BIOLOGICAL MATERIALS RESOURCE GRANTS **Federal Award Date:** 04/02/2015
Department of Health and Human Services
National Institutes of Health
OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Grant Number: 2P40OD010938-35 REVISED
FAIN: P40OD010938

Principal Investigator(s):
CHRISTIAN R ABEE, DVM

Project Title: Squirrel Monkey Breeding and Research Resource

Gonzales, Renee
The University of Texas
MD Anderson Cancer Center
Exec Director, Sponsored Programs
1515 Holcombe Blvd, Unit 1626
Houston, TX 770304009

Award e-mailed to: AwardNotice@mdanderson.org

Period Of Performance:
Budget Period: 04/01/2015 – 01/31/2016
Project Period: 04/01/1997 – 01/31/2020

Dear Business Official:

The National Institutes of Health hereby revises this award (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to UNIVERSITY OF TX MD ANDERSON CAN CTR 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 P40OD010938. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

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

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

Sincerely yours,

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

Additional information follows

SECTION I – AWARD DATA – 2P40OD010938-35 REVISED

Award Calculation (U.S. Dollars)

Salaries and Wages	$161,343
Fringe Benefits	$45,176
Personnel Costs (Subtotal)	$206,519
Other Costs	$285,948
Federal Direct Costs	$492,467
Federal F&A Costs	$285,631
Approved Budget	$778,098
Total Amount of Federal Funds Obligated (Federal Share)	$778,098
TOTAL FEDERAL AWARD AMOUNT	$778,098
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$0

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
35	$778,098	$778,098
36	$768,371	$768,371
37	$768,371	$768,371
38	$768,371	$768,371
39	$768,371	$768,371

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

Fiscal Information:

CFDA Name:	Research Infrastructure Programs
CFDA Number:	93.351
EIN:	1746001118A1
Document Number:	POD010938I
PMS Account Type:	P (Subaccount)
Fiscal Year:	2015

IC	CAN	2015	2016	2017	2018	2019
OD	8014500	$778,098	$768,371	$768,371	$768,371	$768,371

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

NIH Administrative Data:
PCC: CMR03 / **OC**: 414B / **Released**: eRA Commons User Name 04/01/2015
Award Processed: 01/15/2015 11:58:50 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 2P40OD010938-35 REVISED

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

SECTION III – TERMS AND CONDITIONS – 2P40OD010938-35 REVISED

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

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

period.

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

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

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

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) P40OD010938. 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/.

Treatment of Program Income:
Additional Costs

SECTION IV – OD Special Terms and Conditions – 2P40OD010938-35 REVISED

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

Revised to change the F&A rate from 60% to 58% in Years 36-39.

All previous terms and conditions remain in effect.

SUBJECT FOA
This award is subject to the conditions set forth in PAR 14-005, "Animal and Biological Material Resource Center (P40)," which are hereby incorporated by reference as special terms and conditions of this award. Copies of this Funding Opportunity Announcement can be found at the following link: http://grants.nih.gov/grants/guide/pa-files/PAR-14-005.html

ORIP FUNDING PLAN FOR FY2015

This competing award reflects the NIH Fiscal Policy for Grant Awards for FY2015 (see NIH Guide Notice NOT-OD-15-050) and the implementation of the ORIP FY2015 grants funding policy: http://dpcpsi.nih.gov/orip/rf/fyg_fp2015

RECYCLING FUTURE BUDGET PERIOD START DATES
In order to redistribute awards more evenly throughout the fiscal year, this grant has been issued with a 10-month initial budget period with 12 months of monetary support. The continuation award for this grant will cycle each year on February 1st. Information for where to submit reports may be found at: http://grants.nih.gov/grants/submitapplication.htm.

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.

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

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

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

STAFF CONTACTS

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

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

Program Official: Manuel H Moro
Email: morom@mail.nih.gov **Phone**: 301-435-0960 **Fax**: 301 480-3819

SPREADSHEET SUMMARY
GRANT NUMBER: 2P40OD010938-35 REVISED

INSTITUTION: UNIVERSITY OF TX MD ANDERSON CAN CTR

Budget	Year 35	Year 36	Year 37	Year 38	Year 39
Salaries and Wages	$161,343	$159,326	$159,326	$159,326	$159,326
Fringe Benefits	$45,176	$44,611	$44,611	$44,611	$44,611
Personnel Costs (Subtotal)	$206,519	$203,937	$203,937	$203,937	$203,937
Other Costs	$285,948	$282,374	$282,374	$282,374	$282,374
TOTAL FEDERAL DC	$492,467	$486,311	$486,311	$486,311	$486,311
TOTAL FEDERAL F&A	$285,631	$282,060	$282,060	$282,060	$282,060
TOTAL COST	$778,098	$768,371	$768,371	$768,371	$768,371

Facilities and Administrative Costs	Year 35	Year 36	Year 37	Year 38	Year 39
F&A Cost Rate 1	58%	58%	58%	58%	58%
F&A Cost Base 1	$492,467	$486,311	$486,311	$486,311	$486,311
F&A Costs 1	$285,631	$282,060	$282,060	$282,060	$282,060

BIOLOGICAL MATERIALS RESOURCE GRANTS **Federal Award Date:** 03/26/2015
Department of Health and Human Services
National Institutes of Health
OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Grant Number: 2P40OD010938-35
FAIN: P40OD010938

Principal Investigator(s):
CHRISTIAN R ABEE, DVM

Project Title: Squirrel Monkey Breeding and Research Resource

Gonzales, Renee
The University of Texas
MD Anderson Cancer Center
Exec Director, Sponsored Programs
1515 Holcombe Blvd, Unit 1626
Houston, TX 770304009

Award e-mailed to: AwardNotice@mdanderson.org

Period Of Performance:
Budget Period: 04/01/2015 – 01/31/2016
Project Period: 04/01/1997 – 01/31/2020

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $778,098 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to UNIVERSITY OF TX MD ANDERSON CAN CTR 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 P40OD010938. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

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

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

Sincerely yours,

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

Additional information follows

SECTION I – AWARD DATA – 2P40OD010938-35

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TOTAL FEDERAL AWARD AMOUNT	$778,098
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39	$778,098	$778,098

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

Fiscal Information:

CFDA Name:	Research Infrastructure Programs
CFDA Number:	93.351
EIN:	1746001118A1
Document Number:	POD010938I
PMS Account Type:	P (Subaccount)
Fiscal Year:	2015

IC	CAN	2015	2016	2017	2018	2019
OD	8014500	$778,098	$778,098	$778,098	$778,098	$778,098

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

NIH Administrative Data:
PCC: CMR03 / **OC**: 414B / **Released**: eRA Commons User Name 03/20/2015
Award Processed: 01/15/2015 11:58:50 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 2P40OD010938-35

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c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget

period.

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Additional Costs

SECTION IV – OD Special Terms and Conditions – 2P40OD010938-35

SUBJECT FOA
This award is subject to the conditions set forth in PAR 14-005, "Animal and Biological Material Resource Center (P40)," which are hereby incorporated by reference as special terms and conditions of this award. Copies of this Funding Opportunity Announcement can be found at the following link: http://grants.nih.gov/grants/guide/pa-files/PAR-14-005.html

ORIP FUNDING PLAN FOR FY2015
This competing award reflects the NIH Fiscal Policy for Grant Awards for FY2015 (see NIH Guide Notice NOT-OD-15-050) and the implementation of the ORIP FY2015 grants funding policy: http://dpcpsi.nih.gov/orip/rf/fyg_fp2015

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

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

STAFF CONTACTS

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

Program Official: Manuel H Moro
Email: morom@mail.nih.gov **Phone**: 301-435-0960 **Fax**: 301 480-3819

SPREADSHEET SUMMARY
GRANT NUMBER: 2P40OD010938-35

INSTITUTION: UNIVERSITY OF TX MD ANDERSON CAN CTR

Budget	Year 35	Year 36	Year 37	Year 38	Year 39
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Personnel Costs (Subtotal)	$206,519	$203,937	$203,937	$203,937	$203,937
Other Costs	$285,948	$282,374	$282,374	$282,374	$282,374
TOTAL FEDERAL DC	$492,467	$486,311	$486,311	$486,311	$486,311
TOTAL FEDERAL F&A	$285,631	$291,787	$291,787	$291,787	$291,787
TOTAL COST	$778,098	$778,098	$778,098	$778,098	$778,098

Facilities and Administrative Costs	Year 35	Year 36	Year 37	Year 38	Year 39
F&A Cost Rate 1	58%	60%	60%	60%	60%
F&A Cost Base 1	$492,467	$486,311	$486,311	$486,311	$486,311
F&A Costs 1	$285,631	$291,787	$291,787	$291,787	$291,787

PI: **ABEE, CHRISTIAN R**	Title: Squirrel Monkey Breeding and Research Resource	
Received: 05/29/2014	FOA: PAR14-005	Council: 01/2015
Competition ID: FORMS-C	FOA Title: ANIMAL AND BIOLOGICAL MATERIAL RESOURCE CENTERS (P40)	
2 P40 OD010938-35	Dual: RI	Accession Number: 3696361
IPF: 578407	Organization: UNIVERSITY OF TX MD ANDERSON CAN CTR	
Former Number:	Department: Dept of Veterinary Sciences	
IRG/SRG: ZRG1 BBBP-Y (45)R	AIDS: N	Expedited: N
Subtotal Direct Costs (excludes consortium F&A) Year 35: 506,032 Year 36: 506,032 Year 37: 506,032 Year 38: 506,032 Year 39: 506,032	Animals: Y Humans: N Clinical Trial: N Current HS Code: 10 HESC: N	New Investigator: N Early Stage Investigator: N
Senior/Key Personnel:	*Organization:*	*Role Category:*
Christian Abee	The University of Texas MD Anderson Cancer Center	PD/PI
Excluded by Requester	The University of Texas MD Anderson Cancer Center	Co-Investigator

Appendices

Excluded by Requester

OMB Number: 4040-0001
Expiration Date: 06/30/2016

APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

3. DATE RECEIVED BY STATE	State Application Identifier

1. TYPE OF SUBMISSION*

○ Pre-application ● Application ○ Changed/Corrected Application

4.a. Federal Identifier
OD010938

b. Agency Routing Number

2. DATE SUBMITTED	Application Identifier	c. Previous Grants.gov Tracking Number

5. APPLICANT INFORMATION

Organizational DUNS*: 8007721390000

Legal Name*: The University of Texas MD Anderson Cancer Center
Department:
Division:
Street1*: 1515 HOLCOMBE BLVD
Street2: Unit 1676
City*: HOUSTON
County:
State*: TX: Texas
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 770304009

Person to be contacted on matters involving this application
Prefix: First Name*: Renee Middle Name: Last Name*: Gonzales Suffix:
Position/Title: Executive Director, Sponsored Programs
Street1*: The University of Texas MD Anderson Cancer Center
Street2: 1515 Holcombe Blvd, Unit 1626
City*: Houston
County:
State*: TX: Texas
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 770304009
Phone Number*: 713-792-3220 Fax Number: 713-794-4535 Email: osp@mdanderson.org

6. EMPLOYER IDENTIFICATION NUMBER *(EIN) or (TIN)** 1746001118A1

7. TYPE OF APPLICANT* H: Public/State Controlled Institution of Higher Education

Other (Specify):
Small Business Organization Type ○ Women Owned ○ Socially and Economically Disadvantaged

8. TYPE OF APPLICATION*

○ New ○ Resubmission
● Renewal ○ Continuation ○ Revision

If Revision, mark appropriate box(es).
○ A. Increase Award ○ B. Decrease Award ○ C. Increase Duration
○ D. Decrease Duration ○ E. Other *(specify)* :

Is this application being submitted to other agencies?* ○Yes ●No What other Agencies?

9. NAME OF FEDERAL AGENCY*
National Institutes of Health

10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER
93.351
TITLE: Research Infrastructure Programs

11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT*
Squirrel Monkey Breeding and Research Resource

12. PROPOSED PROJECT
Start Date* 04/01/2015
Ending Date* 03/31/2020

13. CONGRESSIONAL DISTRICTS OF APPLICANT
TX-009

SF 424 (R&R) APPLICATION FOR FEDERAL ASSISTANCE

14. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION

Prefix: Dr. First Name*: Christian Middle Name: R Last Name*: Abee Suffix:
Position/Title: Director and Chair
Organization Name*: The University of Texas MD Anderson Cancer Center
Department: Dept of Veterinary Sciences
Division:
Street1*: Michale E. Keeling Center for Comp Med and Research
Street2: 650 Cool Water Drive
City*: Bastrop
County:
State*: TX: Texas
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 786026621
Phone Number*: 512-321-3991 Fax Number: 512-332-5208 Email*: cabee@mdanderson.org

15. ESTIMATED PROJECT FUNDING

a. Total Federal Funds Requested*	$4,048,260.00
b. Total Non-Federal Funds*	$0.00
c. Total Federal & Non-Federal Funds*	$4,048,260.00
d. Estimated Program Income*	$1,054,421.00

16.IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?*

a. YES ○ THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:
DATE:

b. NO ● PROGRAM IS NOT COVERED BY E.O. 12372; OR
○ PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW

17. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001)

● I agree*

** The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.*

18. SFLLL or OTHER EXPLANATORY DOCUMENTATION File Name:

19. AUTHORIZED REPRESENTATIVE

Prefix: First Name*: Renee Middle Name: Last Name*: Gonzales Suffix:
Position/Title*: Executive Director, Sponsored Programs
Organization Name*: The University of Texas MD Anderson Cancer Center
Department:
Division:
Street1*: The University of Texas MD Anderson Cancer Center
Street2: 1515 Holcombe Blvd, Unit 1626
City*: Houston
County:
State*: TX: Texas
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 770304009
Phone Number*: 713-792-3220 Fax Number: 713-794-4535 Email*: osp@mdanderson.org

Signature of Authorized Representative*
TONYA FOREMAN

Date Signed*
05/29/2014

20. PRE-APPLICATION File Name:

21. COVER LETTER ATTACHMENT File Name:F_P40_2014Cover_Letter.pdf

424 R&R and PHS-398 Specific Table Of Contents

Component Summary

Components	Component Project Title	Organization Name	Contact PD/PI Name or Project Lead Name
Overall	Squirrel Monkey Breeding and Research Resource	The University of Texas MD Anderson Cancer Center	Abee, Christian R
Core-001 (516)	Squirrel Monkey Breeding and Research Resource: Resource Core	The University of Texas MD Anderson Cancer Center	Abee, Christian R
Project-001 (446)	Squirrel Monkey Breeding and Research Resource: Applied Research	The University of Texas MD Anderson Cancer Center	Abee, Christian R

Project/Performance
Site Location(s) Summary

Applicant Organization	City	State/Province	Country
The University of Texas MD Anderson Cancer Center	HOUSTON	TX	UNITED STATES

Organization Name	City	State/Province	Country	Component
The University of Texas MD Anderson Cancer Center	Bastrop	TX	UNITED STATES	Core-001 (516)
The University of Texas MD Anderson Cancer Center	Bastrop	TX	UNITED STATES	Overall
The University of Texas MD Anderson Cancer Center	Bastrop	TX	UNITED STATES	Project-001 (446)

Human Subjects
Clinical Trial
Human Embryonic Stem Cells
Vertebrate Animals
Summary

Components	Human Subjects	Clinical Trial	HESC Involved	Vertebrate Animals
Overall	N	N	N	Y
Core-001 (516)	N	N	N	Y
Project-001 (446)	N	N	N	Y

Composite Application Budget Summary

Categories	Budget Period 1	Budget Period 2	Budget Period 3	Budget Period 4	Budget Period 5	TOTALS
Salary, Wages and Fringe Benefits	212,207	212,207	212,207	212,207	212,207	1,061,035
Equipment	0	0	0	0	0	0
Travel	0	0	0	0	0	0
Participant/Trainee Support Costs	0	0	0	0	0	0
Other Direct Costs (excluding Consortium)	293,825	293,825	293,825	293,825	293,825	1,469,125
Consortium Costs	0	0	0	0	0	0
Direct Costs	506,032	506,032	506,032	506,032	506,032	2,530,160
Indirect Costs	303,620	303,620	303,620	303,620	303,620	1,518,100
Total Direct and Indirect Costs	809,652	809,652	809,652	809,652	809,652	**4,048,260**

Total Direct Costs less Consortium F&A

Category	Budget Period 1	Budget Period 2	Budget Period 3	Budget Period 4	Budget Period 5	TOTALS
Total Direct Costs less Consortium F&A	506,032	506,032	506,032	506,032	506,032	**2,530,160**

Funding Opportunity Number: PAR-14-005. Received Date: 2014-05-29T15:39:24.000-04:00

Component Budget Summary

Components	Categories	Budget Period 1	Budget Period 2	Budget Period 3	Budget Period 4	Budget Period 5	TOTALS
Core-001 (516)	Salary, Wages and Fringe Benefits	193,976	193,976	193,976	193,976	193,976	969,880
	Equipment	0	0	0	0	0	0
	Travel	0	0	0	0	0	0
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	293,825	293,825	293,825	293,825	293,825	1,469,125
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	487,801	487,801	487,801	487,801	487,801	2,439,005
	Indirect Costs	292,681	292,681	292,681	292,681	292,681	1,463,405
TOTALS	Total Direct and Indirect Costs	780,482	780,482	780,482	780,482	780,482	**3,902,410**
Project-001 (446)	Salary, Wages and Fringe Benefits	18,231	18,231	18,231	18,231	18,231	91,155
	Equipment	0	0	0	0	0	0
	Travel	0	0	0	0	0	0
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	0	0	0	0	0	0
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	18,231	18,231	18,231	18,231	18,231	91,155
	Indirect Costs	10,939	10,939	10,939	10,939	10,939	54,695
TOTALS	Total Direct and Indirect Costs	29,170	29,170	29,170	29,170	29,170	**145,850**
TOTALS		**809,652**	**809,652**	**809,652**	**809,652**	**809,652**	**4,048,260**

Funding Opportunity Number: PAR-14-005. Received Date: 2014-05-29T15:39:24.000-04:00

Categories Budget Summary

Categories	Components	Budget Period 1	Budget Period 2	Budget Period 3	Budget Period 4	Budget Period 5	TOTALS
R&R Budget - Senior/Key Person Funds Requested	Core-001 (516)	165,893	165,893	165,893	165,893	165,893	829,465
	Project-001 (446)	9,014	9,014	9,014	9,014	9,014	45,070
TOTALS		174,907	174,907	174,907	174,907	174,907	**874,535**
R&R Budget - Other Personnel Funds Requested	Core-001 (516)	28,083	28,083	28,083	28,083	28,083	140,415
	Project-001 (446)	9,217	9,217	9,217	9,217	9,217	46,085
TOTALS		37,300	37,300	37,300	37,300	37,300	**186,500**
R&R Budget - Section A & B. Total Salary, Wages and Fringe Benefits (A+B)	Core-001 (516)	193,976	193,976	193,976	193,976	193,976	969,880
	Project-001 (446)	18,231	18,231	18,231	18,231	18,231	91,155
TOTALS		212,207	212,207	212,207	212,207	212,207	**1,061,035**
R&R Budget - Section C. Total Equipment	Core-001 (516)	0	0	0	0	0	0
	Project-001 (446)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Domestic Travel	Core-001 (516)	0	0	0	0	0	0
	Project-001 (446)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Foreign Travel	Core-001 (516)	0	0	0	0	0	0
	Project-001 (446)	0	0	0	0	0	0

TOTALS		0	0	0	0	0	**0**
R&R Budget - Section D. Total Travel	Core-001 (516)	0	0	0	0	0	0
	Project-001 (446)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Tuition/Fees/Health Insurance	Core-001 (516)	0	0	0	0	0	0
	Project-001 (446)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Stipends	Core-001 (516)	0	0	0	0	0	0
	Project-001 (446)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Trainee Travel	Core-001 (516)	0	0	0	0	0	0
	Project-001 (446)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget - Subsistence	Core-001 (516)	0	0	0	0	0	0
	Project-001 (446)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget ī¿½ Other Participants/Trainee Support Costs	Core-001 (516)	0	0	0	0	0	0
	Project-001 (446)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget ī¿½ Section E. Total Participants/Trainee Support Costs	Core-001 (516)	0	0	0	0	0	0
	Project-001 (446)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**

R&R Budget ï¿½ Materials and Supplies	Core-001 (516)	0	0	0	0	0	0
	Project-001 (446)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget ï¿½ Publication Costs	Core-001 (516)	0	0	0	0	0	0
	Project-001 (446)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget ï¿½ Consultant Services	Core-001 (516)	0	0	0	0	0	0
	Project-001 (446)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget ï¿½ ADP/Computer Services	Core-001 (516)	0	0	0	0	0	0
	Project-001 (446)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget ï¿½ Subawards/Consortium/Contractual Costs	Core-001 (516)	0	0	0	0	0	0
	Project-001 (446)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget ï¿½ Equipment or Facility Rental User Fees	Core-001 (516)	0	0	0	0	0	0
	Project-001 (446)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget ï¿½ Alterations and Renovations	Core-001 (516)	0	0	0	0	0	0
	Project-001 (446)	0	0	0	0	0	0

TOTALS		0	0	0	0	0	**0**
R&R Budget ï¿½ Other Direct Cost 1	Core-001 (516)	293,825	293,825	293,825	293,825	293,825	1,469,125
	Project-001 (446)	0	0	0	0	0	0
TOTALS		293,825	293,825	293,825	293,825	293,825	**1,469,125**
R&R Budget ï¿½ Other Direct Cost 2	Core-001 (516)	0	0	0	0	0	0
	Project-001 (446)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget ï¿½ Other Direct Cost 3	Core-001 (516)	0	0	0	0	0	0
	Project-001 (446)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	**0**
R&R Budget ï¿½ Section F. Total Other Direct Cost	Core-001 (516)	293,825	293,825	293,825	293,825	293,825	1,469,125
	Project-001 (446)	0	0	0	0	0	0
TOTALS		293,825	293,825	293,825	293,825	293,825	**1,469,125**
R&R Budget ï¿½ Section G. Total Direct Cost (A thru F)	Core-001 (516)	487,801	487,801	487,801	487,801	487,801	2,439,005
	Project-001 (446)	18,231	18,231	18,231	18,231	18,231	91,155
TOTALS		506,032	506,032	506,032	506,032	506,032	**2,530,160**
R&R Budget ï¿½ Section H. Indirect Costs	Core-001 (516)	292,681	292,681	292,681	292,681	292,681	1,463,405
	Project-001 (446)	10,939	10,939	10,939	10,939	10,939	54,695
TOTALS		303,620	303,620	303,620	303,620	303,620	**1,518,100**
R&R Budget ï¿½ Section I. Total Direct and Indirect Costs (G +H)	Core-001 (516)	780,482	780,482	780,482	780,482	780,482	3,902,410

	Project-001 (446)	29,170	29,170	29,170	29,170	29,170	145,850
TOTALS		809,652	809,652	809,652	809,652	809,652	**4,048,260**

Senior/Key Personnel
Summary

Name	Organization	Role on Project	Components
Abee, Christian R	The University of Texas MD Anderson Cancer Center	PD/PI(Contact)	Overall
Abee, Christian R	The University of Texas MD Anderson Cancer Center	Other: Project Lead	Core-001 (516)
Abee, Christian R	The University of Texas MD Anderson Cancer Center	Other: Project Lead	Project-001 (446)
Excluded by Requester		Other: External Advisory Board Member	Core-001 (516)
		Consultant	Project-001 (446)
		Other: External Advisory Board Member	Core-001 (516)
		Other: Other Significant Contributor	Project-001 (446)
Excluded by Requester	The University of Texas MD Anderson Cancer Center	Other: Other Significant Contributor	Project-001 (446)
	The University of Texas MD Anderson Cancer Center	Co-Investigator	Core-001 (516)
Excluded by Requester		Other: External Advisory Board Member	Core-001 (516)
		Other: External Advisory Board Member	Core-001 (516)
Excluded by Requester	The University of Texas MD Anderson Cancer Center	Co-PD/PI	Core-001 (516)
	The University of Texas MD Anderson Cancer Center	Co-Investigator	Overall
	The University of Texas MD Anderson Cancer Center	Co-PD/PI	Project-001 (446)

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Excluded by Requester

OMB Number: 4040-0010
Expiration Date: 06/30/2016

Project/Performance Site Location(s)

Project/Performance Site Primary Location

● I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	The University of Texas MD Anderson Cancer Center
Duns Number:	8007721390000
Street1*:	Michale E. Keeling Center for Comp Med and Research
Street2:	650 Cool Water Drive
City*:	Bastrop
County:	
State*:	TX: Texas
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	786026621
Project/Performance Site Congressional District*:	TX-009

File Name

Additional Location(s)

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* ○ **Yes** ● **No**

1.a. If YES to Human Subjects

Is the Project Exempt from Federal regulations? ○ Yes ○ No

If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6

If NO, is the IRB review Pending? ○ **Yes** ○ **No**

IRB Approval Date:

Human Subject Assurance Number

2. Are Vertebrate Animals Used?* ● **Yes** ○ **No**

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ● Yes ○ No

IACUC Approval Date:

Animal Welfare Assurance Number A3343-01

3. Is proprietary/privileged information included in the application?* ○ **Yes** ● **No**

4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* ○ **Yes** ● **No**

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ○ Yes ○ No

4.d. If yes, please explain:

5. Is the research performance site designated, or eligible to be designated, as a historic place?* ○ **Yes** ● **No**

5.a. If yes, please explain:

6. Does this project involve activities outside the United States or partnership with international collaborators?* ○ **Yes** ● **No**

6.a. If yes, identify countries:

6.b. Optional Explanation:

	Filename
7. Project Summary/Abstract*	F_OVERALL_Project_Summary_Abstract.pdf
8. Project Narrative*	F_OVERALL_Project_Narrative.pdf
9. Bibliography & References Cited	F_OVERALL_References.pdf
10.Facilities & Other Resources	F_FACILITIES.pdf
11.Equipment	F_EQUIPMENT.pdf

PROJECT SUMMARY: OVERALL

This application is a competing renewal of the “Squirrel Monkey Breeding and Research Resource” (SMBRR), P40 OD010938 which has received continuous NIH grant support since 1980. The SMBRR is the only national research resource of laboratory born squirrel monkeys available to NIH grantees, intramural research programs of federal agencies including the FDA, NSF, and the NIH, and other sponsors of biomedical research (private foundations, pharmaceutical companies, and contract research organizations). Because some squirrel monkey species are no longer available from source countries and there are no other breeding colonies of pedigreed squirrel monkeys available for biomedical research, the SMBRR is a unique research resource that cannot be duplicated or replaced. The overall goals of the SMBRR are to provide a national research resource of squirrel monkeys; provide squirrel monkey derived biological materials; provide education and training opportunities to scientists, colony managers, and animal caregivers; and, provide investigators with facilities and expertise to conduct studies using squirrel monkeys. The scarcity of squirrel monkeys, difficulties associated with captive breeding, challenges associated with their care and use in research, all contribute to the need for this national research resource. The SMBRR has integrated multiple disciplines into a program designed to meet the needs of investigators who utilize the resources provided by the SMBRR. The SMBRR has focused much of its effort on understanding the natural biology, reproductive biology, and diseases of squirrel monkeys with an emphasis on models of human disease. In the coming years, the SMBRR will continue to improve the resources it provides and continue to add new information about the biology and research value of squirrel monkeys. Squirrel monkeys continue to be used extensively in neuroscience research, drug addiction research, malaria research, and fundamental evolutionary biology. New areas of research requiring squirrel monkeys continue to emerge. As these new research areas develop, the SMBRR plays an essential role by providing the animals, biological resources, and the expertise needed to carry out research in squirrel monkeys. In the next five years, the SMBRR will increase the animals and related resources that can be provided to the scientific community. The SMBRR plans to organize and sponsor a squirrel monkey genomics workshop. Biomedical scientists who use squirrel monkeys to study human diseases and geneticists will share their expertise to determine how genome sequencing and subsequent identification of SNPs can be used to increase the value of the squirrel monkey model in human health research. The proposed applied research projects (Applied Research Component) will add new information about squirrel monkeys. This information will further refine and add value to the resources provided by the SMBRR.

Project Narrative

The "Squirrel Monkey Breeding and Research Resource" (SMBRR) maintains the only self-sustaining national research resource of laboratory-born squirrel monkeys, their tissues and other biological materials, and the expertise to carry out research in this important research animal. Scientists with NIH grants utilize squirrel monkeys to study many diseases that threaten human health including alzheimer's disease and other disorders of the central nervous system, drug addiction, malaria, and viral diseases. The resources provided by the SMBRR reduce the need for importation of squirrel monkeys by providing highly defined animals and biomaterials that scientists can use to either reduce the number of animals needed or eliminate the need for living animals in their research.

FACILITIES AND OTHER RESOURCES

The laboratory space at the Michale E. Keeling Center for Comparative Medicine and Research (KCCMR) of the University of Texas MD Anderson Cancer Center (UTMDACC) consists of a basic science research laboratories, clinical diagnostic laboratories, anatomical pathology laboratories, and immunology laboratories. Equipment and facilities are described below.

Clinical:
There are seven clinical veterinarians and four veterinary pathologists that share clinical and pathology diagnostic service responsibilities at the KCCMR. The veterinary staff of six laboratory animal veterinarians includes four board certified laboratory animal medicine veterinarians (Drs. Abee, Excluded by Requester Excluded by and 2 TBN) experienced with squirrel monkeys and four board certified veterinary pathologists Excluded by Requester and TBN) experienced with multiple nonhuman primate species. The TBN positions are under active recruitment and will be filled soon.

Animal:
The SMBRR includes a colony of approximately 559 squirrel monkeys (*Saimiri* spp.). This is the only NIH-supported national research resource that specializes in New World (Neotropical) primates. The SMBRR maintains the only biomedical research resource of Bolivian squirrel monkeys (*Saimiri boliviensis boliviensis*). Housing is described under facilities below. The KCCMR is AAALAC accredited and maintains an approved PHS Assurance through the Office of Laboratory Animal Welfare (OLAW).

Computer:
Personal Computers are provided to each faculty member. All KCCMR desktop and laptop computers are "refreshed" (replaced with a new computer) every three years. Computers are provided to faculty members, area supervisors, laboratories, and clinical staff. The KCCMR has three dedicated computer support staff, a Support Services Analyst, a database programmer, and an Associate Applications System Analyst to maintain computers and software.

Office:
Office space is provided to faculty members and supervisory staff members within the SMBRR. Most of the SMBRR management team members have their offices in the Comparative Medicine Research Building (CMRB) described below.

FACILITIES

The Michale E. Keeling Center for Comparative Medicine and Research (KCCMR) is located on a 381-acre campus near Bastrop, TX. The KCCMR is a research center within the UTMDACC that has been AAALAC accredited since 1979. The mission of the KCCMR is to conduct biomedical research aimed at improving human health and welfare by developing, maintaining, and using specialized animal models of human diseases. The KCCMR houses the UTMDACC Department of Veterinary Sciences (DVS). The DVS is composed of 15 faculty members that include 7 clinical veterinarians, 4 veterinary pathologists, 2 primate behaviorists, and 2 basic scientists with expertise in cellular immunology and pharmacology/toxicology. The KCCMR is composed of seven major buildings totaling approximately 275,000 sq. ft. not including Excluded by Excluded by Requester

Comparative Medicine Research Building (CMRB) was designed and constructed in 2009 to meet the needs of the Squirrel Monkey Breeding and Research Resource (SMBRR). The CMRB was constructed at a cost of $52,000,000 as part of the recruitment of Dr. Abee's research team from the University of South Alabama. The Excluded by Requester and includes state-of-the-art housing areas for squirrel monkeys and owl monkeys. This construction was partially supported by $4,000,000 NCRR (C06 RR020129) awarded to support facility improvements for the SMBRR. There is approximately a Excluded by Requester Excluded by Requester designed to house breeding groups of squirrel monkeys. Additional areas include surgical facilities, IVF laboratories, BSL-3 suite (approximately 3,800 sq. ft.), and approximately 16,000 net sq. ft. of pathology and research laboratories.

Excluded by Requester

The SMBRR has a dedicated fully equipped assisted reproductive technology laboratory in the CMRB with 2 Thermo water-jacketed incubators with controls for CO2 and O2 levels. The lab has dedicated refrigerator and separate freezer, a Stoelting pipette puller, a Platinum model BioGenic Systems Programmable liquid nitrogen freezer, an Zeiss inverted observer D1 AXIO microscope with heated stage, dual Eppendorf TransferMan NK2 injectors, and Zylos-tk laser and camera system. Also, a laminar flow hood and Zeiss Stemi 2000-CS dissecting microscope with portable table is included in the lab. Both microscopes are supported on vibration isolating tables. A Dell PC computer is present to allow data entry, control of inverted microscope operational features, the laser and camera. Images can be moved view CDs as this unit is isolated from other computer systems to maintain security. This laboratory has backup power supplies, monitored temperature, nitrogen and carbon dioxide gas supplies with automatic backup systems. The lab is located in a restricted area with pass-through to adjacent surgical suite for gamete and embryo movement.

In addition to the areas described above, the CMRB contains more than 20,000 sq. ft. of support spaces including cage wash (clean and soiled), clinic rooms, diet preparation lab, imaging room, technician workstations, staff break rooms, staff shower and change rooms.

OTHER RESOURCES

Security: The KCCMR campus is authorized personnel only. Visitors must request entry at the front gate. The on-site University of Texas Police Department - Houston (UTPH) provides security for the KCCMR. Police Department personnel are available 24-hours per day. Animal areas and buildings are monitored remotely and card access is required.

Veterinary Services: Veterinary services are provided by seven clinical veterinarians, four of whom are diplomates of the American College of Laboratory Animal Medicine (ACLAM), and four veterinary pathologists who are diplomates in the American College of Veterinary Pathologists (ACVP).

Christian R. Abee, D.V.M., M.S., DACLAM	Primary: KCCMR, Director; Chair, Dept. Vet. Sciences Back-up: Chimpanzee, Rhesus, Squirrel monkey,
Excluded by Requester	Primary: Pathology, Section Chief Back-up: Chimpanzee, Rhesus

Excluded by Requester	Primary: Owl monkey Backup: Squirrel monkey, Chimpanzee, Rhesus
	Primary: Chimpanzee Back-up: Biohazard Chimpanzee, Rhesus
	Primary: Pathology
	Primary: Chimpanzee Back-up: Chimpanzee, Rhesus
	Primary: Squirrel monkey Backup: Owl monkey, Chimpanzee, Rhesus
	Primary: Pathology Backup: Rhesus

(At this time, two clinical veterinarian positions and one veterinarian pathologist position are in active recruitment.)

Each veterinarian has daily contact with the section supervisor, animal technicians and animal attendants. They perform rounds, clinical treatments, surgery, and administrative duties. Animal technicians and attendants survey their animal areas throughout the day. They report problems immediately to their supervisor, who in turn contacts the veterinarian. Verbal followed by written reports are prepared when observations reveal a problem. Personnel are instructed to contact the section veterinarian directly or another staff veterinarian, if the area veterinarian is not available. Weekend and holiday care is provided on a rotational schedule. Veterinarians are available after hours by pager and cell phone for veterinary emergencies. Pathologists are available after hours for diagnostic and investigative services, if required.

Surgery: A well-equipped surgical suite consisting of a major surgery, postoperative recovery room, instrument prep, and scrub room are available in support of the clinical and research activities within this project. The Squirrel Monkey Clinic serves as an anesthetic induction and prep room for major surgical cases. The postoperative recovery room also serves as a nursery room during the squirrel monkey birthing season. The scrub room is equipped to serve as the surgeon's scrub/prep area and for the storage of scrub suits masks, caps, shoe covers, surgical linens and gowns. The scrub room is equipped with a large pedal-operated, two station scrub sink. All packs are prepared in the instrument prep room. This room is equipped with work counters for pack preparation, ultrasonic instrument cleaner, stainless steel shelving and a Getinge 433/ 533LS autoclave. Gas sterilization is done using a Sterrad NX Sterilization System (hydrogen peroxide).

Radiology and Imaging: A well-equipped radiology unit is available to support the diagnostic and research support needs of the SMBRR. Veterinarians or veterinary technologists schedule and supervise the taking and developing of radiographs (x-rays). The unit x-ray machine is licensed and meets state safety requirements. Ancillary safety equipment such as leaded gloves and aprons and lead-lined shields, are provided for personnel authorized to work in radiology. Personnel are also provided film badges (whole body) and are monitored monthly for levels of radiation exposure. Employer and employee responsibilities concerning radiation hazards, as set forth by the Texas State Department of Health, are posted in a prominent location in the radiology unit. The UTMDACC Radiation Safety Office and the Texas State Department of Health perform periodic quality control inspections. An automatic x-ray film processor leads from the dark room into the viewing and filing room. This room is also equipped with a bank of view boxes for film interpretation and a file cabinet for storage of radiographs. We have the capability of taking digital radiographs, and radiographs can by be viewed by veterinarians from their office computers. The radiographs can be sent digitally for consultation when needed. The SMBRR also has real-time ultrasound with variable frequency array and image storage capabilities. Echocardiography and obstetric\gynecologic procedures are done with a Siemens Medical Solutions Aspen® ultrasound unit with a variety of application-specific multi-frequency transducers. The system performs digital two-dimensional, M-mode, color Doppler (continuous, pulse) imaging for echocardiography. This system (valued at $250,000) was donated by the Siemens Corporation to the SMBRR at no cost to the grant.

Pathology: The Pathology Section provides comprehensive diagnostic, collaborative, and research-related pathology services and a tissue/biological fluids banking program. This section includes Clinical and

Anatomical Pathology Laboratories and shares resources with the Department's flow cytometry and molecular diagnostic laboratories. The Pathology Section has available a staff of 15, including 4 veterinary pathologists, 4 medical technologists, 2 animal resources technologists (to support tissue and biological fluids collection and banking), 2 histology technicians, 1 senior histology technician, 1 laboratory manager and 1 administrative assistant. Clinical Pathology provides hematology, coagulation, clinical chemistry, microbiology, serology, parasitology, flow cytometry (diagnostic markers), molecular diagnostics [nucleic acid extraction, polymerase chain reaction (PCR), reverse transcriptase (RT)-PCR, real-time PCR], and tissue banking. In addition, the Clinical Pathology Laboratory provides tissue culture services for establishing and maintaining cell lines, primary cultures of tissues, and body fluids obtained from primates housed at the KCCMR. Radioimmunoassay and ELISA are performed upon request for selected serum and tissue analytes. Anatomical Pathology provides necropsy, histopathology, cryostat sectioning of frozen tissue, and immunohistochemistry services.

The Pathology Section is responsible for the tissue and biological fluids bank for the SMBRR. Formalin-fixed tissues collected at necropsy include all major organs (e.g., heart, liver, kidney, lung, brain, spinal cord, intestines, major lymph nodes, eyes, endocrine glands, musculoskeletal, and others). Over the last 34 years since the original award of this national research resource, an archive of formalin-fixed tissues has been developed that could be used for immunohistochemical analyses, in-situ hybridization studies, and various retrospective analyses. In addition to fixed tissues, frozen tissues (-80°C freezer) are routinely collected at necropsy. Tissues collected and archived include heart, liver, kidney, lung, spleen, and lymph node. Frozen tissues have the potential to be used in immunohistochemical analyses, viral isolation, pharmaceutical evaluation, and DNA and RNA analyses.

Immunology Laboratory Services: The Immunology laboratory provides a centralized service for peripheral blood mononuclear cells separation from blood and tissues; proliferation assays for T and B cells; ELISPOT assay for cytokines; ELISA assay for Cytokines; immunoglobulin and endocrine factors; Cytokine Bead array method for cytokine detection; four color Flow cytometry for determination of cell surface markers; determination of intracellular cytokines by Flow cytometry; methods for vaccine development. The laboratory is also equipped to handle biohazardous materials such as HIV, SHIV and Hepatitis C. The Luminex system can analyze immunoassays, complex genetic analysis, and enzymatic assays in one format. The reagents, (antibodies, oligonucleotides, substrates, etc.) are attached to unique fluorescent microscopic beads (microspheres). The unique fluorescent emission for a given microsphere enables the Luminex to identify discrete measurements of multiple microsphere based reactions from a single sample.

Computer Software and Hardware: The UTMDACC has provided computer hardware and relevant software for the KCCMR campus and the SMBRR. The KCCMR uses a high-speed, 1 gigabyte, Ethernet local area network (LAN). Buildings are connected to a central hub via fiber-optic cable. Individual computers are connected to the network either through cat-6a cable or through campus-wide wireless access points. Two-gigabyte transmission lines between the KCCMR and the UTMDACC in Houston allows high-speed connectivity for enhanced Internet access and videoconferencing. The KCCMR has approximately 98 desktop computers, 45 laptop computers, and 13 Ricoh network printers (two of which are color). UTMDACC provides computers running the Microsoft Windows 7 operating system and the Microsoft Office software (Excel, Access, PowerPoint, and Word). Additional software is available for database management, reporting and data analysis, including the Adobe (Acrobat and Photoshop) Crystal Reports, and statistical/graphing software (such as SPSS and GraphPad Prism).

Data Management: The Unified Animal Records System (UARS) is a comprehensive animal colony database developed that supports the SMBRR. These programs are currently being expanded to manage colony records for all primate species at the KCCMR. The data are organized within a relational database, with information indexed back to the animal's ID number. By tagging the data with the date it was collected, it is possible to move, retrospectively, through sets of information to trace an animal's clinical and experimental treatments. This method is powerful both from a clinical approach, where it is necessary to trace an animal across several data fields, and from an experimental approach, where data from many animals can be drawn together for analysis.

The **Colony Demographic and Colony Forecast Model (CDFM)** was developed by SMBRR to provide a method of determining basic life-death and reproduction statistics for the squirrel monkey colony, but it can

and is used for many captive populations of nonhuman primates. The CDFM uses population census data to calculate survivorship and fertility functions, as well as forecast the population structure. The model consists of a series of linked spreadsheets in which the user enters the census and birth information. The model can then use this to calculate demographic and reproductive statistics about specific populations under study. Additional spreadsheets use the survivorship and fertility statistics to forecast the size and structure of the population. The current model takes both a deterministic, for short term forecasting, and stochastic approach, for longer-term forecasts. Demographic modeling is a useful mathematical tool for managing animal colonies in a controlled habitat. The statistics generated allow us to quantify life-history events within the squirrel monkey resource and to project how management decisions will affect the population's availability into the future.

Informational Resources: The KCCMR library has an extensive array of resources compiled over the past 32 years to facilitate those tasks taken on by students, clinicians and basic scientists alike. The library contains journal subscriptions and textbooks that focus primarily on primate medicine and husbandry, laboratory animal medicine and research, veterinary pathology and cancer research.

The UTMDACC Research Medical Library has a staff of 15 professional librarians and provides an extensive array of services, journals and collections that are available for diagnostic and research purposes to all faculty and students. Currently, the library has 18,955 total print books, 11,123 total electronic books, 5,606 online journal subscriptions, 27,538 bound journal volumes, 630 audiovisuals and 144 online databases (e.g., PubMed, Ovid, and Current Contents). If a resource is not available online, the library subsidizes the costs for routine requests which are typically completed in 2-3 working days. Additional access to online resources and databases is available through registration with the Texas Health Science Libraries Consortium.

KCCMR Preclinical Studies Program: As part of UTMDACC's translational research strategic initiative of real-time technology development and transfer, a Good Laboratory Practice (GLP) compliant preclinical studies program was established at the KCCMR. An on-site Quality Assurance Unit (QAU) monitors the GLP Program. Laboratories and equipment have been validated for GLP, the program and facilities have been inspected/audited by FDA and outside study sponsors. All GLP study management and personnel are trained under the Center's GLP Training Program managed by the QAU. GLP service offerings include:

- Professional services include planning, implementation, and management of on-site preclinical laboratory study protocols using animal models: nonhuman primates, livestock, and rodents. Study Directors are provided by the Center.
- Clinical Pathology Laboratory Services are under the supervision of a Board-Certified Veterinary Clinical Pathologist. Services include: Chemistry Profiles, Hematology, Coagulation Analysis, Urinalysis, Microbiology, Parasitology, and Serology.
- Anatomical Pathology Services and Histopathology Evaluations are performed by two Board-Certified Veterinary Pathologists and a support staff of three Histology Technicians.
- An environmentally controlled GLP archive facility is maintained for storage of study data, reports and tissues.

In addition, the KCCMR is in the process of converting from manual to automated data collection, reporting, and archiving, through the acquisition of a Pathology/Toxicology data management software system (Provantis 8™, Instem). The existing Facilities Management System (FMS) is in the process of being upgraded to a state of the art building automation and facilities management system compatible with the electronic information distribution and networking infrastructure of today's industry standards. Both systems will be fully validated and GLP and Part 11 compliant.

Occupational Health and Safety Program: For hazard identification and risk assessment, the KCCMR follows institutional policies concerning the use of hazardous agents that are in compliance with the NIH guidelines for Research Involving Recombinant DNA Molecules, the CDC/NIH Biosafety of Microbiological and Biomedical Laboratories and the recent publication of the National Research Council, Occupational Health and Safety in the Care and Use of Research Animals. In addition, designated personnel establish written protocols for each hazardous investigation and do not change or modify these protocols without written authorization and modification by the appropriate biosafety group. The KCCMR frequently interacts with the Office of Sponsored Research, the Institutional Biosafety Committee, the Office of Radiation Safety and the Office of Environmental

Health and Safety at UTMDACC to monitor and coordinate hazardous procedures. Departmental faculty and supervisors ensure safety training occurs and biohazard procedures are followed.

The Environmental Health and Safety Program ensures that employees are appropriately immunized and receive the appropriate personal protective equipment and training in proper use of this equipment. This program is overseen by the Director of MD Anderson Employee Health and Well-being directed by G. A. Thomas, M. D. and the Office of Environmental Health and Safety directed by Mathew Berkheiser, Ph.D.

Physical Plant: Physical Plant support and personnel are available 24-hours per day. A Johnson Controls Metasys® Facility Management System (FMS) uses computer monitoring to provide control, information, and alarms for various equipment, systems, and spaces. Temperature and humidity are monitored by the FMS system in all indoor animal housing areas. Pre-set limits and alarm notifications have been determined. When operating conditions deviate from the pre-set limits, the FMS issues an alarm at the Operator Workstation and auto-dials appropriate staff pages and The University of Texas Police Department personnel.

Environmental Enrichment and Behavior: The environmental enrichment program for squirrel monkeys is directed by Excluded by Requester Ph.D. The primary objectives of the environmental enrichment program are to promote species typical behavior and reduce morbidity and mortality in social groups. Excluded by Requester also directs the environmental enrichment program for owl monkeys. The primary focus of this program is providing effective environmental enrichment, implementation of strategies for successful social group formation, and development of behavioral intervention strategies that lead to reduced morbidity within the colony. An enrichment technician, supervised by Excluded by Requester devotes % Effort her effort to the squirrel monkey colony. Costs associated with the enrichment program are included in the squirrel monkey per diem. Management of environmental enrichment focuses on four different areas: structural, inanimate objects, feeding and social components.

Excluded by Requester of Texas A & M University: Although all animals in the SMBRR and most studies will be carried out Excluded by Requester within the CMRB, some parts of the proposed study of Pelvic Organ Prolapse will be carried out at the Excluded by Requester Texas. This second activity site is Excluded by Requester Excluded by Requester Excluded by Requester that will be used for the studies of Pelvic Organ Prolapse Excluded by Requester include a GE real-time ultrasound with variable frequency transducer for high resolution examination of squirrel monkeys and Trio 3T MR unit with 8 channel wrist coil for MRI of squirrel monkeys. These units are accessible to animals on a scheduled basis and protocols are in place for allowing animals to be safely examined without interaction with patients. These equipment items and the MRI facilities are managed for research uses. Animals from the SMBRR that will be examined in the Excluded by Requester facility will be transported using personnel and vehicle that are designated for this purpose from the SMBRR so as not to interact with animal care personnel or areas where animals are managed at Excluded by Requester Excluded by Requester Excluded by Requester Ultrasound and MR images are stored in DICOM format on CDs and re adily t ransfer red to two workstations equipped with 3-D Doctor software for tracing, modeling and measurement of features. Images are backed up and can be made available to other collaborating investigators using FTP sites or CDs for file transfer. Excluded by Requester has office space, computers, and software for support of technicians, residents, fellows, and visiting scientists to utilize these images. Dr. Excluded by Requester has trained 4 fellows, 2 technicians, 3 residents for performing tracings of images in a uniform fashion.

MAJOR EQUIPMENT

Equipment available to the Squirrel Monkey Breeding and Research Resource (SMBRR) includes:

Animal Care: 12 LC 1551 – S cages, 13 LC 1302 cages; 12 aluminum air transport cages, 4 aluminum restraint cages, 4 Isolette incubators, 1 Henry Schein Vet Base Ultima 500 Ultrasonic dental descaler, 1 intensive care unit, 1 industrial balance, 1 MedRx Otic irrigation system, 3 electronic platform scales, 8 refrigerators (2.7 cu. ft.-822.5 cu. ft.), 3 box type freezers (25.1 cu.ft each), 1 Chevrolet Truck-1993 (½ ton), 3 blood pressure monitors (Propaq 100 series, Propaq 102 EL, Propaq 104 EL), 1 portable surgical lamp, 2 commercial washers, 2 commercial dryers, 1 Whirlpool washing machine, 3 John Deere Gator, 1 Kawasaki Mule, 58 Harford 4.3 cages, 6 Harford 6.0 cages, 24 aluminum transport tunnels, 6 stainless squeeze transports, 10 capture nets, 2 escape 6' nets, 1 Chevy van-1991, 1 Chevy truck-2003 (½ ton), 1 Propaq 102,1 iSTAT blood analyzer.

Surgical Equipment: (dental, minor and major surgical procedures) 3- SurgiVet® University Anesthesia Machines; 2- SurgiVet® SAV2500 Ventilators; 2- SurgiVet® Advisor® Vital Signs Monitors; 6- Gaymar® T/Pumps; 1- SurgiVet® V9400 Capnograph/ Agents Monitor; 1- Maxant Techline Radiograph Viewer; 4- Centurion™ Surgical Lights; 2- Amico Corporation Gas Supply Manifold Columns; 2- VSSI Adjustable Height/ Tilting V- top Surgical tables; 4- Mayo stands; 1- IV stand; 2- Basin stands; 2- Surgical Kick Buckets; 2- Blue-Bell Bio-Medical Carts; 1- Stainless Steel Table w/ Wheels; Surgical and dental instruments.

Endoscopy (colonoscopy, gastroscopy, bronchoscopy): 1 Olympus 140 cm Pediatric flexible endoscope 7.8mm, 17" Sony color monitor, Sony video capture system.

Radiology and Imaging Equipment: A TRuDr nx DICOM Digital Radiography Enterprise Imaging Solution with a Digital radiograph detector 4030E with a 20 foot cable with 7.3 million Active Pixels 127 mm(sq) Pixel Size: 3.94 lp/mm resolution, 4.0 second exposure display time, 16" x 12" viewable image area, fluid-protect seal and claw scratch surface design for veterinary applications. There is a 24"LCD Widescreen Display with speakers. The Acquisition Workstation has an integrated synchronization of X-ray generator/ receptor/ work station with DICOM send ready, reporting, telemedicine, one click acquire controller interface.

Anatomical Pathology Laboratory Equipment: (diagnostic and research necropsy, histopathology, immunohistochemistry, and other specialized anatomical pathology support) 1 Lipshaw autopsy table with downdraft circulation, 1 portable/adjustable height autopsy table, 3 Lipshaw autopsy saws, 1 Biological Safety cabinet, Class II, Type A, 3 portable surgery lights, 1 Olympus stereomicroscope, 1 Nikon N80 35 mm camera, 1 Nikon FE2 35 mm camera, 1 Nikon 6006 35 mm camera, 1 Nikon Culpix 990 digital camera, 1 Fleetwood meat saw, 1 Ohaus balance, 1 Lipshaw balance, 5 positive pressure HEPA-filtered air suits, 2 Thermo Shandon Gross lab stations, 1 Shandon Cassette labeler, 1 Shandon Pathcentre tissue processor, 1 Leica ASP3000 tissue processor, 2 Shandon Histocentre 2 embedding centers, 1 Linistain GIX Random Access Stainer, 1 bench fume expeller, 1 Olympus BX-40 dual observation microscope with digital camera, 2 Olympus BX-41 dual observation microscopes with digital cameras, 1 Olympus Vanox AHBT3 research microscope, 1 Olympus BHTU microscope, 1 Olympus BX-51 10-head microscope, 3 flammable and acid storage cabinets, 1 IEC Minotome Cryostat – International Equipment Lab, 1 DAKO immunohistochemistry autostainer.

Clinical Pathology Laboratory Equipment: 1 Siemens Advia 120 hematology analyzer, 1 Olympus AU400e Chemistry Analyzer, 1 Beckman Coulter ACL 7000 Coagulation Analyzer, 1 Olympus BX-40 dual observation microscope with 35 mm camera, 1 Olympus BH-2 dual observation microscope, 1 Olympus BH-2 microscope, 1 chromatography refrigerator, 1 blood rotator, 1 Shandon Cytospin 3 centrifuge, 1 IEC HN-SII centrifuge, 1 Centra 7R centrifuge, 1 Serofuge II centrifuge, 1 Jouan DR412 refrigerated centrifuge, 3 Temp Blok Module heaters, 1 Lancer dishwasher, 1 Biological Safety Cabinet (Class II, Type A), 2 Bacti-incinerators,1 42"C air incubator, 1 35"C CO_2 incubator, 1 25"C air incubator, 1 35"C air incubator, 1 Zeiss stereomicroscope, 1 fume hood, 1 Tissue-Tek fume absorber, 1 Ohaus Dial-O-Gram balance, 1 Ohaus CT200 balance, 1 Acumet pH meter, 1 refrigerated Sorvall RC04 centrifuge, 6 ultra-low freezers, 1 -20"C freezer, 2 refrigerator/freezers, 1 blood bank refrigerator, 2 refrigerators, 1 steam autoclave, 2 micro-

centrifuges, 1 Barnstead Nanopure water system, 1 Millipore RO water system.

Immunological Resources Instruments: Liquid Scintillation Counter (Wallac 1409), Wizard y-Counter (Wallac 1470), Luminex technology based Millipore Cytokine bead array system, Cell Harvestor (Skatron/ Molecular Device), Biological safety hoods (NuAire), Biological CO2 Incubators (Forma Scientific), Refrigerated Centriguge (Sorvall), Ultra-Centrifuge (Sorvall), Microscope (Olympus), Fluorescent microscope (Olympus), 96-well microplate reader (TiterTek multiskan MCC-340), Freezer (-80C) and (-20C), Liquid nitrogen storage. Flow Cytometry Instrument: A Becton Dickinson FACSCalibur multi-purpose flow cytometer, equipped with CellQuest Pro data acquisition and analysis software and a Becton Dickinson FACSArray Bioanalyzer System are available for clinical and research applications. The FACSCalibur contains a 488-nm, argon-ion laser and 635-nm red diode laser. The FACSArray contains a 532 nm green diode laser and a 635-nm red diode laser. Currently, these instruments support multiple applications including immunophenotyping, intracellular cytokine staining, cytometric bead array and apoptosis assays.

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Prefix: Dr. First Name*: Christian Middle Name R Last Name*: Abee Suffix:

Position/Title*: Director and Chair
Organization Name*: The University of Texas MD Anderson Cancer Center
Department: Dept of Veterinary Sciences
Division:
Street1*: Michale E. Keeling Center for Comp Med and Research
Street2: 650 Cool Water Drive
City*: Bastrop
County:
State*: TX: Texas
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 786026621

Phone Number*: 512-321-3991 Fax Number: 512-332-5208 E-Mail*: cabee@mdanderson.org

Credential, e.g., agency login: eRA Commons User Name

Project Role*: PD/PI Other Project Role Category:

Degree Type: Degree Year:

	File Name
Attach Biographical Sketch*:	Abee_Biosketch.pdf
Attach Current & Pending Support:	

PROFILE - Senior/Key Person

Excluded by Requester

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OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix: Dr.
First Name*: Christian
Middle Name: R
Last Name*: Abee
Suffix:

2. Human Subjects

Clinical Trial? ● No ○ Yes
Agency-Defined Phase III Clinical Trial?* ○ No ○ Yes

3. Permission Statement*

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

● Yes ○ No

4. Program Income*

Is program income anticipated during the periods for which the grant support is requested? ● Yes ○ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount ($)*	Source(s)*
1	172,200.00	Animal and BioBank Sales
2	188,559.00	Animal and BioBank Sales
3	208,824.00	Animal and BioBank Sales
4	230,688.00	Animal and BioBank Sales
5	254,150.00	Animal and BioBank Sales

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5. Human Embryonic Stem Cells

Does the proposed project involve human embryonic stem cells?* ● No ○ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ❑ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)

Inventions and Patents*: ○ Yes ● No

If the answer is "Yes" then please answer the following:

Previously Reported*: ○ Yes ○ No

7. Change of Investigator / Change of Institution Questions

❑ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

❑ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application (for RESUBMISSION or REVISION only)	
2. Specific Aims	F_OVERALL_Specific_Aims.pdf
3. Research Strategy*	F_OVERALL_Component_Research_Strategy.pdf
4. Progress Report Publication List	
Human Subjects Sections	
5. Protection of Human Subjects	
6. Inclusion of Women and Minorities	
7. Inclusion of Children	
Other Research Plan Sections	
8. Vertebrate Animals	VERTEBRATE_ANIMALS.pdf
9. Select Agent Research	
10. Multiple PD/PI Leadership Plan	
11. Consortium/Contractual Arrangements	
12. Letters of Support	F_OVERALL_Letters_of_Support.pdf
13. Resource Sharing Plan(s)	F_OVERALL_Resource_Sharing_Plan.pdf
Appendix (if applicable)	
14. Appendix	Excluded by Requester

Specific Aims: Overall

The **Squirrel Monkey Breeding and Research Resource (SMBRR)** is organized into a **Resource Component** focused entirely on managing the National Research Resource aspects of the SMBRR and an **Applied Research Component** with research projects that seek to improve the resources provided from the SMBRR or increase their value to the scientific community. During this proposed period of support, we plan to focus on adding value to the resources that are provided to the biomedical research community by improving reproductive efficiency, expanding services and resources provided to the scientific community, and conducting applied research that either improves how the resource is managed or adds value to the resources provided by the SMBRR. Our overall goal is to meet or exceed the needs of the biomedical research community for the resources that the SMBRR can provide. The following specific aims are proposed:

Resource Component (Christian Abee, D.V.M. and Excluded by Requester

1. Continue to improve and expand resources provided to the biomedical research community by:
    a. Evaluating the use of dried blood spots (DBS) for banking biological material;
    b. Expanding information provided on the SMBRR website to better address the needs of scientists who use squirrel monkeys in their research;
    c. Using information gained through our Applied Research studies to increase the value of the resources provided by the SMBRR.
2. Continue to improve reproduction in the breeding colony by:
    a. Using genetic management and colony management tools developed by the SMBRR and others to make better decisions regarding the sex/age classes for optimal reproduction;
    b. Using knowledge gained in our applied research on Pelvic Organ prolapse to reduce the incidence rate of dystocia and associated perinatal morbidity/mortality;
    c. Organizing and hosting a squirrel monkey genomics workshop.

Applied Research Component

Reproductive Biology Research: Excluded by Requester **Lead Investigator)**

1. Determine and describe cause(s) and potential preventive treatments on Pelvic Organ Prolapse in squirrel monkeys using serial MRI for three successive pregnancies by:
    a. Comparing effects of vaginal delivery to elective c-section on pelvic floor striated muscles
    b. Comparing mode of delivery on anatomic position endpoints in animals related to delivery route
    c. Using serial MRI to follow three successive pregnancies to measure the effect of successive obstetrical challenges
    d. Testing tools developed in this study to reduce dystocias leading to stillbirth and obstetrical injury in breeding females to improve production of healthy squirrel monkeys for research

Applied Genomics Research: Excluded by Requester **and** Excluded by Requester **Co-Lead Investigators)**

1. Identify novel genome-wide SNPs by whole genome sequencing of 6-8 squirrel monkeys from the resource colony and alignment to the reference sequence
2. Assign specific chromosomal locations to new SNPs by anchoring the existing scaffolding of the reference sequence.
3. Validate candidates SNPs by re-sequencing or real-time PCR.

Behavior Research: Excluded by Requester **Lead Investigator)**

1. Determine how squirrel monkeys housed at KCCMR use their available three-dimensional space.
2. Compare cage use and social activity during all phases of the reproductive cycle.
3. Investigate longitudinal changes in social group activity

Immunology Research: Excluded by Requester **Lead Investigator)**

1. Identify new cross reactive molecular and immunological research reagents for squirrel monkeys cells
2. Investigate specific cells such as Dendritic cells (DC), NK (Natural killer cells and NKT (Natural killer T cells) to further support the value of squirrel monkeys as an animal model for human studies
3. Test adjuvants such as α-alphagalactosylceramide, and CpG for vaccine delivery in squirrel monkeys.

Research Strategy: Overall

Background:

This competing renewal grant application requests support for grant years (GY) 35 through 39 of the **Squirrel Monkey Breeding and Research Resource (SMBRR)**. The SMBRR was established in 1980 through a P40 grant mechanism in response to a Request for Applications (RFA) from the Animal Resources Branch of the Division of Research Resources, NIH. The Animal Resources Branch is now the Division of Comparative Medicine in the Office of Research Infrastructural Programs (ORIP) within the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI) in the Office of the NIH Director (OD).

The SMBRR is located at the Michale E. Keeling Center for Comparative Medicine and Research (KCCMR). The KCCMR was established in 1974 as part of the University of Texas MD Anderson Cancer Center's (UTMDACC) research mission. The KCCMR occupies a 381-acre campus in Central Texas approximately 35 miles east of Austin. The KCCMR began the development of NIH-supported national research resources of nonhuman primates in 1976 with the establishment of the Chimpanzee Biomedical Research Resource (CBRR), followed by the Rhesus Monkey Breeding and Research Resource (RMBRR) in 1988. When Dr. Abee became Director of the KCCMR, the Owl Monkey Breeding and Research Resource (OMBRR) and the SMBRR were relocated from the University of South Alabama (USA) to the KCCMR. The UTMDACC has provided very strong institutional support to the SMBRR. In order to provide state-of-the-art facilities for the SMBRR, UTMDACC provided funding so that Dr. Abee could design and construct a 74,000 sq. ft. multi-function research building (Comparative Medicine Research Building, CMRB). The SMBRR moved into the Excluded by Requester of dedicated space and an additional 10,000 sq. ft. of shared support space. The total cost of the CMRB was $52,000,000. Of the $52,000,000 total construction cost, UTMDACC provided $48,000,000 and $4,000,000 was provided by a CO6 NIH construction grant that was awarded to Dr. Abee to partially support the construction of new facilities for the SMBRR. Research resources and services within the CMRB that support the SMBRR include: pathology, histology, and clinical pathology laboratories supervised by four board-certified veterinary pathologists, six clinical veterinarians provide backup veterinary medical support Excluded by Requester who is the primary clinical veterinarian for the SMBRR. An information and data services (IDS) section headed by Excluded by Requester is composed of a database programmer, a computer Support Services Analyst, and an Associate Applications System Analyst. The SMBRR has an outstanding animal caregiver staff, supervised by Excluded by Requester and Excluded by Requester who have 35 years combined experience caring for squirrel monkeys.

The members of the SMBRR's management and research teams include: Dr. Abee (PI), Excluded by Requester (Co-Investigator), Excluded by Requester (Co-PI Excluded by Requester genetic management consultant), and the External Advisory Board (EAB) composed of Excluded by Requester

Excluded by Requester The leaders of the research projects in the Applied Research Component are Excluded by Requester

Excluded by Requester

Significance:

It has long been recognized that the squirrel monkey (*Saimiri* spp.) is an important primate model in biomedical research. Squirrel monkeys and marmosets are the most commonly used Neotropical primates in biomedical research (Tardif et al. 2011; Abee, 2000). In the late 1970's, the NIH recognized that supply and availability of squirrel monkeys from source countries had become very vulnerable and that a self-sustaining breeding resource in the United States was the only way to assure continued availability of squirrel monkeys. However, attempts at establishing self-sustaining breeding colonies of squirrel monkeys had been unsuccessful. For this reason, the RFA that established the NIH funding mechanism for a squirrel monkey resource called for a breeding resource that would focus on improving reproduction so that a self-sustaining domestic resource could be achieved. The concerns of the NIH about sources and availability of squirrel monkeys from source countries were well founded. By 1987, the government of Bolivia joined Brazil and Colombia in banning export of squirrel monkeys. The loss of the Bolivian squirrel monkey (*Saimiri boliviensis boliviensis*) created an especially serious problem for many research programs that found this species the most desirable for their research. Importation of the other frequently used *Saimiri* species has remained unreliable. Availability of squirrel monkeys through importers is further complicated by the difficulties in air transport from South America as most airlines no longer transport primates. When feral squirrel monkeys can be obtained, the difficulties associated with uncertain age, disease history, pedigree, and intercurrent diseases create serious obstacles to research use.

Efforts to develop domestic breeding colonies of squirrel monkeys have spanned 65 years. The National Heart Institute awarded the first grant to establish a breeding colony of squirrel monkeys in 1949 (Gross et al. 1968). Taub *et al.* (1978) reported difficulties with captive reproduction in *Saimiri*. They reported that reproductive success in peer-raised laboratory-born female squirrel monkeys was poor compared to feral origin animals. Johnsen and Whitehair (1986) reviewed breeding colony statistics from several institutions and reported that the squirrel monkey was more difficult to breed in captivity than most other laboratory primates. Squirrel monkeys, unlike Old World primates, are seasonally polyestrus rather than menstrual cyclers. The breeding season occurs from December to March and births occur from June through August. The breeding season consists of a series of ovulatory cycles that vary in length between six and twelve days (Diamond et al. 1984). Although ovulatory cycles all occur at the same time of year, females do not cycle in synchrony within the same cage (Williams and Abee 1986), and there are no external signs of cycle stages. Squirrel monkeys are seasonally polyestrus, but they can be induced to ovulate in the nonbreeding season. Schuler *et al.* (Schuler et al. 2006) reported multiple ovarian stimulations of squirrel monkeys using pregnant mare serum gonadotropin (PMSG). As an estrous cycling animal, a strategy similar to that used in mice can be used to obtain oocytes from immature animals (Abee et al. 1996). Schuler *et al.* (2007b) used ultrasound guided follicular aspiration to harvest oocytes from hormonally stimulated squirrel monkeys. These studies have allowed us to learn a great deal about the reproductive biology of the squirrel monkey and allowed the SMBRR to test the feasibility of using assisted reproductive technology in squirrel monkeys. Although these techniques can be used in squirrel monkeys, they are far more time consuming, expensive, and less efficient than natural breeding. It is for these reasons that the SMBRR has focused its efforts on improving natural reproduction.

Squirrel monkeys continue to be among the most commonly used of Neotropical primates in biomedical research in this country (Abee 2000; Tardif et al. 2011). The need for squirrel monkeys continues to exceed domestic supply. More than 2,100 articles, about 400 articles per year, cited squirrel monkeys from 2009 to 2014 (Google Scholar query, May 2014).

The NIH Workshop, "Neotropical Primates in Biomedical Research" which was sponsored by and held at the NIH in September 2010, has reaffirmed the need for resources of Neotropical primates. The report published from the workshop (Tardif et al. 2011) emphasized the limited availability of these primates and recommended that mechanisms to support breeding colonies of the most needed New World primate species should be sought to ensure a domestic source. The SMBRR is unique in addressing this recommendation as it is the only NIH-supported national research resource that specializes in a New World (Neotropical) primate species. The only other source of squirrel monkeys is through primate suppliers that import feral squirrel monkeys from Guyana. As described above, availability is unreliable and the animals have unknown medical histories and pedigrees. When imported squirrel monkeys are available, the only species that can be imported is the common squirrel monkey (*Saimiri sciureus sciureus*). More than 75% of the SMBRR's squirrel monkeys are Bolivian squirrel monkeys (*Saimiri boliviensis boliviensis*). This species is no longer available from importers due to a ban on export of squirrel monkeys from source countries. NIH sponsored investigators have used Bolivian squirrel monkeys extensively.

Research needs for squirrel monkeys has increased over the last 10 years. We believe this is due to multiple factors including the reduced zoonotic disease risk compared to macaques, their small size which facilitates easier handling and housing, the increasing availability of reagents known to work in squirrel monkeys, and availability of laboratory born squirrel monkeys from the SMBRR. For these reasons, the SMBRR sells virtually all that can be harvested from the colony each year. Although the number of squirrel monkeys and BioBank specimens requested varies from year to year, annual animal requests exceeds production. Tables of animal sales and BioBank requests are in the Appendix of the Resource Component.

SMBRR resources are made available to investigators on a local, regional, and national basis. The SMBRR has made resources available to investigators within our institution and to local investigators as illustrated in the letter of support from Excluded by Requester **(see letter of support)**. Excluded by Requester has been working with the SMBRR for over two years to determine whether squirrel monkeys may be susceptible to HIV infection (Meyerson et al. 2014). Squirrel monkeys are of special interest in HIV research because they lack functional "restriction factors" against HIV which is a major barrier in most species of Old World monkeys, including macaques. Proprietary Info

Proprietary Info

Proprietary Info Excluded by Requester work may open a new area of research importance for the squirrel monkey model in the years to come. This is an example of how the SMBRR is working with a local/regional investigator to identify a new model for an important human disease. The following paragraphs provide examples of resources provided by the SMBRR.

Preliminary studies to determine whether the squirrel monkey can serve as a model of polyoma virus disease are underway at the SMBRR. This is an example of another new/emerging research area in which the squirrel monkey may impact human disease research (Houff et al. 1983; Verschoor et al. 2008; Zaragoza et al. 2005). The work of Excluded by Requester is showing considerable promise in using the squirrel monkey as a model of this infectious disease. Because Excluded by Requester has a continuing need to access the SMBRR animals, facilities, and staff in support of his research, he has been appointed to an adjunct faculty position in the Department of Veterinary Sciences at the KCCMR Excluded by Requester **letter of support is included in this application.** In it, Excluded by Requester describes his need for access to squirrel monkeys and the importance of research to better understand polyoma virus disease.

Squirrel monkeys are used extensively in neuroscience, vision and hearing research. The squirrel monkey model offers advantages over rodent models in that cortical organization of the squirrel monkey brain more closely resembles humans (Gao et al. 2014). Studies using squirrel monkeys have also contributed to our understanding of injury-induced reorganization of the sensory cortex and somatotopic reorganization of the brain stem and thalamus (Chen et al. 2012; Dancause et al. 2006; Qi et al. 2014; Wang et al. 2013). Contributions to vision research include gene therapy in color vision (Mancuso et al. 2009; Roy et al. 2010; Shapley 2009), adaptation of the vestibule-ocular reflex (Migliaccio et al. 2010), and topography of cones, rods, and optic nerve axons. Auditory research has included auditory frequency discrimination (Malone et al. 2013; Rhode et al. 2010) and mapping of the auditory cortex and projections throughout the brain (Cheung et al. 2009; Rhode et al. 2010). Examples of neuroscientists who use squirrel monkeys from the SMBRR are provided in the **letters of support:** Excluded by Requester Excluded by Requester

The field of **Behavioral Pharmacology**, particularly drug addiction research, has used squirrel monkeys for many years (Rowlett, et al. 2005; Valdez et al. 2007; Achat-Mendes et al. 2012). The letter of support from Excluded by Requester **(see letter of support)** explains how her research at the FDA has benefitted from resources provided by the SMBRR in helping her set up her research program Excluded by Requester studies the effects of tobacco product constituents. Her decision to use the squirrel monkey model was based on the extensive body of literature in which squirrel monkeys have been used in behavioral pharmacology and the availability of information from the SMBRR on how to care for squirrel monkeys in a laboratory environment. She plans to purchase 24 squirrel monkeys from the SMBRR in the coming months. Excluded by Requester **(Harvard Medical School) letter of support** describes the contribution the SMBRR has made to his research program that focuses on drug addiction and its behavioral and physiological sequelae. He recently purchased 10 squirrel monkeys and plans to purchase an additional 20 to 30 within the next two years.

The squirrel monkey is an important animal model for malaria vaccine development studies (Collins et al. 2010; Collins et al. 2009c; Horii et al. 2010). Because *Plasmodium* sp. are host specific, animal models used to study human malaria must be susceptible to the same strains that cause disease in humans. The Bolivian squirrel monkey has been shown to be a superior model for studies of the pathogenesis of *P. falciparum* Indochina I (Whiteley et al. 1987), developing lesions and clinical signs similar to those reported in the human disease. Squirrel monkeys are used to screen *P. falciparum* vaccine candidates for humans (Collins et al. 2000). Bolivian, Peruvian, and Guyanese squirrel monkeys are all susceptible to infection with different strains of *P. vivax*, but each squirrel monkey species/subspecies responds differently depending on the strain of the parasite used (Collins et al. 2005; Collins et al. 2009b; Galland 2000). Carvalho *et al*, (2010) reported positive findings using *Saimiri boliviensis* as a model for *P. vivax* vaccine testing. Differences in susceptibility and response to experimental malaria infections underscore the importance of species identification when using squirrel monkeys. Collins *et al*. (Collins et al. 2009a) reported that *Saimiri boliviensis* is a suitable model for testing sporozoite and liver stage vaccines against the Salvador I strain of *P .vivax*. **The supporting letter from** Excluded by Requester **describes the importance of the Bolivian squirrel monkey and the SMBRR for current and future studies of malaria treatment and vaccine development.** Malaria remains one of the top three diseases causing human mortality worldwide. **The SMBRR is the only resource of Bolivian squirrel monkeys in the world.**

The SMBRR has expanded its resources and outreach within the scientific community over the years beyond providing squirrel monkeys and biological materials to the biomedical research community. There are a number of accomplishments of the SMBRR that contribute in various ways to enrich NIH grantee community. Some selected accomplishments as listed below:

Selected Accomplishments and Value to the Biomedical Research Community:

1. Investigators within the SMBRR have organized and participated in workshops related to primate resources for biomedical research. After moving to the KCCMR, the SMBRR has become a part of

the **Primate Training and Enrichment Workshop** (PTEW) hosted by the KCCMR. Excluded by Requester leads the PTEW, and Excluded by Requester coordinates SMBRR participation. The PTEW is a four and half day workshop that emphasizes enrichment of captive nonhuman primates and the use of positive reinforcement training to shape behavior of primates used in research. The SMBRR provides PTEW workshop attendees (195 in the last 5 years, 2009-2014) an opportunity to practice hands-on training of squirrel monkeys, something that was not possible prior to inclusion of the SMBRR in the PTEW workshop program. During the next five years, we expect the PTEW will provide training experiences for 150-200 veterinarians, colony managers, and animal care technicians. Also, Dr. Abee served as a co-organizer and presenter at the **NIH-sponsored workshop on Neotropical Primates in Biomedical Research in September 2010**. More than 100 scientists from both the extramural grant community and the NIH intramural research program attended this workshop (Tardif, et al., 2011). In 2011, 2012, and 2013 Excluded by Private Source presented short courses on diseases and care of squirrel monkeys at the

2. The SMBRR provides training to investigators and veterinarians in the care and use of squirrel monkeys. Over the years, the SMBRR has responded to numerous requests for squirrel monkey training with "**Mini-Residencies**": 2-5 day individual, intensive training experiences on squirrel monkey care and use. This training has evolved into a four-day course entitled, "**Squirrel Monkey 101**" taught by SMBRR faculty and staff. To address the need for undergraduate training with squirrel monkeys, the SMBRR created the "**Nursery Intern Program**", a summer program for college students that provides students with experience in squirrel monkey nursery care. These students also attend primatology classes taught by SMBRR faculty and staff. **This program has had nineteen students from the US and Latin America since 2009**. In January 2009, the KCCMR welcomed its first resident fellow in the "**Training Clinical Veterinarians in Nonhuman Primate Clinical Medicine" (R25 RR024503)** program. This NIH-grant supported veterinary residency program provides two-years of intense clinical training to veterinarians who have already completed a laboratory animal medicine training program. Since 2009, four laboratory animal veterinarians have completed this program.

3. The **SMBRR has played an important role in the development of professional and scientific careers.** Twenty-one veterinary students in the last five years have rotated through the SMBRR during their 3rd or 4th years of veterinary school. Veterinary schools that have been represented in this program include: Texas A&M University, Oklahoma State University, Colorado State University, Iowa State University, Tuskegee University, University of Illinois, and the National University of Costa Rica. Due to popularity of this pre-doctoral training experience, we have an 18-month waiting list of students wishing to participate. Also, 20 post-DVM four-week externships for laboratory animal medicine trainees have been provided at the SMBRR.

4. The SMBRR website (smbrr.kccmr.org) has been expanded in the last two years with the addition of detailed descriptions of the natural history, reproductive biology, normal values, SMBRR Standard Operating Procedures, and bibliographic citations for the squirrel monkey. The website has also been expanded to include similar information about the owl monkey (*Aotus* spp.). Our website has become an important educational tool for scientists, veterinarians, and the general public. We continue to develop content and add it to the SMBRR website. We have now integrated the SMBRR website into the KCCMR website providing a direct link to the other nonhuman primate programs maintained at the KCCMR (www.kccmr.org). The website provides information on the center and how to access the resources available to NIH grantees.

5. The SMBRR helped develop a national breeding and research resource of owl monkeys (*Aotus* spp.) that received NIH grant support totaling $3,105,672 from 2005 to 2009. Owl monkeys are Neotropical primates that have been used extensively in malaria and ophthalmological research. The investigators and staff of the SMBRR were instrumental in the development of this resource. The **Owl Monkey Breeding and Research Resource (OMBRR)** is the only breeding and research resource of owl monkeys in the United States, and it owes much to the SMBRR for providing expertise on how to develop and operate this resource.

6. Three squirrel monkey and one owl monkey B-lymphoblast cell lines generated at the SMBRR have been characterized and are now available from the American Type Culture Collection (ATCC) (catalog numbers CRL-2311, CRL-2312, CRL-2699, and CRL-2762). In addition to these cell lines, studies carried out by investigators at the SMBRR to better understand squirrel monkey immune responses Excluded by Requester Excluded by Requester have identified new immunological reagents that cross-react with squirrel monkey lymphocyte subsets. A table listing these reagents is provided in the Appendix to the Resource Component.

7. The SMBRR provided the tissues and animal laboratory support to sequence squirrel monkey DNA Excluded by Requester Director and Principal Investigator, BACPAC Resources, Children's Hospital Oakland Research Institute created the first squirrel monkey BAC library. Cell lines from the donor animal have been established within the NSF-funded Integrated Primate Biomaterials and Information Resource and primary cDNA is now available from a large number of tissues. Tissues from the index squirrel monkey (*Saimiri boliviensis boliviensis*) has been archived at the San Diego Zoo. Members of the SMBRR worked with

The Broad Institute of MIT and the Harvard Genome Sequencing Platform, to sequence the entire Bolivian squirrel monkey genome. The DNA donor for sequencing the squirrel monkey genome is the female half-sibling of the male squirrel monkey used to create the BAC library. The genome of the squirrel monkey has been published and is now available [http://www.broadinstitute.org/software/allpaths-lg/blog/?p=350 (2011)]. **The SMBRR is the sole source of the squirrel monkeys used for all DNA sequencing and BAC cDNA library development that has been done. A letter of support and collaboration from** Excluded by Requester **is included in the letters of support.** Excluded by Requester

8. The SMBRR has maintained a leadership role in developing new and improved methods for research and clinical procedures in squirrel monkeys. We published the first report (Yeoman et al. 1997) describing the development of vibrostimulation for semen collection to replace the more invasive electroejaculation methods previously used. This painless procedure eliminated the need for anesthesia and replaced it with brief manual restraint (less than 5 minutes). Investigator's in the SMBRR have also developed **ultrasound guided oocyte retrieval** in the squirrel monkey (Schuler et al. 2007a). This technique eliminates the need for open abdomen or laparoscopic surgery for oocyte retrieval in squirrel monkeys.

9. The SMBRR was successful in accomplishing the original NIH goal to develop a self-sustaining breeding resource and continues to improve reproduction in the breeding colony. In 1980, when the SMBRR was established, no laboratory had been successful in creating a self-sustaining breeding colony of this genus. Since its establishment in 1980, the SMBRR has made great progress in captive reproduction of squirrel monkeys that now rivals the reproductive success observed in rhesus monkeys.

Resources generated by SMBRR are made available rapidly and efficiently using an easily accessible website that includes a **Biologics Request Form**. This form can be printed from the KCCMR website (www.kccmr.org) and sent by email attachment or regular mail. In the next grant period, this form will be converted to an online form. The online form will simplify and accelerate the request process.

The **SMBRR serves the needs of multiple NIH Institutes, Centers and Offices (ICOs)** as shown in the List of Projects/Investigators Receiving Resources in the Appendix of the Resource Component. This Table lists investigators and grants that have been served by the SMBRR during the current period of support. The SMBRR provides a description of resources available at our center on the SMBRR website, through presentations at national meetings, and through Current Listings of the Primate Resource Referral Service. This twice-monthly newsletter lists nonhuman primates available for research and related research resources. Through these multiple mechanisms the SMBRR informs the scientific community of the resources available. **Research resources available from the SMBRR** include squirrel monkeys of specific age, known pedigree, verified species, medical history, and sex. Other specific requirements regarding animals can usually be met depending on the request. At this time, the SMBRR is able to provide approximately 70 squirrel monkeys per year,. Tissues and biological fluids such as serum, whole blood, and urine can be provided upon request. Biological materials are provided from frozen, banked collections or freshly collected based the request criteria. Information regarding reagents that can be used in squirrel monkeys, the natural history of squirrel monkeys, and SOPs for the care and use of laboratory housed squirrel monkeys can be obtained from our website. Additionally, we are often contacted to provide expert advice to research programs across the US that are using squirrel monkeys.

The **SMBRR is supported from three primary sources**. These include the P40 center grant, program income from sales of animals and BioBanked materials, and institutional support. In the current grant year, the P40 grant total budget is $482,810 Total Direct Cost, program income is $139,038, and institutional support is $60,000. Therefore, in the current year (GY34), the P40 grant will contribute about 71% of the total operating cost of the SMBRR with program income and institutional support contributing approximately 29%. In GY 39, the P40 grant will account for 64% of the total operating cost with program income and institutional support accounting for 36%.

The NIH will allow a 5% increase in direct cost in competing renewals, but will not allow annual budget increases during the five years of requested support. Therefore, the contribution from the P40 grant will decrease as a percentage of total operating cost in each succeeding year as program income increases and P40 grant support remains level. The finances of the SMBRR are shown below:

SMBRR Current and Projected Funding from all sources:

	Current Support GY 34	GY 35	GY 36	GY 37	GY 38	GY 39

P40 OD010938-34*	$482,810	$506,033	$506,033	$506,033	$506,033	$506,033
P40 Grant-Related Income**	$139,398	$172,200	$188,559	$208,824	$230,688	$254,150
Institutional Support***	$60,043	$30,000	$30,000	$30,000	$30,000	$30,000
Total Funding for SMBRR	$682,251	$708,233	$724,592	$744,857	$766,721	$790,183

*Total Direct Costs
**Grant-Related Program Income is derived from projected sales of animals.
***Institutional support will vary from GY to GY, but we anticipate that it will average $30,000 per year. These funds will be used to support the cost of the EAB, the genetics consultant, genome sequencing, and the squirrel monkey genomics workshop in GY36. Institutional support is provided from endowment income available to Dr. Abee as part of his endowed professorship.

The sales of squirrel monkeys and BioBank resources have increased during the current period of support to more than $700,000 from 2010 through the first quarter of 2014. As shown in the Table above, increases in program income will help to support the SMBRR as NIH grant support continues to become less as a percentage of total operating cost. Program income combined with P40 support provides a good financial foundation to help assure continuation of the SMBRR into the future. It is important to note that P40 grant support remains absolutely critical in maintaining the SMBRR as a national research resource even as this grant support continues to decline as a percent of total operating cost. The UTMDACC leadership strongly supports the SMBRR and will make certain that space and other institutional resources are provided to assure the strength of the SMBRR in future years. UTMDACC leadership supports the allocation of institutional resources to the SMBRR, but this institutional support is contingent on P40 grant support. The commitment of the institution to maintaining national primate research resources, such as the SMBRR, is demonstrated by a long history of institutional support provided to similar resources at the KCCMR. The Chimpanzee Biomedical Research Resource (established 1976) and the Rhesus Monkey Breeding and Research Resource (established 1988) are examples. Both of these resources continue to be supported by MD Anderson. When the SMBRR and the OMBRR were moved to the KCCMR, MD Anderson provided more than $1,000,000 to move these colonies and provided $48,000,000 to build the Comparative Medicine Research Building (CMRB) to house the SMBRR. The estimated construction cost of the SMBRR space in the CMRB was $12,000,000.

Plans to continue the SMBRR beyond this potential grant award are in place. Dr. Abee has been the PI/Center Director of the SMBRR from its establishment in 1980. Plans are in place for continuing the SMBRR in the event of his retirement or departure from the KCCMR (neither are currently anticipated). The SMBRR is fortunate that its leadership has been very stable for many years. Excluded by Requester has been a member of SMBRR management team since 1982. He is knowledgeable about all aspects of the SMBRR and he has developed excellent ties with the users of the resources. Excluded by is a recognized leader in the care, use, and behavior of squirrel monkeys. Excluded by Requester has agreed (contingent on NIH program approval) to assume the PI/center directorship of the SMBRR should Dr. Abee retire or leave the institution. The faculty and staff of the Keeling Center are highly experienced in the care, use, and maintenance of primate research resources, so the infrastructure is in place to continue these programs into the future. **A letter to Dr. Manuel Moro (NIH OD-ORIP, Div. Comparative Medicine program official) indicating the strong support of the UTMDACC senior leadership from the Provost, Dr. Ethan Dmitrovsky, and the Vice Provost for Science and Institutional Official, Dr. Helen Piwnica-Worms is included in the Letters of Support.**

VERTEBRATE ANIMALS

All procedures involving squirrel monkeys will be carried out at the Michale E. Keeling Center for Comparative Medicine and Research (KCCMR) of the University of Texas M. D. Anderson Cancer Center (UTMDACC) in Bastrop, Texas. The Squirrel Monkey Breeding and Research Resource (SMBRR) is a national research resource of three squirrel monkey species, *Saimiri boliviensis boliviensis*, *Saimiri sciureus sciureus*, and *Saimiri boliviensis peruviensis*. Because this project involves maintaining a breeding colony of squirrel monkeys, all ages and both sexes of squirrel monkeys will be maintained in the project. The KCCMR is AAALAC accredited and has a PHS Assurance on file with the Office for Laboratory Animal Welfare (OLAW).

Proposed Animal Use: The SMBRR currently maintains 509 squirrel monkeys of the three species listed above. Most of these animals are in a breeding colony that serves as a national research resource of this genus available to NIH grantees that need squirrel monkeys for their research. All animals provided from the SMBRR are provided to institutions with PHS assurances and there must be an approved IACUC protocol for the animals requested from the SMBRR. The SMBRR also carries out studies designed to provide new information about the natural biology of squirrel monkeys with an emphasis on studies of natural social behavior, diseases of squirrel monkeys that resemble human diseases, and studies to better understand the immunology of the squirrel monkey.

The squirrel monkey colony consists of both males and females. Squirrel monkeys range in age from newborn to more than 20 years.

The UTMDACC Institutional Animal Care and Use Committee (IACUC) meets monthly to review proposed research protocols and to assure that the guidelines put forth by the PHS Policy on Humane Care and Use of Laboratory Animals and NIH *Guide* are followed; facilities and programs are evaluated by the IACUC every six months. This Institution has an Animal Welfare Assurance on file with the NIH Office of Laboratory Animal Welfare (ref. A-3343-01) and is a USDA-registered research facility.

Justification for the Use of Squirrel Monkeys: The procedures performed on the three species of animals described in this application will occur as part of normal operations to address medical and management problems and research approved by the IACUC. The justification for the number of animals described is that they equal the total number of animals maintained in each colony, all of which require medical care and oversight. The species chosen reflect the most commonly used squirrel monkeys in biomedical research.

Veterinary Care: All of the veterinarians at the KCCMR have extensive experience in the clinical care and biomedical research use of nonhuman primates. Excluded by Requester each have more than 20 years experience working with squirrel monkeys. The technical and husbandry staff receives regular training and approximately 80% of the KCCMR husbandry staff is AALAS certified. Daily observations and regularly scheduled physical examinations are important in preventive medicine and in detecting early, subtle signs of disease. Colony staff and supervisors view all colony animals during observations at least twice daily. An established and well-integrated Behavioral Management and Enrichment program is directed by Excluded by Requester a primate behaviorist with more than 25 years experience with squirrel monkeys.

Guidelines for Minimizing Discomfort, Pain or Distress: All non-painful procedures in squirrel monkeys are carried out with gentle manual restraint or with sedation using Ketamine HCl administered by experienced staff. General anesthesia for painful procedures is provided using injectable ketamine & xylazine, or isoflurane inhalation anesthesia that is induced by mask under manual restraint.

Anesthetic Monitoring and Recovery: During routine short anesthesia periods when ketamine and xylazine are used as the anesthetic agents, the animal's condition is monitored by close observation of its breathing pattern and the color of its mucus membranes, and auscultation of its heart and lung sounds. Major surgery requires use of an inhalation agent and may include continuous monitoring of blood pressure, electrocardiogram, anesthetic agent, oxygen saturation and other parameters. During the recovery period, animals are placed in a lateral position to allow drainage and prevent aspiration of secretions, and they are periodically observed until they are able to maintain a sitting posture.

Analgesia: A variety of oral and injectable analgesics, ranging in strength from nonprescription analgesics to potent narcotics, are available at the discretion of the clinical veterinarian. Buprenorphine is the most frequently used analgesic. In evaluating the need of analgesics, the guidelines from PHS policy "Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Education" are followed (Interagency Research Animal Committee, 1985). Specifically, "Unless the contrary is established, investigators should consider that procedures that cause pain or distress in human beings may cause pain or distress in other animals." In addition, close monitoring, coupled with knowledge of the normal behavior of the individual animal, is used to detect subtle signs of discomfort that indicate a need for analgesia.

Euthanasia Policy: Euthanasia is administered for humane reasons based upon the decision of the attending veterinarian. Methods of euthanasia are in compliance with the AVMA Guidelines for Euthanasia of Animals 2013 Edition Version 2013.0.1 (www.avma.org). Euthanasia, in instances when it becomes necessary, is carried out using an overdose of barbiturate administered intravenously.

References – Overall Component

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Resource Sharing Plan

The Squirrel Monkey Breeding and Research Resource (SMBRR) has developed multiple approaches to sharing the resources that are maintained and provided by the center. The SMBRR provides a description of resources available at our center on the SMBRR website, through presentations at national meetings, and through Current Listings of the Primate Resource Referral Service. This twice-monthly newsletter lists nonhuman primates available for research and related research resources. Through these multiple mechanisms the SMBRR informs the scientific community of the resources available.

Access to Resource Materials: From the SMBRR website, there are links for contact information and a request form (see Appendix in Resource Component, PDF Animal/Biologics Request Form) that can be used by investigators to request animals or biologics from the SMBRR. The **Animal/Biologics Request Form** asks for specific information about the needs of the investigator, time requirements, and if the biologic must be collected from animals rather than from the BioBank, the requester is asked to provide a written protocol for collection and transport of the materials to ensure that the request is obtained, processed, and shipped appropriately to meet their needs. Once a request for animals or biologics is received by the SMBRR, the requirements of the request are compared to available inventory in the BioBank or animal sampling and a decision is made whether the request can be filled. This is usually done within a day or two. The investigator is notified that the requested resources are available and arrangements are made for shipping or transfer. If the specific items requested are not available, the investigator is notified and given an opportunity to modify the request. If there are no suitable animals or biological samples available, the investigator is placed on a waiting list until an appropriate specimen is available. This could require waiting for an animal to mature to an appropriate age or weight, or waiting until material can be collected during a necropsy. In most cases, requests for resources can be met immediately. There have been a small number of requests for animals that exceeded availability. We remain concerned that demand for squirrel monkeys will exceed supply so we continue to search for innovative ways to leverage the number of animals available to meet research needs. This can sometimes be accomplished by using some squirrel monkeys to meet multiple research needs. Drs. Abee, Excluded by Requester work with investigators to determine when this approach is possible. **During the proposed period of support, we will move from the current paper driven animal and BioBank request form to an online ordering process that will streamline the request process and provide investigators with more rapid feedback.**

Investigator and Student Access: Due to the increasing complexity of conducting research with nonhuman primates, the need for special expertise, the high cost of primates, and difficulties in transporting primates, there is a growing trend toward conducting research within primate resources rather than transporting the animals to the investigator's institution. This trend is very likely to grow as institutions that lack the facilities and expertise opt to conduct their studies at facilities that specialize in the use of nonhuman primates. The SMBRR has recognized this trend and has initiated efforts to provide leadership. The Comparative Medicine Research Building (CMRB) where the SMBRR is housed has been designed to provide space for visiting scientists/research teams so they can work directly in the SMBRR and associated support spaces. Because Dr. Abee is both the PI of the SMBRR and the Director of the Keeling Center, he has the authority to provide space to visiting scientists, students, and others so that use of the SMBRR can be made available to NIH grantees and others who wish to conduct research with squirrel monkeys.

Website: Scientists needing resources and/or information from the SMBRR can rapidly access the SMBRR website with their internet browser. Using a search engine and typing "squirrel monkey resource" or "squirrel monkey research resource", the first hit is the SMBRR. The SMBRR website provides information about the resource, its mission and availability. The SMBRR provides access to information on how to access to the resource, as well as information concerning the management and handling of squirrel monkeys. From the website, visitors can access our standard operating procedures for daily husbandry, use of anesthetics, newborn and nursery rearing techniques. Normal values for serum chemistries, hematology, and body weights are also available. From the results of immunology studies carried out in the SMBRR, we continue to update a listing of biologic reagents that have been demonstrated to cross-react with squirrel monkey leukocyte subsets. The website has been designed and tagged in such a way as to consistently appear near the top of lists generated by computer searches. Using search terms like "squirrel monkey" with terms such as "resource", "breeding", "husbandry", and "availability" will return the SMBRR site within the first 5-10 sites reported.

External Advisory Board (EAB): The EAB is consulted annually regarding the resources that are made available. The EAB advises on what resources should be added and whether specific resources should be modified or cease to be maintained. The members of the EAB provide recommendations on how to improve availability of resources provided by the SMBRR.

OMB Number: 4040-0001
Expiration Date: 06/30/2016

APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

5. APPLICANT INFORMATION **Organizational DUNS*:** 8007721390000

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Person to be contacted on matters involving this application

Prefix:	First Name*:	Middle Name:	Last Name*:	Suffix:
	Renee		Gonzales	

Position/Title: Executive Director, Sponsored Programs
Street1*: The University of Texas MD Anderson Cancer Center
Street2: 1515 Holcombe Blvd, Unit 1626
City*: Houston
County:
State*: TX: Texas
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 770304009
Phone Number*: 713-792-3220 Fax Number: 713-794-4535 Email: osp@mdanderson.org

7. TYPE OF APPLICANT* H: Public/State Controlled Institution of Higher Education

Other (Specify):
Small Business Organization Type ❍ Women Owned ❍ Socially and Economically Disadvantaged

11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT*
Squirrel Monkey Breeding and Research Resource: Resource Core

12. PROPOSED PROJECT

Start Date*	Ending Date*
04/01/2015	03/31/2020

OMB Number: 4040-0010
Expiration Date: 06/30/2016

Project/Performance Site Location(s)

Project/Performance Site Primary Location

● I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	The University of Texas MD Anderson Cancer Center
Duns Number:	8007721390000
Street1*:	Michale E. Keeling Center for Comp Med and Research
Street2:	650 Cool Water Drive
City*:	Bastrop
County:	
State*:	TX: Texas
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	786026621
Project/Performance Site Congressional District*:	TX-009

File Name

Additional Location(s)

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* ○ **Yes** ● **No**

1.a. If YES to Human Subjects

Is the Project Exempt from Federal regulations? ○ Yes ○ No

If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6

If NO, is the IRB review Pending? ○ **Yes** ○ **No**

IRB Approval Date:

Human Subject Assurance Number

2. Are Vertebrate Animals Used?* ● **Yes** ○ **No**

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ○ Yes ○ No

IACUC Approval Date:

Animal Welfare Assurance Number

3. Is proprietary/privileged information included in the application?* ○ **Yes** ● **No**

4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* ○ **Yes** ● **No**

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ○ Yes ○ No

4.d. If yes, please explain:

5. Is the research performance site designated, or eligible to be designated, as a historic place?* ○ **Yes** ● **No**

5.a. If yes, please explain:

6. Does this project involve activities outside the United States or partnership with international collaborators?* ○ **Yes** ● **No**

6.a. If yes, identify countries:

6.b. Optional Explanation:

	Filename
7. Project Summary/Abstract*	F_RESOURCE_CORE_Project_Summary_Abstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	F_RESOURCE_CORE_References.pdf
10.Facilities & Other Resources	
11.Equipment	

RESOURCE COMPONENT PROJECT SUMMARY

The Squirrel Monkey Breeding and Research Resource (SMBRR) provides squirrel monkeys, tissues, biological fluids, information on the care and use of squirrel monkeys, and research services to the biomedical research community. The breeding colonies of the SMBRR include three species/subspecies of squirrel monkeys: Bolivian squirrel monkeys (*Saimiri boliviensis boliviensis*) comprising about 71%; Guyanese or common squirrel monkeys (*Saimiri sciureus sciureus*) comprising about 25%; and Peruvian squirrel monkeys (*Saimiri boliviensis peruviensis*) comprising about 4%. Due to bans on export of Bolivian squirrel monkeys, the SMBRR is the only source in the world of this important squirrel monkey species and the only source of laboratory-born and pedigreed squirrel monkeys of any species. Priority with respect to access to these resources is given to NIH grantees, the NIH intramural research program, and federal agencies including the FDA and NSF. Resources are also provided to other sponsors of biomedical research (private foundations, pharmaceutical companies, and contract research organizations). The overall goals of the resource component of the SMBRR are to provide a national research resource of squirrel monkeys and squirrel monkey derived biological materials; provide education and training to scientists, veterinarians, colony managers, and animal caregivers who work with squirrel monkeys; and, support investigators who need facilities and expertise to conduct studies using squirrel monkeys. New areas of research in which squirrel monkeys are needed continue to emerge. As these new areas of research develop, the SMBRR plays an essential role by providing the animals, biological resources, and the expertise needed. In the next five years, the SMBRR will increase the animals and related resources that can be provided to the scientific community, organize and host a squirrel monkey genomics workshop, and continue to add value to the squirrel monkey as a model in human health research. The scarcity of squirrel monkeys, difficulties associated with captive breeding, challenges associated with their care and use in research, all contribute to the need for this national research resource.

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Prefix: Dr. First Name*: Christian Middle Name R Last Name*: Abee Suffix:

Position/Title*:	Professor and Chair
Organization Name*:	The University of Texas MD Anderson Cancer Center
Department:	Dept of Veterinary Sciences
Division:	
Street1*:	Michale E. Keeling Center for Comp Med and Research
Street2:	650 Cool Water Drive
City*:	Bastrop
County:	
State*:	TX: Texas
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	786026621

Phone Number*: 512-321-3991 Fax Number: 512-332-5208 E-Mail*: cabee@mdanderson.org

Credential, e.g., agency login: eRA Commons User Name

Project Role*: Other (Specify) Other Project Role Category: Project Lead

Degree Type: Degree Year:

File Name

Attach Biographical Sketch*:

Attach Current & Pending Support:

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 8007721390000

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2015 **End Date*:** 03-31-2016 **Budget Period: 1**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Christian	R.	Abee		PD/PI	Institutional Base Salary	EFFORT			18,150.00	5,082.00	23,232.00
2.	Excluded by Requester					Co-PD/PI					63,379.00	17,746.00	81,125.00
3.						Co-Investigato					48,075.00	13,461.00	61,536.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **165,893.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Team Lead, Animal Resources	EFFORT			7,539.00	2,111.00	9,650.00
1	Research Asst				14,401.00	4,032.00	18,433.00
2	**Total Number Other Personnel**					**Total Other Personnel**	**28,083.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**193,976.00**

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

Funding Opportunity Number: PAR-14-005. Received Date: 2014-05-29T15:39:24.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 8007721390000
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2015 **End Date*:** 03-31-2016 **Budget Period: 1**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 8007721390000
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2015 **End Date*:** 03-31-2016 **Budget Period: 1**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Animal Care Costs	293,825.00
Total Other Direct Costs	**293,825.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**487,801.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. F & A	60.0	0.00	292,681.00
		Total Indirect Costs	**292,681.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number) DHHS, Arif Karim, 415-437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**780,482.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 8007721390000

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2016 **End Date*:** 03-31-2017 **Budget Period: 2**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Christian	R.	Abee		PD/PI	Institutional Base Salary	EFFORT			18,150.00	5,082.00	23,232.00
2.		Excluded by Requester				Co-PD/PI					63,379.00	17,746.00	81,125.00
3.						Co-Investigator					48,075.00	13,461.00	61,536.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **165,893.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical	EFFORT					
1	Team Lead, Animal Resources				7,539.00	2,111.00	9,650.00
1	Research Asst				14,401.00	4,032.00	18,433.00
2	**Total Number Other Personnel**					**Total Other Personnel**	**28,083.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**193,976.00**

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

Funding Opportunity Number: PAR-14-005. Received Date: 2014-05-29T15:39:24.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 8007721390000
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2016 **End Date*:** 03-31-2017 **Budget Period: 2**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 8007721390000
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2016 **End Date*:** 03-31-2017 **Budget Period: 2**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Animal Care Costs	293,825.00
Total Other Direct Costs	**293,825.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**487,801.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. F & A	60.0	0.00	292,681.00
		Total Indirect Costs	**292,681.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number) DHHS, Arif Karim, 415-437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**780,482.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 8007721390000

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2017 **End Date*:** 03-31-2018 **Budget Period: 3**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Christian	R.	Abee		PD/PI	Institutional Base Salary	EFFORT			18,150.00	5,082.00	23,232.00
2.	Excluded by Requester					Co-PD/PI					63,379.00	17,746.00	81,125.00
3.						Co-Investigator					48,075.00	13,461.00	61,536.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **165,893.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical	EFFORT					
1	Team Lead, Animal Resources				7,539.00	2,111.00	9,650.00
1	Research Asst				14,401.00	4,032.00	18,433.00
2	**Total Number Other Personnel**					**Total Other Personnel**	**28,083.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**193,976.00**

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

Funding Opportunity Number: PAR-14-005. Received Date: 2014-05-29T15:39:24.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 8007721390000
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2017 **End Date*:** 03-31-2018 **Budget Period: 3**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 8007721390000
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2017 **End Date*:** 03-31-2018 **Budget Period: 3**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Animal Care Costs	293,825.00
Total Other Direct Costs	**293,825.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**487,801.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. F & A	60.0	0.00	292,681.00
		Total Indirect Costs	**292,681.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number) DHHS, Arif Karim, 415-437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**780,482.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 8007721390000

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2018 **End Date*:** 03-31-2019 **Budget Period: 4**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Christian	R.	Abee		PD/PI	Institutional Base Salary	EFFORT			18,150.00	5,082.00	23,232.00
2.		Excluded by Requester				Co-PD/PI					63,379.00	17,746.00	81,125.00
3.						Co-Investigator					48,075.00	13,461.00	61,536.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **165,893.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Team Lead, Animal Resources	EFFORT			7,539.00	2,111.00	9,650.00
1	Research Asst				14,401.00	4,032.00	18,433.00
2	**Total Number Other Personnel**					**Total Other Personnel**	**28,083.00**

Total Salary, Wages and Fringe Benefits (A+B) **193,976.00**

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

Funding Opportunity Number: PAR-14-005. Received Date: 2014-05-29T15:39:24.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 8007721390000
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2018 **End Date*:** 03-31-2019 **Budget Period: 4**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 8007721390000
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2018 **End Date*:** 03-31-2019 **Budget Period: 4**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Animal Care Costs	293,825.00
Total Other Direct Costs	**293,825.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**487,801.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. F & A	60.0	0.00	292,681.00
		Total Indirect Costs	**292,681.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number) DHHS, Arif Karim, 415-437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**780,482.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 8007721390000

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2019 **End Date*:** 03-31-2020 **Budget Period:** 5

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Christian	R.	Abee		PD/PI	Institutional Base Salary	EFFORT			18,150.00	5,082.00	23,232.00
2.		Excluded by Requester				Co-PD/PI					63,379.00	17,746.00	81,125.00
3.						Co-Investigator					48,075.00	13,461.00	61,536.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **165,893.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Team Lead, Animal Resources	EFFORT			7,539.00	2,111.00	9,650.00
1	Research Asst				14,401.00	4,032.00	18,433.00
2	**Total Number Other Personnel**					**Total Other Personnel**	**28,083.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**193,976.00**

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

Funding Opportunity Number: PAR-14-005. Received Date: 2014-05-29T15:39:24.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 8007721390000
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2019 **End Date*:** 03-31-2020 **Budget Period: 5**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 8007721390000
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2019 **End Date*:** 03-31-2020 **Budget Period: 5**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Animal Care Costs	293,825.00
Total Other Direct Costs	**293,825.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**487,801.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. F & A	60.0	0.00	292,681.00
		Total Indirect Costs	**292,681.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number) DHHS, Arif Karim, 415-437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**780,482.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

BUDGET JUSTIFICATION

RESOURCE COMPONENT

Personnel – Resource*

	GY 35	GY 36	GY 37	GY 38	GY 39
Professional Personnel					
Abee, C.R., D.V.M., PI (Core Leader)	23,232	23,232	23,232	23,232	23,232
Excluded by Requester Co-PI	81,125	81,125	81,125	81,125	81,125
Excluded by Requester Co-Investigator	61,536	61,536	61,536	61,536	61,536
Technical Personnel					
Excluded by Requester Team Leader, Animal Resources	9,650	9,650	9,650	9,650	9,650
Research Assistant I	18,433	18,433	18,433	18,433	18,433
Total Salaries and Benefits	$193,976	$193,976	$193,976	$193,976	$193,976

*** Although it is anticipated that salaries will increase annually, NIH Fiscal Policy does not allow inflationary increases to be included in this budget.**

Christian R. Abee, D.V.M. % Effort **effort,** EFFORT **mos)** is the principal investigator for the Squirrel Monkey Breeding and Research Resource (SMBRR). Dr. Abee is the Director of the Michale E. Keeling Center for Comparative Medicine and Research (KCCMR) and Professor and Chair of the Department of Veterinary Sciences at the University of Texas MD Anderson Cancer Center. Dr. Abee is responsible for the overall direction of the SMBRR including oversight of the SMBRR management team, implementation of recommendations of the External Advisory Board (EAB) and direction and support Excluded by Requester the Co-PI. He will provide oversight and direction of both the Resource and Applied Research Components of the SMBRR. Dr. Abee will devote % Effort Dr. Abee's salary is subject to the NIH salary cap in all years.

Excluded by Requester

Excluded by Requester

Excluded by Requester

Excluded by Requester

Excluded by Requester

External Advisory Board (EAB) – Resource Component

The EAB of the SMBRR is composed of highly experienced leaders in their fields. Excluded by Requester has agreed to serve as chair of the EAB. The EAB will meet at the SMBRR for a one-day site visit each year. In addition, there will be two teleconference meetings each year. Therefore, the EAB will meet three times a year. The EAB will review, advise, and make recommendations on applied research and management activities. The EAB will provide perspective on the national research needs that can/should be met by the SMBRR, and advise the PI and Co-PI of the SMBRR regarding priorities realizing that funding limitations require setting priorities. All four members of the EAB have experience with Neotropical primates and other experiences that are relevant to the SMBRR. It is anticipated that the meetings/teleconference/honoraria for the EAB will cost approximately $8,000 per year. Dr. Abee will use institutional funds from an endowment to cover the cost of the EAB. Letters from Excluded by Requester agreeing to serve on the SMBRR EAB are provided in this application. With an estimated cost of $8,000 per year, the EAB cost will total $40,000 over the 5-year project period. This will be funded entirely from institutional support. See Institutional Support table below for detail.

Genetic Management Consultant – Resource Component

Excluded by Requester has agreed to serve as consultant on genetic management of the squirrel monkeys breeding colonies. Excluded by will work Excluded by Requester (Co-PI) on selection of breeding males and females to prevent inbreeding and control contributions of founder's pedigrees within the breeding colonies. Excluded by will travel to the SMBRR at least once a year and will be in frequent televideo and telephone communication with Drs. Abee Excluded by Requester The cost for genetic management services in the Resource Component will be paid using institutional support. It is anticipated that genetic management services will be

Other Expenses - Resource Component

	GY 35	GY 36	GY 37	GY 38	GY 39
Animal Care Costs (animal Per Diem) Number of animals 350 animals x 365 days x $2.30 per day	$293,825	$293,825	$293,825	$293,825	$293,825

Animal *per diem* costs are calculated at $2.30/animal/day for all years. NIH budget rules do not allow budgeting for inflationary increases. The current squirrel monkey census is 559 animals. The number of animals in the colony for which support is requested for each year is only 350 adults and juveniles. Funding for the remaining animals beyond the 350 budgeted, is provided from program income.

The KCCMR maintains detailed accounting records for expenditures incurred for the care of the squirrel monkey colony. This is based on an annual Cost Analysis that was most recently carried out in the first quarter of 2014. The *per diem* rate has been determined using the "Cost Analysis and Rate Setting Manual for Animal Research Facilities" (NIH/NCRR May 2000). The *per diem* rate includes the costs associated with the following activities:

- Colony management and supervisory staff
- Animal care personnel, primate enrichment technicians, and administrative personnel
- Routine and emergency veterinary care and pathology services
- General supplies such as expendable office supplies, routine maintenance supplies, and other supplies which are not included in Facilities & Administrative costs
- Feed, bedding, special diets, and diet preparation supplies
- Environmental enrichment materials and other enrichment devices and supplies
- Medical supplies including antibiotics, anesthetics, analgesics
- Routine animal husbandry supplies including cleaning supplies, uniforms, etc.

SMBRR Current and Projected Funding from all sources:

	Current Support GY 34	GY 35	GY 36	GY 37	GY 38	GY 39
P40 OD010938-34*	$482,810	$506,033	$506,033	$506,033	$506,033	$506,033
P40 Grant-Related Income**	$139,398	$172,200	$188,559	$208,824	$230,688	$254,150
Institutional Support***	$60,043	$30,000	$30,000	$30,000	$30,000	$30,000
Total Funding for SMBRR	$682,251	$708,233	$724,592	$744,857	$766,721	$790,183

*Total Direct Costs

**Grant-Related Program Income is derived from projected sales of animals.

***Institutional support will vary from GY to GY, but we anticipate that it will average $30,000 per year. These funds will be used to support the cost of the EAB, the genetics consultant, genome sequencing, and the squirrel monkey genomics workshop in GY36. Institutional support is provided from endowment income available to Dr. Abee as part of his endowed professorship.

Program income is estimated in the table below based on the estimated number of animals that will be sold and the anticipated sale price in each grant year. No estimate is included for sale of BioBank materials as this is difficult to estimate.

Program Income Estimation for GY35-39

	GY 35	GY 36	GY 37	GY 38	GY 39
# of animals provided by SMBRR	70	73	77	81	85
Price per animal	2,460	2,583	2,712	2,848	2,990
	$172,200	$188,559	$208,824	$230,688	$254,150

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals ($)	
Section A, Senior/Key Person		**829,465.00**
Section B, Other Personnel		**140,415.00**
Total Number Other Personnel	10	
Total Salary, Wages and Fringe Benefits (A+B)		**969,880.00**
Section C, Equipment		**0.00**
Section D, Travel		**0.00**
1. Domestic	0.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		**0.00**
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		**1,469,125.00**
1. Materials and Supplies	0.00	
2. Publication Costs	0.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	1,469,125.00	
9. Other 2	0.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		**2,439,005.00**
Section H, Indirect Costs		**1,463,405.00**
Section I, Total Direct and Indirect Costs (G + H)		**3,902,410.00**
Section J, Fee		**0.00**

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix: Dr.
First Name*: Christian
Middle Name: R
Last Name*: Abee
Suffix:

2. Human Subjects

Clinical Trial? ● No ○ Yes
Agency-Defined Phase III Clinical Trial?* ○ No ○ Yes

3. Permission Statement*

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

● Yes ○ No

4. Program Income*

Is program income anticipated during the periods for which the grant support is requested? ● Yes ○ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount ($)*	Source(s)*
1	172,200.00	Animal and BioBank Sales
2	188,559.00	Animal and BioBank Sales
3	208,824.00	Animal and BioBank Sales
4	230,688.00	Animal and BioBank Sales
5	254,150.00	Animal and BioBank Sales

PHS 398 Cover Page Supplement

5. Human Embryonic Stem Cells

Does the proposed project involve human embryonic stem cells?* ● No ○ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ❑ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)

Inventions and Patents*: ○ Yes ● No

If the answer is "Yes" then please answer the following:

Previously Reported*: ○ Yes ○ No

7. Change of Investigator / Change of Institution Questions

❑ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

❑ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application (for RESUBMISSION or REVISION only)	
2. Specific Aims	F_RESOURCE_CORE_Specific_Aims.pdf
3. Research Strategy*	F_RESOURCE_CORE_Research_Strategy.pdf
4. Progress Report Publication List	
Human Subjects Sections	
5. Protection of Human Subjects	
6. Inclusion of Women and Minorities	
7. Inclusion of Children	
Other Research Plan Sections	
8. Vertebrate Animals	VERTEBRATE_ANIMALS.pdf
9. Select Agent Research	
10. Multiple PD/PI Leadership Plan	
11. Consortium/Contractual Arrangements	
12. Letters of Support	F_RESOURCE_Letters_of_Support.pdf
13. Resource Sharing Plan(s)	
Appendix (if applicable)	
14. Appendix	Excluded by Requester

Specific Aims: Resource Component

The Squirrel Monkey Breeding and Research Resource (SMBRR) provides squirrel monkeys, tissues, biological fluids, information on the care and use of squirrel monkeys, and research services to the biomedical research community. The breeding colonies of the SMBRR include three species/subspecies of squirrel monkeys: Bolivian squirrel monkeys (*Saimiri boliviensis boliviensis*) comprising about 71%; Guyanese or common squirrel monkeys (*Saimiri sciureus sciureus*) comprising about 25%; and Peruvian squirrel monkeys (*Saimiri boliviensis peruviensis*) comprising about 4%. The overall goals of the resource component of the SMBRR are to provide a national research resource of squirrel monkeys and squirrel monkey derived biological materials; provide education and training to scientists, veterinarians, colony managers, and animal caregivers who work with squirrel monkeys; and, support investigators who need facilities and expertise to conduct studies using squirrel monkeys. In the next five years, the SMBRR will meet these goals by accomplishing the following specific aims:

Resource Component (Christian Abee, D.V.M. and Excluded by Requester

1. Continue to improve and expand resources provided to the biomedical research community by:
    a. Evaluating the use of dried blood spots (DBS) for banking biological material;
    b. Expanding information provided on the SMBRR website to better address the needs of scientists who use squirrel monkeys in their research;
    c. Using information gained through our Applied Research studies to increase the value of the resources provided by the SMBRR.
2. Continue to improve reproduction in the breeding colony by:
    a. Using genetic management and colony management tools developed by the SMBRR and others to make better decisions regarding the sex/age classes for optimal reproduction;
    b. Using knowledge gained in our applied research on Pelvic Organ prolapse to reduce the incidence rate of dystocia and associated perinatal morbidity/mortality;
    c. Organizing and hosting a squirrel monkey genomics workshop.

Research Strategy: Resource Component

The Squirrel Monkey Breeding and Research Resource (SMBRR) was established in 1980 in response to a Request for Application (RFA) from the Division of Research Resources of the NIH to develop a self-sustaining national research resource of squirrel monkeys (*Saimiri* spp.) and biological materials from squirrel monkeys. Prior to the establishment of the SMBRR, all attempts to develop self-sustaining breeding resources of this species had been unsuccessful. To date, the SMBRR remains the only research resource of squirrel monkeys in the United States. Therefore, the SMBRR serves the scientific community by providing the only source of laboratory-born squirrel monkeys of known pedigree, medical, and experimental history. The SMBRR has continued to improve the resources provided to the NIH grantee community over the past 34 years. In this proposed period of support, the SMBRR will continue to improve reproductive efficiency, seek new ways to meet the needs of the biomedical research community, and progress toward recovering a greater percentage of the cost of maintaining this national research resource. The breeding colony is composed of three species of squirrel monkeys: the Common Squirrel Monkey (*Saimiri sciureus sciureus)*; the Bolivian Squirrel Monkey (*Saimiri boliviensis boliviensis*); and a very small group of Peruvian Squirrel Monkeys (*Saimiri boliviensis peruviensis*). It is planned to phase out the Peruvian Squirrel Monkey group as it is too small to maintain genetic diversity and there is very little research need for this subspecies. The SMBRR was moved from the Proprietary Info in 2008-2009 to the Michale E. Keeling Center for Comparative Medicine and Research (KCCMR), which is part of the University of Texas MD Anderson Cancer Center (UTMDACC).

The need for squirrel monkeys has remained strong during the current period of support and all indications are that research needs will continue to meet or exceed resources that can be produced (**see Letters of Support in the Overall Component of this application**). The SMBRR has remained flexible over the years to allow the resource to meet the changing needs of the biomedical research community. The SMBRR is well positioned to address the growing trend in research that requires resources of nonhuman primates to have the capability to provide the animal resources to other institutions, but also, have the capability to provide the facilities and expertise so that investigators can carry out the research at the center where the SMBRR is located. NIH grantees are offered multiple ways to access the resources of the SMBRR. These include purchase and shipment of animals and biological materials to the grantee's home institution, access to animals on-site at the SMBRR, and access to the technical and scientific expertise to conduct the research at the SMBRR. The SMBRR also provides information on our website to help other programs/institutions work with squirrel monkeys. The SMBRR continues to search for ways to make resources more valuable to the research community.

Resource Production and Use

Breeding Resource: The SMBRR has grown from 509 animals in May 2009 to 559 as of April 1, 2014 while providing 373 squirrel monkeys to research groups in other institutions. We anticipate that an additional 80 infants will be born in 2014, which will increase the colony census to more than 570 by the fall of 2014. Table 1 shows the current composition of the colony by species, sex, and age class.

Table 1. Current SMBRR colony census, April 1, 2014

Species	Sex	Infant (<=1)	Juvenile (<=3)	Adult (4+)	Total
S. b. boliviensis	Female	25	74	197	296
	Male	34	45	22	101
	Total	59	119	219	397
S. b. peruviensis	Female	0	0	21	21
	Male	0	0	0	0
	Total	0	0	21	21
S. s. sciureus	Female	16	23	47	86
	Male	17	22	16	55
	Total	33	45	63	141

In order to determine the number of squirrel monkeys, age classes, and sex ratio that can be harvested each year, we use our Colony Demographic and Forecast Model (CDFM) described in the Data Management section below. The CDFM provides a listing of colony harvest information that is then used to make resource management decisions. We are projecting a harvest of 70-80 animals per year for the next five years.

Assumptions on numbers of females becoming pregnant each year are based on historical information with improvements in reproduction included in the projection based upon the average improvement in reproduction achieved over the previous five years.

Table 2 provides a comparison of two reproduction "snapshots" of three-year averages from our previous period of support (2005 to 2007) compared to a three-year average during the current period of support (2011-2013). Because the entire breeding colony was moved Proprietary Info to Texas in 2008-2009, we have not included this period in the comparison depicted in Table 2. **During our current period of support, we have successfully addressed two major aims by increasing pregnancy rates and percentage of live births and decreasing perinatal mortality.** This Table shows that we have made progress toward both of these. Although we are pleased with this progress, we plan to improve reproductive outcomes in the next five years by further reducing perinatal loss through better management of social groups and improved selection of breeding females that have a high probability of reproductive success (see Reproductive Biology and Behavior in the Applied Research Component).

Table 2. Average 3-year reproductive statistics prior to the move from Univ. of South Alabama the move to the KCCMR

		2005-2007	2011-2013
As % of Breeding Females	Pregnancies	65%	73%
As % of Pregnancies	Live Births	76%	90%
	Fetal Mortality	24%	10%
	Neonatal Mortality (<30 days)	22%	10%

Pregnancies as a percentage of breeders have increased from 65% to 73% and perinatal mortality (stillbirths, abortions, and neonatal deaths) has been reduced by more than half. These improvements were the result of multiple management changes that include: moving the breeding colony from the Proprietary Info Proprietary Info into facilities specifically designed for squirrel monkeys at the KCCMR; better perinatal management with our summer nursery intern program, use of ultrasound to better estimate and manage parturition, implementation of C-section intervention based on our experiences with dystocia in squirrel monkeys; and, the use of newly designed breeding pens specifically designed for squirrel monkeys.

Reproductive Performance: Reproductive performance of the SMBRR breeding colony has maintained high rates of production for the past grant period. The percent of breeders that become pregnant each year has risen above 70% since moving the colony into new facilities at the KCCMR. Table 3 shows reproductive performance of the colony over the last full five years. Only partial year information is available for 2014. This improvement in pregnancy rates has been accomplished in part by gradually expanding the intermediate age classes of females within the colony so that the mean age of breeding females falls within the age range considered to be reproductively optimal.

Table 3. Breeding Colony Statistics

	2009	2010	2011	2012	2013	2014	Average
Breeding Females	154	156	174	154	172	116	**154**
Pregnancies	85	103	119	111	135	74#	**105**
Pregnancies / Breeder (%)	55%	66%	68%	72%	78%	64%	**67%**
Live Births / Pregnancy (%)	83%	84%	94%	90%	83%		**87%**
Fetal Wastage / Pregnancies (%)	17%	16%	6%	10%	17%		**13%**

						Totals
Live births (total)	71	86	112	101	113	**483**
Female	40	39	48	61	52	**240**
Male	31	47	64	40	61	**243**
Abortion (total)	10	7	3	7	13	**40**
Female	0	2	0	2	1	**5**
Male	3	3	1	3	5	**15**
Unknown	7	2	2	2	7	**20**
Stillbirth (total)	5	10	4	3	9	**31**

Female	2	5	1	1	6	**15**
Male	3	5	3	2	3	**16**

[#] Examinations to determine the number of pregnant animals is in process. We expect a similar number of pregnancies as in 2013

Resource Use and Leveraging Research Funding: An important measure of the success of the SMBRR is the number of funded projects that have used the resource. Our progress in making resources available to investigators throughout the country is measured in part by the number of investigators receiving animals and tissues/fluids. Table 4 below provides a summary of the animals and biologic samples provided from the resource over the past grant period. A listing of investigators and grants served by the SMBRR is provided as an Appendix. In summary, we have provided investigators from 28 institutions 373 animals and we have satisfied 374 BioBank requests in the last five years (Table 4). During the current period of support, the SMBRR has provided resources to NIH grants totaling more than $10,600,000 based on a recent query of the NIH eReporter database (projectreporter.nih.gov/reporter.cfm). Budgets for the FDA projects, the NIH intramural research program projects, and NSF grants, are not available, so we are not able to determine the total funding of the research programs that have received resources from the SMBRR.

Table 4. Summary of animals provided and BioBank completed from 2009 to April 1, 2014 (See Appendix for a complete listing)

	2009	2010	2011	2012	2013	2014
Animal Sales	55	53	100	77	34	54*
BioBank access Requests	35	8	83	134	77	37*

* First three months of the year only

Although it might be thought that the value of a national breeding and research resource is wholly measured by the number of animals sold or the number of animals used by NIH grantees, there are other, less tangible, resources that are also important. Investigators across the US who need help in designing studies using squirrel monkeys or who need advice on husbandry and/or veterinary medical care of squirrel monkeys contact the SMBRR for help. This is provided through oral and written communication and through the SMBRR website (www.kccmr.org) where our squirrel monkey husbandry and enrichment Standard Operating Procedures are published. Additionally, the SMBRR has provided training to veterinarians seeking careers in laboratory animal medicine, behaviorists seeking to enhance their understanding of the behavioral management of squirrel monkeys, and animal caregivers from other institutions who seek training in the care of squirrel monkeys. Investigators from the SMBRR frequently give presentations on the care and management of squirrel monkeys. Excluded by Requester has presented short courses in Peru in 2011, 2012, and 2013 on squirrel monkey general pathology and husbandry at the University of San Marcos in Lima, Peru. Excluded is currently hosting a veterinarian from Brazil, Excluded by Requester and a veterinary student from the National University of Costa Rica. Excluded by Requester was awarded a postdoctoral fellowship from the Science Without Borders program supported through the government of Brazil. Excluded by Requester will study ways to better predict delivery dates of squirrel monkeys. This information will allow us to better manage parturition and reduce perinatal morbidity and mortality Excluded by Requester is participating as a co-mentor in this project (see Applied Research Component for information regarding Excluded by Requester participation Excluded by Requester will return to Brazil to train veterinarians in techniques learned at the SMBRR. Additional information about the educational contributions of the SMBRR is provided in the Overall Component of this application. All of these activities add value to the scientific community by providing additional knowledge and capability in the care and use of squirrel monkeys in biomedical research.

Letters of support (see Letters of Support in Overall Component) are included from Excluded by Requester

Excluded by Requester

Excluded by Requester **These investigators have each described how the SMBRR has benefitted their research. We urge reviewers to read these letters to develop a better perspective of the valuable role the SMBRR has played and will continue to play in their research.**

As shown in Appendix of Animals and BioBank resources provided, the need for squirrel monkeys and BioBanked specimens continued to be strong over the past five years. During the current period of support, the SMBRR has provided resources to 39 NIH grants and contracts (28 academic institutions), three NIH intramural research programs, 2 NSF grants, numerous research foundations and private research organizations, and the FDA. We anticipate that continued improvements in reproduction and reductions in perinatal deaths will increase the number of squirrel monkeys that can be provided from the SMBRR by two to three percent per year over the next five years.

Genetic Management of the Squirrel Monkey Breeding Colony

The management team of the SMBRR has focused most of its genetic management efforts in the past on maintaining pedigrees and minimizing breeding of related animals. With this renewal, we plan to increase the sophistication of our genetic management to add value to the resources we provide. To help us accomplish this, we have asked Excluded by Requester letter in the Resource Component agreeing to serve as our genetic management consultant. The paragraphs below provide an explanation of our plans for this renewal period.

DNA markers: DNA testing for cases with uncertain or unknown pedigrees of squirrel monkeys within the SMBRR is not necessary. To date, no harems (breeding configuration composed of one breeding male and multiple breeding females) have included more than one adult male that resulted in unknown paternity. Maternity is ascertained by observation of parturition and subsequent maternal nursing, with no observed cases of kidnapping by dominant females. Therefore, there are no outstanding parentage questions that would require use of genetic markers. Regarding Founder DNA typing, there was only one case of a hybrid squirrel monkey born to a female that was pregnant upon acquisition; that occurred many years ago and the hybrid individual was never allowed to breed. Consequently, there are no cases of between-species/subspecies breeding that produced offspring. All squirrel monkeys in the population belong to the Bolivian subspecies, *Saimiri boliviensis boliviensis* or the Guyanese species, *Saimiri sciureus sciureus* with the exception of a very small population of Peruvian squirrel monkeys (*Saimiri boliviensis peruviensis*) that are kept separate and will be gradually phased out of the resource. Necessary analytical work on Founders and descendant pedigrees, including estimation of percent retained genetic variation, will be performed purely by pedigree analysis (see below).

DNA extraction procedures: We will use the DNAeasy Blood & Tissue Kit (Qiagen #69506; 250/$665.00; Valencia, CA) for DNA extraction. Whole blood samples will be drawn from sedated animals according to veterinary care protocols and stored on wet ice until extractions begin, within two hours of draw. DNA extractions will follow manufacturer's protocol. Briefly, 3 ml blood samples will be first lysed with a Proteinase K buffer, then loaded onto DNAeasy mini-spin columns and centrifuged. Following 2 washes to remove contaminants including enzyme inhibitors, the DNA is eluted in 1X TE buffer. The protocol is highly efficient and typically produces yields of 6 mg genomic DNA per 100 ml whole blood. Information on all DNA samples will be logged into a master database (MS-Access) where they can be traced back to specific individuals in colony pedigree records and to specific freezer locations. The DNA samples themselves will be aliquoted into 2.0 ml freezer microtubes with caps (Sarstedt #72.694.007, Nümbrecht Germany), labeled with a waterproof marker, and then stored in -20°C freezers.

Population genetics and pedigree analyses: Our squirrel monkey population database includes pedigree, reproduction, and mortality records on 4890 squirrel monkeys. Currently, there are 559 animals in the breeding resource, including 397 Bolivian squirrel monkeys (*Saimiri boliviensis boliviensis*) composed of 197 male and 22 female breeders; 141 Common squirrel monkeys (*Saimiri sciureus sciureus*) composed of 47 male and 16 female breeders; and 21 Peruvian squirrel monkeys (*Saimiri boliviensis peruviensis*) which are currently being phased out through attrition and sales. The decision to phase out this subspecies was made because we have too few to maintain genetic diversity and there is very little research need for this subspecies. Each species/subspecies is maintained completely separately with no interbreeding. Pedigrees are 6 generations deep, with a mean generation length of 8.7 years. Excluded by Requester has performed all necessary genetic analyses and will use the background demographic data to provide genetic management recommendations. This will include plans to minimize genetic subdivision by transfer of genetically valuable young males among harems, rationally selected harem compositions based on genetic value and minimal inbreeding coefficients, and breeding plans to minimize inbreeding in harems while maximizing genetic heterogeneity. As possible, any genetic marker data will be applied to monitor Gene Diversity. We will focus on Gene Diversity (GD) rather than empirical estimates of Heterozygosity (H)

because, unlike H, GD is directly related to the amount of additive genetic variance for quantitative traits (Falconer and Mackay 1996). Known pedigrees will be used to estimate average kinship coefficients and the number of founder genomes present among the colony offspring (Ely et al. 2005). Strategies based purely on genetic markers will be avoided because they are typically less informative than pedigree-based estimates (Fernandez et al. 2005). Genetic diversity of the colony will be maintained by recruitment of genetically valuable infants, as determined by low mean kinship, into breeding groups. Following previously set standards (Kanthaswamy et al. 2010), we will define values of F from 0 to 0.075 as negligible, 0.076 to 0.15 as moderate, from 0.16 to 0.20 as high, and >0.25 as very high. Animals with moderate or higher levels of inbreeding (kinship coefficients >0.15) will be preferentially culled from their breeding groups and offered for sale. Due predominantly to the large size of the Founder generation (98 males and 380 females), the colony as a whole is genetically diverse. At colony inception, the genetically effective population size as estimated from sex ratio was Ne=312. This large effective size resulted in minimal genetic drift, with the population losing only 0.2% of its genetic variation during production of the F1 generation. The founding generation of females had an average of 3.2 offspring per female Founder, with reasonably narrow variance in reproduction (s^2=5.4). The founding male generation had 16.4 offspring per male Founder, with wide reproductive variance (s^2=348). This was due to the production of >90 offspring by two prolific male Founders in the early growth phase of the population, which left a large genetic footprint on the descendant population composing the F1 generation. Further analysis is needed and will be conducted by estimating the number of founder genomes (Lacy 1989) in the contemporary F6 population and equalizing Founder representation by making the necessary breeding arrangements involving under-represented lineages. Fortunately, the large number (N=478) of Founders originally imported from wild populations in South America represented a broad sample of genetic variation naturally present in wild populations and are still maintained in the current colony. Genetic divergence among corral breeding groups will be monitored by F_{st} statistics and be prevented by transferring at least one young adult male from each harem into its adjacent harem each year. This practice will maximize the genetically effective population size. Through our detailed program of genetic management, the initial genetic variations found among the founder stock will be maintained for many generations into the future.

Pedigrees will be used for genetic and pedigree management, by estimating average kinship coefficients, heterozygosity and gene diversity, and founder genome representation (Ely et al. 2005). Genetic diversity of the colony will be maintained by identification of genetically under-represented animals (low mean kinship) as future breeders, with genetically over-represented animals (kinship coefficients > 0.0625) to be culled for sale. Genetic divergence among breeding groups will be monitored with F_{st} statistics and prevented by equalizing male reproduction and by transferring up to 1 young male per group into adjacent groups each year (Kanthaswamy and Smith, 2002; Kanthaswamy et al., 2010). Our genetic management strategies will continue to maximize effective population size and preserve the high degree of genetic variation among founders for many future generations of captive breeding.

Excluded by [redacted] will perform population genetic analyses with Arlequin (Excoffier and Lischer 2010), and pedigree analyses with Endog (Gutierrez and Goyache 2005) and PMx (Lacy et al. 2012). Any necessary database file transfers to PMx will be performed using mPed (Jansson et al. 2014). Otherwise, the colony database manager and demographer will format database files into the appropriate format readable by other software packages. The overall strategy will be to minimize population subdivision among harems by annual male transfer, maximizing genetic heterogeneity by transferring genetically valuable males, and minimizing inbreeding by culling over-represented animals from the population. Data obtained using these genetic management tools will be compared with data obtained from the pedigree data management system (PEDSYS), developed by Bennett Dyke (1996). We continue to use PEDSYS for management of the colony. Although an older system, PEDSYS provides a quick, easy interface to obtain kinship relationships for potential mating relationships. We have written programs that provide data from the Unified Animal Records System (UARS) (see Data Management section below) in a format PEDSYS can import and process. We will continue to use PEDSYS to help make informed decisions about breeding group formation.

Lineage & PMx: These two programs, PMx (Lacy et al. 2012) and the pedigree visualization tool Lineage (Pollak 2002) are packages developed for Zoos to manage captive populations. Together they provide demographic and genetic analysis tools to assist with breeding programs. PMx calculates demographic parameters. There is a component that makes projections of colony stability and size into the future. The data compliments data generated from the Colony Demographic and Forecast Model (CDFM) (see Data Management section below) and will be used to validate assumptions about colony harvesting and colony growth.

Genetics Workshop: The SMBRR, together with the KCCMR, will also develop and host a workshop on squirrel monkey research and genomics. Users of SMBRR resources during the last 5-year cycle will be

invited to attend the workshop. Attendees will give 15-20 min talks to generically cover their research area(s), and there will also be break-out groups and round-table discussions. Representatives from the Broad Institute (see letter from Excluded by Requester the Human Genome Sequencing Center at the Baylor College of Medicine (see letter from Excluded by Requester will participate and discuss what can be done using squirrel monkey genomics. Emphasis will be placed on relating research applications to genomics to identify areas that could be most powerfully advanced by the availability of genome-wide SNP markers. Information derived from this workshop will be used to inform our future efforts to add value to the SMBRR through applied genomics research. For example, research priorities could be determined from participants' observations, comments and stated preferences regarding which areas could benefit most from genomics-based approaches. Resources necessary for validation of putative SNPs by resequencing could then be given to the highest-ranking priority areas. Another outcome could be development of SNP subsets covering specific genomic regions of interest that are relevant to specific high-priority research applications. For example, one priority for malaria researchers might be identification of a dense subset of SNP markers in and around interleukin and interferon genes potentially related to malaria severity and susceptibility. Excluded by Requester is on the Editorial Board of the Journal of Medical Primatology. Proceedings of the Workshop will be written up for possible publication there.

Squirrel Monkey BioBank

The availability of banked specimens has reduced the need for living animals as tissue and biological fluid donors. The tissue bank contains over 9000 frozen tissues, serum, blood, and other samples. The SMBRR plans to continue to add specimens of tissues and other biological materials to the BioBank that we will make available to NIH grantees. Based on requests over the past two years, we anticipate the need will increase in the next five years.

During the next five years, we plan to consult with the SMBRR External Advisory Board (EAB) to seek advice on what biological samples should be included in the BioBank. BioBank samples are catalogued in the Unified Animal Records System (UARS) database and attached to the animal's record within the database so that experimental and clinical histories and pedigrees can be accessed with a listing of stored biological samples that are available. Also, the SMBRR continues to expand its listing of reagents that can be used in squirrel monkey research. This growing list of reagents is posted on the SMBRR website providing rapid and easy access to scientists searching for reagents known to work in squirrel monkeys.

Dried blood spot (DBS) storage of blood samples:

The SMBRR BioBank continues to expand as more samples are collected. In an effort to find better and less costly ways to provide specimens from the SMBRR BioBank, we plan to explore the feasibility of using DBS. DBS has been used in human medicine primarily in neonatal screens for innate errors of metabolism and more recently for toxicological purposes (Lehmann et al. 2013; Lehner et al. 2013; Sewell et al. 2012). More recently, DBS has been used to measure a variety of clinical analytes, examples include proteins, small organic molecules, small inorganic molecules, nucleic acids and lipids (Lehmann et al. 2013). DBS has also been used to test for prevalence and genetic diversity of SIV viruses in 8 species of African monkeys (Aghokeng et al. 2010), determination of prevalence and genetic diversity of Simian T-lymphotropic viruses in 4 species of African monkeys (Sintasath et al. 2009), and determination of the origin of Plasmodium vivax through analyses of related parasites in wild chimpanzee and gorilla populations (Weimin et al. 2014). The use of DBS for clinical chemistry, toxicology, viral testing, and genetic analyses including DNA and RNA collection is rapidly expanding in human and veterinary medicine. The SMBRR Biobank utilizes formalin storage of tissues, liquid nitrogen storage of some samples, and storage of serum at both -20° C and -80° C. All of these types of storage are costly, require freezers, or liquid nitrogen dewars. As more methods develop using DBS technology, the need for freezers for long-term storage of blood samples may be reduced if DBS can be used. During the next grant period, we plan to split some blood samples and store them using DBS and conventional

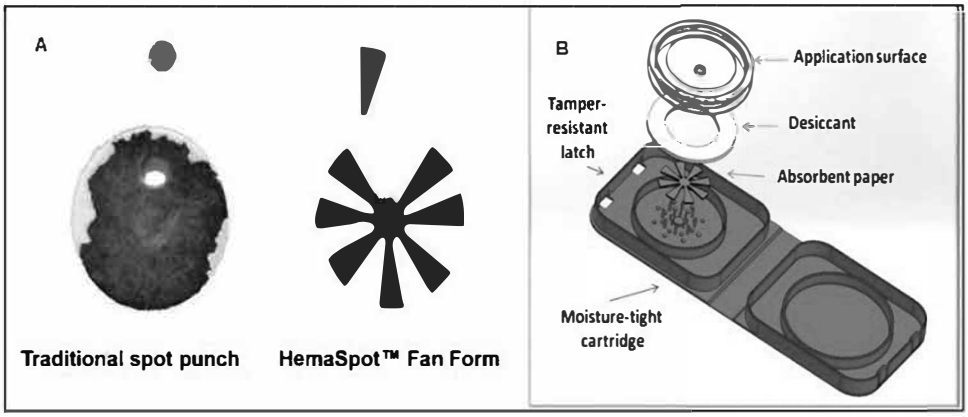

Figure 1. (A) HemaSpot fan form and (B) graphical image of storage device

freezing. Figure 1 above shows the blade design of the HemaSpot™ and a break out display of the storage device. This is a new approach to DBS storage that is especially useful in banking. This technology has been developed by Spot On Sciences (info@SpotOnSciences.com), a biotechnology company located in Austin, TX, approximately 35 miles from the SMBRR. With a single sample of blood applied to the HemaSpot fan, 9 separate samples can be derived (the 8 blades of the fan plus the center spot). Using blades of the Fan Form, multiple analyses will be done and compared. The HemaSpot storage device can store DBSs for years at room temperature. We will consult with Excluded by Requester on ways to validate DBS storage of squirrel monkey blood. Excluded by Requester who is experienced in directing primate diagnostic laboratories, is a member of the SMBRR's External Advisory Board (see EAB below).

Access to Resources:

Access to Resource Materials: From the SMBRR website, there are links for contact information and a PDF form (see Appendix: Animal/Biologics Request Form) that can be used by investigators to request animals or biologics from the resource. This form requests specifics about the needs of the investigator, time requirements, and if the biologic must be collected from animals rather than from the BioBank. The requester is asked to provide a written protocol for collection and transport of the materials to ensure that they are appropriate for their use.

Once a request for animals or biologics is received by the SMBRR, the requirements of the request are compared to available inventory in the BioBank or animal sampling and a decision is made whether the request can be filled. Once this occurs, usually within a day or two, the investigator is notified that the requested resources are available and arrangements are made for shipping or transfer. If the specific items requested are not available, the investigator is notified and given an opportunity to modify his/her request. If there are no suitable animals or biological samples available, the investigator will be placed on a waiting list until an appropriate specimen is available. This could require waiting for an animal to mature to an appropriate age or weight, or waiting until material can be collected during a necropsy. In most cases requests for resources can be met immediately. There have been a small number of requests for animals that exceeded availability. We remain concerned that demand for squirrel monkeys will exceed supply so we continue to search for innovative ways to leverage the number of animals available to meet research needs. This can sometimes be accomplished by using some squirrel monkeys to meet multiple research needs. Drs. Abee, Excluded by Requester work with investigators to determine when this approach is possible.

During the proposed period of support, we will move from the current paper driven animal and BioBank request form to an online ordering process that will streamline the request process and provide investigators with rapid feedback.

Investigator and Student Access: Due to the increasing complexity of conducting research with nonhuman primates, the need for special expertise, the high cost of primates, and difficulties in transporting primates, there is a growing trend toward conducting research within primate resources rather than transporting the animals to the investigator's institution. This trend is very likely to grow as institutions that lack the facilities and expertise opt to conduct their studies at facilities that specialize in the use of nonhuman primates. The SMBRR has recognized this trend and has initiated efforts to provide leadership. The Comparative Medicine Research Building (CMRB), where the SMBRR is housed, has been designed to provide space for visiting scientists/research teams so they can work directly in the SMBRR and associated support spaces. Because Dr. Abee is the PI of the SMBRR, Chair of the Department of Veterinary Sciences, and Director of the KCCMR, he has the authority to provide space to visiting scientists, students, and others so that use of the SMBRR can be made available to NIH grantees and others who wish to conduct research with squirrel monkeys. Using this approach, Excluded by Requester was able to travel to the KCCMR and conduct pilot studies utilizing the veterinary, technical, and animal support staff of the SMBRR (see letter from Excluded by Requester in Letters of Support).

Website: Scientists needing resources and/or information from the SMBRR can rapidly access the SMBRR website (www.smbrr.kccmr.org) with their internet browser. A screenshot of the SMBRR webpage is provided in the Appendix. The website provides access to information about the SMBRR and information about the management and handling of squirrel monkeys. From the website, visitors can access our standard operating procedures for daily husbandry, use of anesthetics, newborn and nursery rearing techniques. Tables showing normal values for serum chemistries, hematology, and body weights are also available. We continue to update a table of reagents that have been proven to cross-react with specific squirrel monkey leukocyte

subsets. The Table, **Reagents that cross-react with squirrel monkey leukocyte subsets** is provided in the Appendix as an example of information available on the SMBRR website.

The SMBRR website has been designed and tagged in such a way as to consistently appear near the top of lists generated by computer searches. Using search terms like "squirrel monkey" with terms such as "resource", "breeding", "husbandry", and "availability", it will return the SMBRR site within the first 5-10 sites reported.

Data and Records Management

Data generated by the SMBRR is captured in a series of databases written and maintained by the Information and Data Services (IDS) at the KCCMR. [Excluded by Requestor] Co-PI of the SMBRR is the faculty supervisor of the IDS. The records system is a comprehensive colony records database that contains unified colony information for all primate species at the KCCMR (squirrel monkey, owl monkey, rhesus, and chimpanzee), using Oracle. The Oracle system provides a wide range of validated behind-the-scenes data management and auditing capabilities.

The KCCMR has developed several databases to manage information about the business and animal records for the primate colonies maintained at the center. Current animal related databases consist of a **Laboratory Information System** (LIS) to manage results from the clinical diagnostic laboratory and the **Unified Animal Records System** (UARS) to manage animal, medical, and inventory records. The LIS is a web-based interface designed to provide the clinical veterinarians with quick, easy access to laboratory results such as hematology, serum chemistry, microbiology, etc. Results from computer interfaced devices in the laboratory, as well as manually entered results, are available real-time to the clinic and office computers of the veterinarians. Because the system is web-based, results are available from any computer or handheld device connected to the center's secure intranet, as well, as offsite through a secured VPN connection.

The **UARS** consists of two sections; **Electronic Medical Records** (EMR) contains annotated medical records and diagnostic laboratory results and the **Animal Management Records** (AMR) contains data on the individual animals, their sex, species, and cage history. The data are organized within a relational database, with information indexed back to the animal's ID. By tagging the data with the date of collection, it is possible to move retrospectively through sets of information to trace an animal's clinical and experimental treatments. This method is powerful both from a clinical approach, where it is necessary to trace an animal across several data fields, and from an experimental approach, where data from many animals can be drawn together for analysis.

The **EMR** are organized around the procedures done to the animal and panels of information collected. Procedures, such as sample collection, ultrasounds, etc, are entered as they are done. Procedures can be broken down into those in which something happened to the animal, such as administration of a treatment or medication, and those that have results associated with them, such as measurement of the bi-parietal diameter of a fetus during ultrasound. Procedures can also be scheduled, generating a calendar of upcoming events for the care staff. For example, a list of veterinary treatments for all animals requiring veterinary care can be generated. Similarly, experimental procedures can be scheduled in the same way. Panels consisting of groups of procedures with results can be grouped for data collection and presentation. Examples of a panel are animal physicals, which consist of groups of procedures typically done during a routine physical examination.

The **AMR** includes records of all squirrel monkeys that have been part of the SMBRR. These records include the basic, static information about individuals (e.g., birthdate, sex, sire, dam, etc.), as well as dynamic information such as current location, social group, and reproductive status. Historical records of dynamic information are available making it possible to trace changes in status and location over time.

During the next five years, we will continue to update the data systems at the KCCMR that are used to support the SMBRR as new reporting and data collection requirements are added. In order to facilitate data availability, we will integrate portable computer tablets and smart phones with the database using the KCCMR center-wide wireless network. This will provide care staff and investigators with immediate access to animal records at all times regardless of their location. **The UARS contains the life records of all the animals that have been acquired by or born into the SMBRR; currently 4,890 squirrel monkeys**. These records provide the opportunity to conduct various retrospective studies of the squirrel monkey population.

We have integrated our **Colony Demographic Model** and **Colony Forecast Model** into a single spreadsheet called the **Colony Demographic and Forecast Model (CDFM).** The CDM and CFM were developed by the SMBRR and were described in previous competing renewal applications. The CDFM generates reproductive summary information from population census data. We have developed a stochastic forecast model and validated it against actual historical demographic statistics from the squirrel monkey colony (Akkoc and Williams 2005). The goal for the next five years is to move CDFM from spreadsheets to a compiled program. We will use Visual Basic to write the program that will utilize the Oracle platform. This will

allow us to better secure the program against accidental modifications, to provide a better user interface, and to provide for additional computations not possible within a spreadsheet model.

Center Support Structure

The same management team has led the SMBRR for many years. Dr. Abee, the PI, works closely with Excluded by Requester Co-PI, and Excluded by Requester Co-Investigator, Excluded by Requester Research Assistant, Excluded by Requester the Animal Resources Team Leader, and Excluded by Requester Colony Manager of the SMBRR. Dr. Abee is responsible for coordinating the overall mission of the SMBRR Excluded by Requester responsible for veterinary care. There are four additional clinical veterinarians who support Excluded by Requester as necessary. Excluded by Requester has been a part of the SMBRR leadership since 1982. He provides direct supervision of Excluded by Requester the Research Assistant Excluded by Requester coordinates and prepares research protocols within the SMBRR. works out the logistics of shipping animals and BioBank materials, and assists with research projects Excluded by Requester also supervises the animal records databases used in support of the SMBRR, and he works directly with investigators in other institutions who need to access resources or carry out studies at the SMBRR. Excluded by Requester directs environmental enrichment and behavioral management for the SMBRR Excluded by Requester AALAS certified Laboratory Animal Technologist, supervises Excluded by Requester who supervises the team of animal care technicians that work in the squirrel monkey breeding colony.

Timelines for achieving milestones, whether they relate to the Applied Research Component or Resource Component of the SMBRR, are discussed on a continuing basis by the management team consisting of those named above, and every four months with the External Advisory Board (EAB). The EAB functions include one meeting on-site and two teleconference meetings per year. During these meetings, we discuss progress toward meeting specific aims and we review resources provided, and progress in the Applied Research projects.

The coordination and integration of SMBRR activities is carried out by Excluded by Requester on a day-to-day basis, with support from Dr. Abee when departmental/institutional resources are needed. Dr. Abee and Excluded by Requester communicate daily on SMBRR matters. Dr. Abee, with support from Excluded by Requester and consultation of the EAB, is responsible for ensuring appropriate prioritization of activities and overall direction of the SMBRR.

SMBRR Financial Status

The table below lists program income for the period 2010-2014.

2010	2011	2012	2013	2014*	Total
$125,700	$225,750	$210,381	$40,250	$66,170	$668,251

*Partial year of program income from first three months (Jan-April 1, 2014)

Program income shown above for 2014 reflects only a partial year. Based on commitments from users of the SMBRR, we anticipate that program income will exceed $120,000 by the end of 2014 bringing the total projected program income for the 5-year period to more than $700,000. Program income has increased substantially over the years reflecting increasing demand for SMBRR resources. Program income in 2011 and 2012 was substantially larger than in 2010 in part because restructuring of the breeding colony allowed us to sell more squirrel monkeys in those years. We anticipate that we will be able to sell 70 animals in the first year of this proposed grant cycle. The table below shows projected program income during the proposed period of support.

Projected Program Income based on the number of animals to be provided by the SMBRR in coming years:

	GY 35	GY 36	GY 37	GY 38	GY 39
# of animals provided by SMBRR	70	73	77	81	85
Price per animal	2,460	2,583	2,712	2,848	2,990
	$172,200	$188,559	$208,824	$230,688	$254,150

We plan to increase the sale price for squirrel monkeys by approximately 5% each year and we project that the number of squirrel monkeys that can be harvested from the colony will increase by 4-5% per year. In this projection, we use only projected sales of squirrel monkeys to estimate program income because the amount of program income from the BioBank is more difficult to predict in future years.

Based on the above projection, program income is anticipated to increase from approximately $700,000 for the current period of support (2010-2015) to $1,054,421 (2015 to 2020). This represents a projected increase in program income of approximately 50% compared to the current 5-year period of support. During the current period of support, **program income has been used to offset costs that have substantially exceeded the amount awarded in the P40 grant.** We anticipate that we will continue to need program income to offset that portion of the cost of the SMBRR that is not supported by the P40 grant. The **Letters of Support** included in the Overall Component of this application provide evidence that the need for SMBRR resources will remain strong. A number of these letters include estimates of the number of squirrel monkeys that will be needed by that investigator. It is important to note that the P40 grant budget remains flat for the next five years based on budget instructions from NIH. This means that inflationary increases in the cost to operate the SMBRR must come from program income and institutional support. This will result in the P40 grant providing a lower percentage of total operating cost in each succeeding year.

In the current year, institutional support will total approximately $60,000 (see table below). This support is the result of the KCCMR paying the difference between the actual squirrel monkey *per diem* cost versus the amount paid by the P40 grant. Administrative budget reductions made by NIH during the current period of support have substantially reduced annual budgets necessitating that no increases in squirrel monkey *per diem* be charged to the grant even though the cost of care has increased. Program Income is used to pay animal *per diems* for the number of animals in the breeding colony that exceed the number of animals that is actually budgeted in the grant. For example, we have budgeted in this application for 350 squirrel monkeys, but the size of the breeding colony varies between 500 and 575 animals each year. The difference between the budgeted number of squirrel monkeys and the actual number in the colony is paid using Program Income and the difference between the per diem charged and the actual per diem cost is paid using institutional support. NIH permits us to budget a 5% increase in total direct cost in this competing renewal. This increase will be used to adjust the *per diem* price charged for squirrel monkeys so that the P40 grant pays a greater percentage of the actual cost of care. This will allow us to direct institutional support toward paying for the studies in the Applied Research Component, consulting costs Excluded by Requestor and the cost of the External Advisory Board (EAB). The NIH has mandated that the budget of this competing renewal not increase from one year to the next. This will necessitate increases in program income in each succeeding year to absorb the increased cost of annual salary increases and inflation. Based on a review of the increasing cost in past years, we anticipate that the actual cost of operations in the SMBRR will increase by about 4% per year. The table below shows all sources of support for the SMBRR.

SMBRR Current and Projected Funding:

	Current Support GY 34	GY 35	GY 36	GY 37	GY 38	GY 39
P40 OD010938	$482,810	$506,033	$506,033	$506,033	$506,033	$506,033
P40 Program Income*	$139,038	$172,200	$188,559	$208,824	$230,688	$254,150
Institutional Support**	$60,043	$30,000	$30,000	$30,000	$30,000	$30,000
Total Funding for SMBRR	$682,251	$708,233	$724,592	$744,857	$766,721	$790,183

*Grant-Related Program Income is derived from sales of animals. It is anticipated that NIH's administrative reductions to the current budget will require all Program Income to pay *per diems* for those animals that exceed the number of animals in the grant budget.

**Institutional support will be provided from endowment income from Dr. Abee's endowed professorship. Endowment income of $30,000 per year will be used to support the proposed projects in the Applied Research Component and the costs associated with the External Advisory Committee (EAB).

Progress toward self-sufficiency can be seen in our projections (above). The substantial budget reductions mandated by NIH during the current funding period have required that a greater and greater percentage of the total cost of the SMBRR be paid from other sources. These sources have been, and will continue to be, Program Income and Institutional Support. In the current year (GY 34) the P40 grant will provide about 71% of the total direct cost of the SMBRR. Although the amount provided by the P40 grant will remain the same in GY35-39, increases in program income will result in the P40 grant paying a smaller percentage of the total

direct cost in each succeeding year. It is projected that the P40 grant will provide 64% of total direct cost in GY39.

SMBRR External Advisory Board (EAB)

The EAB is composed of highly experienced leaders in their fields. Excluded by Requester will serve as chair of the EAB. The EAB will meet at the KCCMR/SMBRR for a one-day site visit each year. In addition, there will be two teleconference meetings each year. Therefore, the EAB will meet either in person or by teleconference three times per year. The EAB will review and advise on applied research and management activities, provide perspective on the national research needs that can/should be met by the SMBRR, and advise the PI (Dr. Abee) and Co-PI Excluded by Requester regarding priorities based on funding limitations. All four members of the EAB have experience with Neotropical primates and other experiences that are relevant to the SMBRR. It is anticipated that the meetings of the EAB will cost approximately $8,000 per year. Dr. Abee will use institutional funds from an endowment to cover the cost of the EAB. Additional information about the members of the EAB is provided in the following paragraphs. Letters from Excluded by Requester agreeing to serve on the EAB are provided in the Letters of Support section in this Resource Core.

Excluded by Requester

Excluded by Requester

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Resource Component Concluding Comments:

This application can only provide limited details regarding many of the methods that have been developed over the years to manage this national research resource. Therefore, we have provided information about performance of the SMBRR over the past five years, and we have provided projections of resources that will be provided in the next five years. The SMBRR has a highly experienced management team that has worked together for many years, and we have assembled a highly experienced EAB to advise us. The reproductive performance of the breeding colony continues to improve. We anticipate that these breeding colony improvements will allow us to continue to increase the number of squirrel monkeys available to the research community. We continue to search for ways to add value to the resources that the SMBRR provides by using what is learned from our applied research projects, through our educational activities, and through outreach to the scientific community. Our educational efforts continue to provide training experiences to professionals who work with squirrel monkeys, and our outreach to scientists continues through our participation in workshops and presentations at scientific meetings on the use of squirrel monkeys in research. We are especially enthusiastic about our plans to provide leadership in squirrel monkey genomics. Our collaborations with the Proprietary Info (See Letters agreeing to collaborate from Excluded by Requester in the Applied Research Component) will help expand our understanding of the squirrel monkey genome. And, our plans to organize and host a squirrel monkey genomics workshop will inform the scientific community of the value of squirrel monkeys and help us continue to refine the resources provided by the SMBRR. For these reasons, we believe the SMBRR is positioned to make new and important contributions to the biomedical research community and to human health.

VERTEBRATE ANIMALS

All procedures involving squirrel monkeys will be carried out at the Michale E. Keeling Center for Comparative Medicine and Research (KCCMR) of the University of Texas M. D. Anderson Cancer Center (UTMDACC) in Bastrop, Texas. The Squirrel Monkey Breeding and Research Resource (SMBRR) is a national research resource of three squirrel monkey species, *Saimiri boliviensis boliviensis*, *Saimiri sciureus sciureus*, and *Saimiri boliviensis peruviensis*. Because this project involves maintaining a breeding colony of squirrel monkeys, all ages and both sexes of squirrel monkeys will be maintained in the project. The KCCMR is AAALAC accredited and has a PHS Assurance on file with the Office for Laboratory Animal Welfare (OLAW).

Proposed Animal Use: The SMBRR currently maintains 509 squirrel monkeys of the three species listed above. Most of these animals are in a breeding colony that serves as a national research resource of this genus available to NIH grantees that need squirrel monkeys for their research. All animals provided from the SMBRR are provided to institutions with PHS assurances and there must be an approved IACUC protocol for the animals requested from the SMBRR. The SMBRR also carries out studies designed to provide new information about the natural biology of squirrel monkeys with an emphasis on studies of natural social behavior, diseases of squirrel monkeys that resemble human diseases, and studies to better understand the immunology of the squirrel monkey.

The squirrel monkey colony consists of both males and females. Squirrel monkeys range in age from newborn to more than 20 years.

The UTMDACC Institutional Animal Care and Use Committee (IACUC) meets monthly to review proposed research protocols and to assure that the guidelines put forth by the PHS Policy on Humane Care and Use of Laboratory Animals and NIH *Guide* are followed; facilities and programs are evaluated by the IACUC every six months. This Institution has an Animal Welfare Assurance on file with the NIH Office of Laboratory Animal Welfare (ref. A-3343-01) and is a USDA-registered research facility.

Justification for the Use of Squirrel Monkeys: The procedures performed on the three species of animals described in this application will occur as part of normal operations to address medical and management problems and research approved by the IACUC. The justification for the number of animals described is that they equal the total number of animals maintained in each colony, all of which require medical care and oversight. The species chosen reflect the most commonly used squirrel monkeys in biomedical research.

Veterinary Care: All of the veterinarians at the KCCMR have extensive experience in the clinical care and biomedical research use of nonhuman primates Excluded by Requester each have more than 20 years experience working with squirrel monkeys. The technical and husbandry staff receives regular training and approximately 80% of the KCCMR husbandry staff is AALAS certified. Daily observations and regularly scheduled physical examinations are important in preventive medicine and in detecting early, subtle signs of disease. Colony staff and supervisors view all colony animals during observations at least twice daily. An established and well-integrated Behavioral Management and Enrichment program is directed by Excluded by Requester Excluded by Requester a primate behaviorist with more than 25 years experience with squirrel monkeys.

Guidelines for Minimizing Discomfort, Pain or Distress: All non-painful procedures in squirrel monkeys are carried out with gentle manual restraint or with sedation using Ketamine HCl administered by experienced staff. General anesthesia for painful procedures is provided using injectable ketamine & xylazine, or isoflurane inhalation anesthesia that is induced by mask under manual restraint.

Anesthetic Monitoring and Recovery: During routine short anesthesia periods when ketamine and xylazine are used as the anesthetic agents, the animal's condition is monitored by close observation of its breathing pattern and the color of its mucus membranes, and auscultation of its heart and lung sounds. Major surgery requires use of an inhalation agent and may include continuous monitoring of blood pressure, electrocardiogram, anesthetic agent, oxygen saturation and other parameters. During the recovery period, animals are placed in a lateral position to allow drainage and prevent aspiration of secretions, and they are periodically observed until they are able to maintain a sitting posture.

Analgesia: A variety of oral and injectable analgesics, ranging in strength from nonprescription analgesics to potent narcotics, are available at the discretion of the clinical veterinarian. Buprenorphine is the most frequently used analgesic. In evaluating the need of analgesics, the guidelines from PHS policy "Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Education" are followed (Interagency Research Animal Committee, 1985). Specifically, "Unless the contrary is established, investigators should consider that procedures that cause pain or distress in human beings may cause pain or distress in other animals." In addition, close monitoring, coupled with knowledge of the normal behavior of the individual animal, is used to detect subtle signs of discomfort that indicate a need for analgesia.

Euthanasia Policy: Euthanasia is administered for humane reasons based upon the decision of the attending veterinarian. Methods of euthanasia are in compliance with the AVMA Guidelines for Euthanasia of Animals 2013 Edition Version 2013.0.1 (www.avma.org). Euthanasia, in instances when it becomes necessary, is carried out using an overdose of barbiturate administered intravenously.

References – Resource Core

Excluded by Requester

LETTERS AGREEING TO PARTICIPATE – Genetic Consultant and External Advisory Board (EAB)

Excluded by Requester

Excluded by Requester

Excluded by Requester

Excluded by Requester

Excluded by Requester

Excluded by Requester

OMB Number: 4040-0001
Expiration Date: 06/30/2016

APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

5. APPLICANT INFORMATION **Organizational DUNS*:** 8007721390000

Legal Name*: The University of Texas MD Anderson Cancer Center
Department:
Division:
Street1*: 1515 HOLCOMBE BLVD
Street2: Unit 1676
City*: HOUSTON
County:
State*: TX: Texas
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 770304009

Person to be contacted on matters involving this application

Prefix:	First Name*:	Middle Name:	Last Name*:	Suffix:
	Renee		Gonzales	

Position/Title: Executive Director, Sponsored Programs
Street1*: The University of Texas MD Anderson Cancer Center
Street2: 1515 Holcombe Blvd, Unit 1676
City*: Houston
County:
State*: TX: Texas
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 770304009
Phone Number*: 713-792-3220 Fax Number: 713-794-4535 Email: osp@mdanderson.org

7. TYPE OF APPLICANT* H: Public/State Controlled Institution of Higher Education

Other (Specify):
Small Business Organization Type ❍ Women Owned ❍ Socially and Economically Disadvantaged

11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT*
Squirrel Monkey Breeding and Research Resource: Applied Research

12. PROPOSED PROJECT

Start Date*	Ending Date*
04/01/2015	03/31/2020

OMB Number: 4040-0010
Expiration Date: 06/30/2016

Project/Performance Site Location(s)

Project/Performance Site Primary Location

● I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	The University of Texas MD Anderson Cancer Center
Duns Number:	8007721390000
Street1*:	Michale E. Keeling Center for Comp Med and Research
Street2:	650 Cool Water Drive
City*:	Bastrop
County:	
State*:	TX: Texas
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	786026621
Project/Performance Site Congressional District*:	TX-009

File Name

Additional Location(s)

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* ○ **Yes** ● **No**

1.a. If YES to Human Subjects

Is the Project Exempt from Federal regulations? ○ Yes ○ No

If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6

If NO, is the IRB review Pending? ○ **Yes** ○ **No**

IRB Approval Date:

Human Subject Assurance Number

2. Are Vertebrate Animals Used?* ● **Yes** ○ **No**

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ○ Yes ○ No

IACUC Approval Date:

Animal Welfare Assurance Number

3. Is proprietary/privileged information included in the application?* ○ **Yes** ● **No**

4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* ○ **Yes** ● **No**

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ○ Yes ○ No

4.d. If yes, please explain:

5. Is the research performance site designated, or eligible to be designated, as a historic place?* ○ **Yes** ● **No**

5.a. If yes, please explain:

6. Does this project involve activities outside the United States or partnership with international collaborators?* ○ **Yes** ● **No**

6.a. If yes, identify countries:

6.b. Optional Explanation:

	Filename
7. Project Summary/Abstract*	F_APPLIED_RESEARCH_Project_Summary_Abstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	F_APPLIED_RESEARCH_References.pdf
10.Facilities & Other Resources	
11.Equipment	

APPLIED RESEARCH PROJECT SUMMARY

The Squirrel Monkey Breeding and Research Resource (SMBRR), P40 OD010938 has received continuous NIH grant support since 1980. The SMBRR's proposed applied research projects include continuations of resource-related research projects in Reproductive Biology, Behavior, and Immunology from the current and previous periods of support while the Applied Genomics Research proposed in this application represents a new direction for the SMBRR. The Reproductive Biology Research project will extend studies currently underway to better understand the cause(s) of Pelvic Organ Prolapse (POP) in squirrel monkeys and in women. The squirrel monkey model of POP closely resembles the disease of women. This project will provide insights into the disease of women, and will also provide new procedures and management approaches that can be used to improve reproductive success in squirrel monkeys. This project will lead to better management of parturition and perinatal care of squirrel monkey infants. The Immunology Research proposed will continue work that was published in 2013 [Excluded by Requester] This project will provide insights into the similarities and differences in squirrel monkey immune cells compared to those of human beings. Additionally, these studies will identify new reagents that cross react with squirrel monkey lymphocyte subsets and adjuvants that can be used to deliver vaccines. The Behavior Research will focus on how squirrel monkeys use space within captive housing and provide insights into social activity in relation to reproductive season. The Applied Genomics Research will focus on basic genome sequencing and subsequent SNP identification in squirrel monkeys. This information will allow investigators using the squirrel monkeys from the SMBRR to identify specific animals that will more closely model particular human diseases by identifying relevant SNPs and other genome sequence information. All of the studies proposed in the Applied Research Component pursue scientific questions about squirrel monkey biology and behavior that will allow us to enhance the value of the resources provided by the SMBRR.

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Prefix: Dr. First Name*: Christian Middle Name R Last Name*: Abee Suffix:

Position/Title*: Professor and Chair
Organization Name*: The University of Texas MD Anderson Cancer Center
Department: Dept of Veterinary Sciences
Division:
Street1*: Michale E. Keeling Center for Comp Med and Research
Street2: 650 Cool Water Drive
City*: Bastrop
County:
State*: TX: Texas
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 786026621

Phone Number*: 512-321-3991 Fax Number: 512-332-5208 E-Mail*: cabee@mdanderson.org

Credential, e.g., agency login: eRA Commons User Name

Project Role*: Other (Specify) Other Project Role Category: Project Lead

Degree Type: Degree Year:

File Name

Attach Biographical Sketch*:

Attach Current & Pending Support:

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 8007721390000

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2015 **End Date*:** 03-31-2016 **Budget Period: 1**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Co-PI	Institutional Base Salary	EFFORT			7,042.00	1,972.00	9,014.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **9,014.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Asst	EFFORT			7,201.00	2,016.00	9,217.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**9,217.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**18,231.00**

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

Funding Opportunity Number: PAR-14-005. Received Date: 2014-05-29T15:39:24.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 8007721390000
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2015 **End Date*:** 03-31-2016 **Budget Period: 1**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 8007721390000
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2015 **End Date*:** 03-31-2016 **Budget Period: 1**

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

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**18,231.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. F & A	60.0	0.00	10,939.00
		Total Indirect Costs	**10,939.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): DHHS, Arif Karim, 415-437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**29,170.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 8007721390000

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2016 **End Date*:** 03-31-2017 **Budget Period: 2**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Co-PI	Institutional Base Salary	EFFORT			7,042.00	1,972.00	9,014.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **9,014.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Asst	EFFORT			7,201.00	2,016.00	9,217.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**9,217.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**18,231.00**

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

Funding Opportunity Number: PAR-14-005. Received Date: 2014-05-29T15:39:24.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 8007721390000
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2016 **End Date*:** 03-31-2017 **Budget Period: 2**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 8007721390000
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2016 **End Date*:** 03-31-2017 **Budget Period: 2**

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

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**18,231.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. F & A	60.0	0.00	10,939.00
		Total Indirect Costs	**10,939.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): DHHS, Arif Karim, 415-437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**29,170.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 8007721390000

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2017 **End Date*:** 03-31-2018 **Budget Period: 3**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Co-PI	Institutional Base Salary	EFFORT			7,042.00	1,972.00	9,014.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **9,014.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Asst	EFFORT			7,201.00	2,016.00	9,217.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**9,217.00**

Total Salary, Wages and Fringe Benefits (A+B) **18,231.00**

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

Funding Opportunity Number: PAR-14-005. Received Date: 2014-05-29T15:39:24.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 8007721390000
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2017 **End Date*:** 03-31-2018 **Budget Period: 3**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 8007721390000
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2017 **End Date*:** 03-31-2018 **Budget Period: 3**

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

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**18,231.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. F & A	60.0	0.00	10,939.00
		Total Indirect Costs	**10,939.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): DHHS, Arif Karim, 415-437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**29,170.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 8007721390000

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2018 **End Date*:** 03-31-2019 **Budget Period: 4**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Co-PI	Institutional Base Salary	EFFORT			7,042.00	1,972.00	9,014.00

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

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **9,014.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Asst	EFFORT			7,201.00	2,016.00	9,217.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**9,217.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**18,231.00**

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

Funding Opportunity Number: PAR-14-005. Received Date: 2014-05-29T15:39:24.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 8007721390000
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2018 **End Date*:** 03-31-2019 **Budget Period: 4**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

Tracking Number: GRANT11658537
Funding Opportunity Number: PAR-14-005. Received Date: 2014-05-29T15:39:24.000-04:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 8007721390000
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2018 **End Date*:** 03-31-2019 **Budget Period: 4**

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

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**18,231.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. F & A	60.0	0.00	10,939.00
		Total Indirect Costs	**10,939.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): DHHS, Arif Karim, 415-437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**29,170.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 8007721390000

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2019 **End Date*:** 03-31-2020 **Budget Period:** 5

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Co-PI	Institutional Base Salary	EFFORT			7,042.00	1,972.00	9,014.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **9,014.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Asst	EFFORT			7,201.00	2,016.00	9,217.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**9,217.00**

Total Salary, Wages and Fringe Benefits (A+B) **18,231.00**

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

Funding Opportunity Number: PAR-14-005. Received Date: 2014-05-29T15:39:24.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 8007721390000
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2019 **End Date*:** 03-31-2020 **Budget Period: 5**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 8007721390000
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: The University of Texas MD Anderson Cancer Center

Start Date*: 04-01-2019 **End Date*:** 03-31-2020 **Budget Period: 5**

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

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**18,231.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. F & A	60.0	0.00	10,939.00
		Total Indirect Costs	**10,939.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): DHHS, Arif Karim, 415-437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**29,170.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

BUDGET JUSTIFICATION: APPLIED RESEARCH COMPONENT

Partial salaries for Excluded by Requester the Co-PI EFFORT and Excluded by Requester a Research Assistant EFFORT are requested to support the studies proposed in the Applied Research Component. Excluded by Requester will be responsible for working directly with Excluded by Requester to develop research protocols, coordinate research projects, schedule procedures, and train staff to carry out these studies. All other funding for these studies will come from institutional sources including Dr. Abee's endowed professorship, departmental funds available to Excluded by Requester and shared funding from other departmental sources.

Personnel – Applied Research Component*

	GY 35	GY 36	GY 37	GY 38	GY 39
Professional Personnel					
Abee, C.R., PI (Project Lead)	-	-	-	-	-
Excluded by Requester Ph.D., Co-PI	9,217	7,832	8,067	8,309	8,558
Excluded by Requester Ph.D. Consultant	-	-	-	-	-
Excluded by Requester Ph.D., Other Significant Contributor	-	-	-	-	-
Excluded by Requester ., Ph.D., Other Significant Contributor	-	-	-	-	-
Excluded by Requester Research Assistant I	9,014	9,014	9,014	9,014	9,014
Total Salaries/Fringe Benefits	$18,231	$18,231	$18,231	$18,231	$18,231

*** Although it is anticipated that salaries will increase annually, NIH Fiscal Policy does not allow inflationary increases to be included in this budget.**

Christian R. Abee, D.V.M., DACLAM, (no calendar mos.), provides overall direction of the Applied Research Component. He will be responsible for allocating resources necessary to carry out the proposed studies. Dr. Abee will work closely with each of the Lead Investigators of the Applied Research projects.

Excluded by Requester

Excluded by Requester

Consultant - Applied Research Component

Excluded by Requester

All other costs for studies in the Applied Research Component beyond the Personnel costs requested above will be paid from institutional funds.

Other Significant Contributors – Applied Research Component

No support is requested in the budget for **Other Significant Contributors**. They are listed here to provide a description of the roles of these individuals within the Applied Research Component. The following investigators will serve as Other Significant Contributors. BioSketches are included.

Excluded by Requester

Excluded by Requester

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals ($)	
Section A, Senior/Key Person		**45,070.00**
Section B, Other Personnel		**46,085.00**
Total Number Other Personnel	5	
Total Salary, Wages and Fringe Benefits (A+B)		**91,155.00**
Section C, Equipment		**0.00**
Section D, Travel		**0.00**
1. Domestic	0.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		**0.00**
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		**0.00**
1. Materials and Supplies	0.00	
2. Publication Costs	0.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	0.00	
9. Other 2	0.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		**91,155.00**
Section H, Indirect Costs		**54,695.00**
Section I, Total Direct and Indirect Costs (G + H)		**145,850.00**
Section J, Fee		**0.00**

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix: Dr.
First Name*: Christian
Middle Name: R
Last Name*: Abee
Suffix:

2. Human Subjects

Clinical Trial? ● No ○ Yes
Agency-Defined Phase III Clinical Trial?* ○ No ○ Yes

3. Permission Statement*

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

● Yes ○ No

4. Program Income*

Is program income anticipated during the periods for which the grant support is requested? ○ Yes ● No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount ($)*	Source(s)*

PHS 398 Cover Page Supplement

5. Human Embryonic Stem Cells

Does the proposed project involve human embryonic stem cells?* ● No ○ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ❑ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)

Inventions and Patents*: ○ Yes ● No

If the answer is "Yes" then please answer the following:

Previously Reported*: ○ Yes ○ No

7. Change of Investigator / Change of Institution Questions

❑ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

❑ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application (for RESUBMISSION or REVISION only)	
2. Specific Aims	F_APPLIED_RESEARCH_Specific_Aims.pdf
3. Research Strategy*	F_APPLIED_RESEARCH_Research_Strategy.pdf
4. Progress Report Publication List	
Human Subjects Sections	
5. Protection of Human Subjects	
6. Inclusion of Women and Minorities	
7. Inclusion of Children	
Other Research Plan Sections	
8. Vertebrate Animals	F_VERTEBRATE_ANIMALS.pdf
9. Select Agent Research	
10. Multiple PD/PI Leadership Plan	
11. Consortium/Contractual Arrangements	
12. Letters of Support	F_RESEARCH_Letters_of_Support.pdf
13. Resource Sharing Plan(s)	
Appendix (if applicable)	
14. Appendix	

Applied Research Component

The proposed Applied Research Component includes resource-related studies in Reproductive Biology, Behavior, and Immunology that are continuations of lines of investigation that have been pursued from the current and previous periods of support. The Applied Genomics Research proposed in this application represents a new direction for the SMBRR. Historically, genetic management in the SMBRR has focused entirely on breeding colony management concentrated on breeding pedigree analysis. That work will continue as described in the Resource Component while genomics research proposed here will focus on basic genome sequencing and subsequent SNP identification of genomic sequences of animals within the SMBRR. This information will allow investigators using the squirrel monkey model to identify specific animals that will more closely model particular human diseases by identifying relevant SNPs and other genome sequence information. All of the studies proposed in the Applied Research Component pursue scientific questions about squirrel monkey biology and behavior that will allow us to enhance the value of the resources provided by the SMBRR.

Specific Aims

Reproductive Biology Research: Excluded by Requester Ph.D. Lead Investigator)

1. Determine and describe cause(s) and potential preventive treatments on Pelvic Organ Prolapse in squirrel monkeys using serial MRI for three successive pregnancies by:
   a. Comparing effects of vaginal delivery to elective c-section on pelvic floor striated muscles
   b. Comparing mode of delivery on anatomic position endpoints in animals related to delivery route
   c. Using serial MRI to follow three successive pregnancies to measure the effect of successive obstetrical challenges
   d. Testing tools developed in this study to reduce dystocias leading to stillbirth and obstetrical injury in breeding females to improve production of healthy squirrel monkeys for research

Applied Genomics Research: Excluded by Requester Ph.D. and Excluded by Requester Ph.D. Co-Lead Investigators)

1. Identify novel genome-wide SNPs by whole genome sequencing of 6-8 squirrel monkeys from the resource colony and alignment to the reference sequence
2. Assign specific chromosomal locations to new SNPs by anchoring the existing scaffolding of the reference sequence.
3. Validate candidates SNPs by re-sequencing or real-time PCR.

Behavior Research Excluded by Requester Ph.D. Lead Investigator)

1. Determine how squirrel monkeys housed at KCCMR use their available three-dimensional space.
2. Compare cage use and social activity during all phases of the reproductive cycle.
3. Investigate longitudinal changes in social group activity

Immunology Research Excluded by Requester Ph.D. Lead Investigator)

1. Identify new cross reactive molecular and immunological research reagents for squirrel monkeys cells
2. Investigate specific cells such as Dendritic cells (DC), NK (Natural killer cells and NKT (Natural killer T cells) to further support the value of squirrel monkeys as an animal model for human studies
3. Test adjuvants such as α-alphagalactosylceramide, and CpG for vaccine delivery in squirrel monkeys.

Applied Research Component: Research Strategy

The applied research projects proposed in Reproductive Biology, Behavior, and Immunology described below are continuations of lines of investigation that have been pursued from the current and previous periods of support. The Applied Genomics Research proposed in this application represents a new direction for the SMBRR. Historically, genetic management in the SMBRR has focused on breeding colony management techniques including pedigree identification and avoidance of inbreeding. That work will continue in the Resource Component while genomics research proposed here will provide more in depth genome sequencing and subsequent SNP identification. This information will allow investigators to identify specific animals that will more closely model particular human diseases by identifying SNPs and other genome sequence information relevant to the disease being studied. All of the studies proposed in the Applied Research Component pursue scientific questions about squirrel monkey biology and behavior that will allow us to enhance the value of the resources provided by the SMBRR.

Reproductive Biology: Squirrel monkey Pelvic Organ Prolapse Excluded by Requester **Lead Investigator)**

Pelvic organ prolapse (POP) is a serious disorder of middle-aged and older women who have experienced one or more vaginal deliveries during their childbearing years. POP can lead to urinary incontinence, infections and chronic pain. In studies carried out in the SMBRR, multiparous squirrel monkeys were found to develop this same disorder. Studies of POP in squirrel monkeys have provided the opportunity to test hypotheses regarding the cause(s) of POP in women and have provided information leading to improvements in the management of the SMBRR breeding colony. Squirrel monkeys are thought to be at high risk of POP due to the very large size of term fetuses in this species.

During the current grant period, tools (ultrasound-based calculator for gestational age and obstetrical course) and procedures (elective C-section with subsequent newborn management practices) were developed and a preventive trial for Pelvic Organ Prolapse (POP) in squirrel monkeys was initiated. In a pilot study, preceding the current resource-related research, MRI results were obtained from seven animals with intact levator ani (LA) nerves Excluded by Requester Significant changes in bladder support, immediate post-partum accumulation of contrast, and coccygeus (COC) muscle volume changes were noted after the first pregnancy, so that the need for an additional intervention to transect the levator ani nerves was deemed unnecessary.

This study was redesigned to follow two groups of 10 females, each for three successive pregnancies. Sixteen animals from the breeding colony and four animals from a separate colony derived from the breeding colony were enrolled in this first ever prospective randomized controlled trial to test whether scheduled cesarean section will reduce pelvic floor injury caused by parturition. Pregnancies were diagnosed and dated using a calculator based on ultrasound measurements of gestational sac volumes and fetal dimensions to monitor obstetric well-being. All subjects received an MRI prior to each breeding season. Following each delivery, additional MRI procedures were performed with one immediate post-partum (1 to 5 days) and one after pelvic floor recovery (2 to 3 months post-partum). All assigned animals have completed their first pregnancies with 3 related MRI procedures. Eighty percent have initiated a second pregnancy with 3 of these 16 having completed the second pregnancy as of May 2014. By the end of calendar year 2014, 16 females are anticipated to have completed the second pregnancy and by the end of calendar year 2015, we anticipate that at least seven animals in each group will have completed their third pregnancy, the sample size needed based on the initial power analysis.

The results for 11 of the first 20 females to complete their first pregnancy are summarized in **Table** 1. All three pairs of pelvic floor muscles have changes associated with timing of the MRI assessment. For LA and obturator internus (OI) muscles, these changes are seen as a reduction in volume immediately after delivery with return to pre-pregnancy values by three months post-partum. These changes were not different between delivery groups. In contrast, COC muscles increased in volume following vaginal delivery, but not cesarean section. This results in a significant interaction ($p = 0.0004$) between groups and times of MRI exams. When the COC muscles were traced, the percent of muscle volume associated with high level of contrast accumulation was increased in the same manner (**Figure 1**). Pelvic floor muscles and connective tissue provide support of pelvic organs. The bladder neck served as a site to evaluate the extent of descent when abdominal pressure is provided during a dynamic MRI. Position of the bladder neck in the two groups at three separate time points is presented in **Figure 2**. Both post-partum exams after spontaneous vaginal delivery demonstrate a significant descent. After cesarean delivery, the evaluation three months post-partum showed descent that was not different from that after vaginal delivery. Bladder neck position immediately after C-

sections were obtained without abdominal pressure due to the abdominal surgery and were not included in the analysis.

We hypothesized that the greatest change would be seen in the COC muscles at the time immediately after spontaneous vaginal delivery, with an improvement by three months post-partum. Because our work with pre-term pregnant multiparous animals showed no significant difference between near-term and post-partum volumes, this indicated that the greatest and most significant amount of damage to the pelvic floor occurred during pregnancy. For this reason, we anticipated that scheduled cesarean delivery without labor would not prevent this injury or the subsequent effects on bladder descent. However, the preliminary results reported in this trial with primaparous females do not support this hypothesis. Instead, we saw an increase in COC muscle volume and corresponding increase in contrast accumulation consistent with tissue edema as reported by Bracken et al (2011) in spontaneous vaginal delivering females. Those with cesarean sections did not have this muscle injury. The COC muscle is located in the region of the pelvis between the posterior aspects of the pelvic bones. The paired muscles attach to the fused vertebra of the sacrum in an area that has been reported to expand during mentum anterior fetal presentation and vaginal delivery in the squirrel monkey. The translational aspect of this work occurs when one appreciates that the impact of vaginal delivery on LA muscle in human pelvic musculature is comparable to that on COC muscle in the squirrel monkey. In human parturition, the LA muscles are most affected by shearing forces of the presenting occiput anterior fetal head, allowing the anterior pelvis to stretch to accommodate the delivering fetus. The findings of this first prospective trial of primary cesarean section is that avoiding engagement of the fetal head into the pelvis and vaginal delivery, spares these muscles from injury and perhaps other connective tissue components. In spite of this potential benefit, a second feature of pregnancy and parturition in nulliparous squirrel monkeys is the prominent descent of the bladder neck seen three months post-partum in both groups. **The implications for women are profound as no such controlled trial can be conducted in patients and, even if possible, results on the pelvic floor could not be fully evaluated until perhaps decades after delivery.**

Table 1. Preliminary comparison of average muscle volumes (mm^3) for three pelvic floor muscles in 2 groups of females including 6 with cesarean sections (Csec) and 5 with spontaneous vaginal deliveries (SVD) measured at three times relative to first delivery.

Group	Prior to pregnancy	1-5 days post-partum	3 months post-partum	P values for Group differences	P values for Time differences
Average of left and right levator ani muscles					
SVD	408 ± 31	372 ± 27	399 ± 32	0.20	0.023
Csec	451 ± 28	396 ± 24	429 ± 30		
Total	429 ± 21^{A}	384 ± 18^{B}	414 ± 22^{A}		
Average of left and right obturator internus					
SVD	379 ± 17	339 ± 25	364 ± 15	0.22	0.00012
Csec	384 ± 16	364 ± 23	403 ± 14		
Total	381 ± 12^{A}	351 ± 17^{B}	383 ± 10^{A}		
Average of left and right coccygeus					
SVD	224 ± 20^{A}	328 ± 35^{B}	224 ± 28^{A}	0.40	0.0010*
Csec	238 ± 18^{A}	235 ± 32^{A}	242 ± 25^{A}		
Total	231 ± 14	281 ± 23	233 ± 19		

^{A,B} Means with difference superscripts differ ($p < 0.05$ using Duncan's post-hoc test after ANOVA)
*Interaction term also significant ($p = 0.0004$) indicating group by time factor interaction

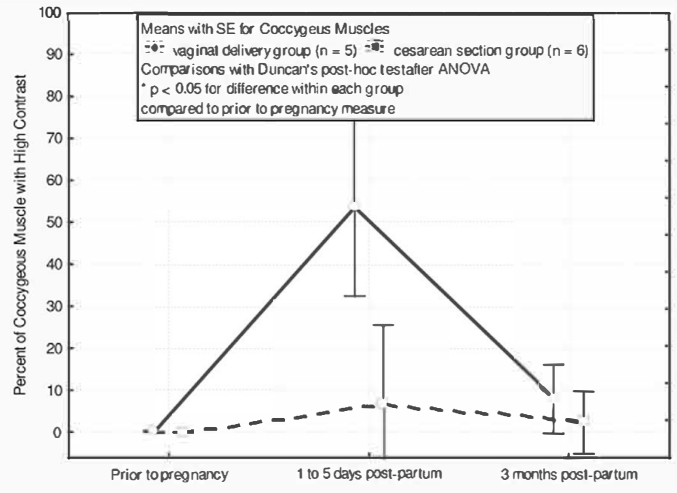

Figure 3. Percent of coccygeus muscle volume with high contrast accumulation. Vaginal delivery group shows increase at 1 to 5 days after delivery compared the group undergoing cesarean section.

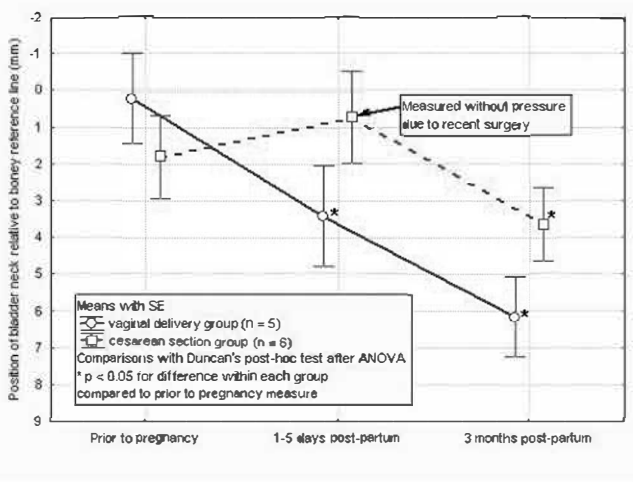

Figure 2. Comparison of bladder neck position within groups shows bladder neck descent at points after vaginal delivery and at 3 months post-partum for females undergoing C-section. Groups did not differ prio to pregnancy (p = 0.38) or 3 months post-partum (p=0.15).

Finally, during the preparation and execution of this trial, several tools, procedures, and management experiences were obtained that can now be used for diagnosis, dating and prospective management of the breeding females to decrease dystocia and stillbirths. During the current breeding year, we recruited a visiting scientist, Excluded by Requester who also has experience with obstetrical ultrasound in Neotropical primates, to work with Excluded by Requester on evaluation of breeding females for pregnancy, testing the obstetrical calculator, and making estimates of fetal head size and presentation near term to predict those females where interventions may be undertaken to prevent fetal and maternal complications. The impact of this change in management practices on colony production, health of infants, and reproductive lifespan of females will be evaluated during the next grant interval.

During the upcoming grant period, we propose to complete the trial described above and to follow the enrolled females through their subsequent time in the colony to document long-term effects on pelvic floor using perineal assessments, as first developed by Coates et al. (1995a,b). These observations will be augmented by a study to obtain similar assessments of all breeding females in the colony in relation to obstetrical history and age using this prolapse assessment system. The composition of the current colony includes a substantial group of females over 10 years of age with reproductive histories of more than five deliveries. These animals were not represented in the previously published study of this colony in 1995 (Coates et al. 1995b).

Applied Squirrel Monkey Genomics Excluded by Requester **and** Excluded by Requester **Co-Lead Investigators)**

The population genetic and pedigree approaches and analyses described earlier will provide a solid and rational program for an ongoing program on colony genetic management. This program will also serve as a foundation to initiate the next phase, namely, an applied squirrel monkey genomics research component. The goal will be to identify, validate and evaluate a large number of informative single nucleotide polymorphisms (SNPs) broadly dispersed across the genome sequence. Ultimately, this genomics resource will serve to identify functional polymorphisms related to disease phenotypes of interest to biomedical researchers who utilize squirrel monkeys.

Squirrel monkeys are vital animal models in many areas in biomedical research. A summary of NIH researchers who use our resource revealed three broad types of research use: malaria, neuroscience, and stem cells. In humans, susceptibility, resistance or severity of malaria is a complex trait involving interactions between multiple host genes, the malarial parasite, and the environment (Fortin et al. 2002). Malaria traits with a genetic component include parasitemia levels, anti-parasite antibody production and lymphocyte proliferation (Fortin et al. 2002; Kwiatkowski 2000; Kwiatkowski 2005). Many candidate genes are believed to influence human susceptibility to malarial infection. These include the Duffy blood group antigen (FY), which encodes the DARC chemokine receptor recognized by the human P. vivax parasite that is biologically similar to the endogenous squirrel monkey *P. simium* (Contamin et al. 2000; Galland 2000; Kwiatkowski 2005). Other genes believed to mediate human response to malaria include genes of the immune system (HLA genes, interleukins

Il-1A, Il-1B, Il-2B, Il-4 and Il-10, interferons Ifn-α and Ifn-γ), tumor necrosis factor alpha (TNFα) gene, the intercellular adhesion molecule-1 (ICAM), hemoglobins C, E and S, α and β-thallasemia G6PD, glycophorin, ABO and haptoglobin blood-groups (Driss et al. 2011; Fortin et al. 2002; Kwiatkowski 2000; Kwiatkowski 2005). Indeed, the list of malaria-related genes is so long that it reveals the shortcomings of the candidate gene approach, namely, that too much expensive genotyping is necessary to conduct genome-wide analyses given that many of these associations remain preliminary. More recent approaches used Genome Wide Association Studies (GWAS) with closely-spaced SNP maps to genomic regions involved in severe malaria, which recently revealed 2 new SNPs and verified earlier reports of HbS in West African case-control studies (Jallow et al. 2009). The second use of our squirrel monkey resource was in neuroscience. These studies included a wide variety of topics, from addiction, neural plasticity and regrowth, glaucoma, chronic pain, drug addiction and stroke. Up to 70% of the risk for addictive behaviors can be attributed to heritable genetic variation (Al-Haggar 2014). Genetic association analysis of SAGE (Study of Addiction—Genes and Environment) case-control data revealed 271 genetic regions including SNPs associated with substance addiction (Guo et al. 2012), while a recent meta-analysis identified 1500 SNPs in 18 molecular pathways involved in human addictions (Li et al. 2008). SNPS have been similarly used to identify genetic risk factors for normal-pressure glaucoma and optic nerve degeneration in glaucoma (van Koolwijk et al. 2012; Wiggs et al. 2012). GWAS studies have also identified SNPs associated with stroke and for subtypes ischemic and atherothrombotic strokes (Gschwendtner et al. 2009; Gudbjartsson et al. 2009; Ikram et al. 2009; Zeller et al. 2012). GWAS studies have also identified genes and SNPs involved in chronic widespread pain and pain perception (James 2013; Peters et al. 2013). Thirdly, stem cell studies have also applied GWAS techniques to good effect. For example, GWAS has revealed that DNA enhancer regions in embryonic stem cells (ES) are greatly enriched for transposable elements associated with various human cancers (Teng et al. 2011). Furthermore, GWAS was used to demonstrate that histone modification sites in ES are enriched for allele-specific methylation sites, which is important in interpreting patterns of expression of disease loci (Prendergast et al. 2012).

In short, all major areas of human biomedical research that also involve squirrel monkeys are already being advanced through the application of SNPs. Relative to the large number of putative candidate genes associated with any of these disorders, we believe it is more parsimonious to focus on identification and development of genome-wide SNPs. This approach will be realized through collaboration with Excluded by Requester Excluded by Requester at the Broad Institute (Alfoldi 2014; Johnson 2014) and Excluded by Requester (**see letters of collaboration**). Thus, the first goal of the applied genomics research component will be to sequence up to 8 more complete squirrel monkey genomes and identify novel genome-wide SNPs including chromosomal locations that will be applicable to squirrel monkey research. The first squirrel monkey DNA sequence was generated from a *S. b. boliviensis* individual drawn from our colony (NCBI 2014; UCSC 2014; WTSI 2014). In collaboration with Excluded by Requester we will use whole genome sequencing (WGS) on another six to eight squirrel monkeys over the first three years of the grant period. Initial sequencing and analysis currently cost $7,000/animal and will be paid with institutional funds. In line with recent genomics industry trends, this cost is expected to decrease substantially over the next few years (Hall, 2013; Wetterstrand, 2014). Animals to be sequenced will be selected from unrelated founder lineages in the breeding colony, in order to gain better understanding of genome-wide diversity and SNP allele frequencies in the resource colony as a whole.

Resulting DNA sequences will be compared to the publically available squirrel assembly from the Broad Institute and available at NCBI (NCBI 2014; UCSC 2014; WTSI 2014). Alignment of these sequences will allow identification of novel SNPs and indels, following current best-practice guidelines (Brownstein et al. 2014; Fawcett et al. 2011). The squirrel monkey reference genome currently consists of 724 unanchored scaffolds but there are no funds available to anchor them to chromosomes using traditional methods such as FISH-mapping (see letter of collaboration from Excluded by Requester Unless remedied, this would mean that neither the reference genome nor any future SNPs could be assigned specific chromosomal locations. We will address this deficiency through collaboration with genome scientists at the Proprietary Info who are developing new DISCOVAR and Hi-C methods to anchor the squirrel monkey genome (Lieberman-Aiden et al., 2009; see letter of collaboration from Excluded by Requester An anchored reference genome plus comparison to 6-8 more whole genome sequences will allow identification of hundreds of thousands of informative SNP sites and design of high-density SNP arrays for genome-wide association studies in squirrel monkeys. This will be extremely valuable for disease studies involving SNP genotyping, whether genome-wide or restricted to specific chromosomal regions of interest. For example, this genome-wide SNP resource will allow identification of the genetic bases to different disease phenotypes (such as resistance to malaria infection, genetic bases of pain

sensitivity, or susceptibility to nerve degeneration in glaucoma). In this way, genome-wide genotyping capacity will become available for squirrel monkeys in various avenues of research of on-going interest to many researchers. This applied genomics research component is the first step toward that long-term goal. By homology to closely related rhesus and cynomologus macaques, we anticipate that comparison of our first new genome to the squirrel monkey SaiBoi1.0 genome assembly (NCBI 2014) should identify 1-2 million chromosomally dispersed SNPs (Ebeling et al. 2011; Fang et al. 2011; Fawcett et al. 2011). Use of WGS on a panel of 6-8 squirrel monkeys should detect a minor allele frequency (MAF) of 0.083 to as little as 6.25% or 1 SNP per 16 chromosomes (Trask et al. 2011). Any questionable candidates SNPs will be validated by resequencing or real-time PCR (Isler et al. 2007; Shi et al. 1999). By comparison, a less comprehensive approach started with only 23,000 candidate SNPs yet identified over 4000 informative SNPs spaced at <1 Mb intervals in rhesus monkeys (Trask et al., 2011; Mahli et al., 2007). Thus our approach should be more than sufficient for dense genome-wide SNP coverage. Results can also be used to design reduced SNP subsets for population genetic applications, including inbreeding, population subdivision or ancestry-informative panels, as needed (Budowle and Van Daal 2008; Hou et al. 2011; Pakstis et al. 2007).

Behavior Research: Analysis of Squirrel Monkey Housing and Use of Space Excluded by Requester **Lead Investigator)**

Housing primates in ethologically appropriate social and physical environments is important for their physical and psychological well-being (Geschwind et al. 2013). For squirrel monkeys, arboreal primates that exhibit a dynamic social structure of seasonal sexual segregation (Lyons et al. 1992), providing satisfactory three-dimensional spacing and ethologically appropriate social groups is challenging. Enclosures must accommodate both high and low-ranking group members, and allow individuals to have a suitable amount of control over inter-individual distance. It has been shown that when given access to additional space, squirrel monkeys will increase the amount of time spent at greater distances from their nearest neighbor (Marriott and Meyers 2005). This indicates a preference for large inter-individual distance and illustrates the significance of spatial and social density.

The subjects of the study will be five social groups of *S. boliviensis* squirrel monkeys housed in single and double pens (each pen measuring 4'widex6'tallx14'deep). Observation will consist of instantaneous scans conducted every ten minutes. One hundred observations per social group will be conducted between 07:30 and 16:30, Monday through Friday. Data will be collected during four time points of each year (breeding season, post-breeding, birthing season, pre-breeding). Data will be collected across the five years of the grant period in order to investigate longitudinal changes in-group behavior.

During the group scans, we will record the location and behavior of each individual within the pen. The locations of the subjects will be determined based on where the hind feet are planted. The ethogram used will consist of enrichment foraging, feeding, travel, non-social, aggressive, affiliative, and resting behavior.

These data will be analyzed along with existing data from three squirrel monkey social groups that were collected in March and April 2011 using identical methods. From these data we will be able to determine how much of the physical three-dimensional space is utilized by the squirrel monkeys, and conversely which areas are neglected, and the preferred locations to feed, play, sleep, etc.

In order to complete the social assessment of space use we will also collect nearest neighbor data for each individual during each group scan. The following categories will be used: in contact, within arm's length (≤ 15cm), short distance (15 ≤ 60cm), and long distance (>60cm away).

From these data, we will be able to determine the frequency with which individuals maintain shorter versus longer inter-individual distances. Values will be compared between single and double pens and between large and small groups.

Squirrel Monkey Immunology Studies Excluded by Requester **Lead Investigator)**

Progress in current grant period: In the current grant support period, we have identified the following cross reactive fluorescence labeled monoclonal antibodies specific to different lymphocytes subsets of squirrel monkey: CD3 (FITC, clone SP34-2, BD Pharmingen), CD4 (PE, clone L200, BD Pharmingen, San Jose, CA), and NK cells (CD16 PE clone 3G8, BD Pharmingen, San Jose, CA), and B cells (CD20+ APC clone L27, BD pharmingen, San Jose, CA) and CD8 (PE, clone B5, Invitrogen, Carlsbad, CA) Excluded by Requester We also investigated differences in the phenotype and function of lymphocytes subsets of young (3-4 years), adult (8-10 years) and aged (16-19 years) squirrel monkeys. In general, animals in all three age groups exhibited comparable numbers of different lymphocyte subsets except for CD20+ B cells that were significantly lower in aged relative to young animals and T cells subsets expressing both CD4 and CD8 (double positive) were

significantly higher in aged relative to young animals. With increasing age, phenotypic differences in central and effector memory T cells subsets were observed, that were more pronounced for the CD8+ T cells. Despite equal proportions of CD3+ T cells among the three age groups, responses of peripheral blood mononuclear cells to T cell mitogens PHA and Con A showed lower IFN-γ producing cells in aged group than that in the young group. Furthermore, aged animals showed significantly higher plasma levels of inflammatory cytokines IL-6, IFN-γ, TNF-α, IL-10 and IL-12. These findings suggest that while the squirrel monkeys in general share phenotypic and functional similarities of lymphocyte subsets with humans in relation to age, specific differences exist in immune function of lymphocytes between young and old animals that could potentially impact experimental outcomes for which the measurement of immunologic endpoints are critical.

Proposed Immunology studies:

The studies proposed here will add value to the squirrel monkey as a model of human disease by providing new information about the immune system of squirrel monkeys and by identifying reagents that cross react with specific squirrel monkey lymphocyte subsets. These studies extend previous research done within the SMBRR Excluded by Requester and will be supported by institutional funds. The study proposed in Specific Aim 3 will be the first in the field to study the mechanism of NKT cell mediated activation of adaptive immune cells in squirrel monkeys. The successful completion of this project will enable us to test the efficacy of this method in this primate model, a critical step before studies in human population.

Specific Aim 1 and 2

To further develop and define squirrel monkeys as a model for immunological studies, we will use a series of commercially available human monoclonal antibodies and reagents to test for cross reactivity to squirrel monkey mononuclear cells using flow cytometric analysis as described before Excluded by Requester Briefly, we will incubate titered amount of antibody with 1x106 PBMC for 15 minutes at room temperature, washed with PBS and acquired at FACSCaliber (BD, SanJose) and analyzed using Flowjo software. We will characterize specialized cells such as myeloid dendritic cells (mDCs), Plasmacytoid dendritic cells (pDCs), NK and NKT cells and their function using commercial cross reactive antibodies and reagents. For mDCs, we will use the surface marker, CD11c, for pDCs CD123, BDCA-2 and BDCA-4, for monocytes CD14, for NK CD3- CD16+ and NKT CD3+CD16+ and CD1d. In humans and rhesus, NKT cells are defined as CD161 and Cd1d markers, however, these makers are not cross reactive in Neotropical primates, therefore, we will define NKT cells as expressing both CD3 and CD16.

Specific Aim 3

NKT cells are important members of innate immunity that are activated in response to specific glycolipids such as α-GalCer presented by dendritic cells (DC) in the context of the CD1d surface molecule. The synthetic glycolipid alpha-galactosylceramide (α-GalCer) is a potent activator of NKT cells that will be used as an adjuvant for immunization approaches to stimulate antigen-specific immune responses. The alpha-galactosylceramide (α-GalCer) will be purchased from Diagnocine LLC (Hackensack, NJ) and dissolved in dimethyl sulfoxide, (Sigma, St. Louis, MO) at a concentration of 1 mg/ml. 10ug of α-GalCer will be used in *in vitro* and or *in vivo* studies to investigate stimulation of NKT cells as well as its function by measuring IFN-γ and IL-4 by ELISA.

VERTEBRATE ANIMALS

All procedures involving squirrel monkeys will be carried out at the Michale E. Keeling Center for Comparative Medicine and Research (KCCMR) of the University of Texas M. D. Anderson Cancer Center (UTMDACC) in Bastrop, Texas. The Squirrel Monkey Breeding and Research Resource (SMBRR) is a national research resource of three squirrel monkey species, *Saimiri boliviensis boliviensis*, *Saimiri sciureus sciureus*, and *Saimiri boliviensis peruviensis*. Because this project involves maintaining a breeding colony of squirrel monkeys, all ages and both sexes of squirrel monkeys will be maintained in the project. The KCCMR is AAALAC accredited and has a PHS Assurance on file with the Office for Laboratory Animal Welfare (OLAW).

Proposed Animal Use: The SMBRR currently maintains 559 squirrel monkeys of the three species listed above. Most of these animals are in the breeding colony that serves as a national research resource of this genus available to NIH grantees that need squirrel monkeys for their research. All animals provided from the SMBRR are provided to institutions with PHS assurances and there must be an approved IACUC protocol for the animals requested from the SMBRR. The SMBRR carries out studies designed to provide new information about the natural biology of squirrel monkeys with an emphasis on studies of natural social behavior, diseases of squirrel monkeys that resemble human diseases, and studies to better understand the immunology of the squirrel monkey. Some studies require only samples obtained from squirrel monkeys during routine veterinary examinations.

The squirrel monkey colony consists of both males and females. Squirrel monkeys range in age from newborn to more than 20 years.

The UTMDACC Institutional Animal Care and Use Committee (IACUC) meets monthly to review proposed research protocols and to assure that the guidelines put forth by the PHS Policy on Humane Care and Use of Laboratory Animals and NIH *Guide* are followed; facilities and programs are inspected and reviewed by the IACUC every six months. This Institution has an Animal Welfare Assurance on file with the NIH Office of Laboratory Animal Welfare (ref. A-3343-01) and is a USDA-registered research facility.

Justification for the Use of Squirrel Monkeys: The procedures performed on the three species of animals described in this application will occur as part of normal operations to address medical and management problems and research approved by the IACUC. The justification for the number of animals described is that they equal the total number of animals maintained in each colony, all of which require medical care and oversight. The species chosen reflect the most commonly used squirrel monkeys in biomedical research.

Veterinary Care: All of the veterinarians at the KCCMR have extensive experience in the clinical care and biomedical research use of nonhuman primates. Excluded by Requester has more than 20 years experience working with squirrel monkeys. The technical and husbandry staff receives regular training and approximately 80% of the KCCMR husbandry staff is AALAS certified. Daily observations and regularly scheduled physical examinations are important in preventive medicine and in detecting early, subtle signs of disease. Colony staff and supervisors view all colony animals during observations at least twice daily. An established and well-integrated Behavioral Management and Enrichment program is directed by Excluded by Requester a primate behaviorist with more than 30 years experience with squirrel monkeys.

Guidelines for Minimizing Discomfort, Pain or Distress: All non-painful procedures in squirrel monkeys are carried out with gentle manual restraint or with sedation using Ketamine HCl administered by experienced staff. General anesthesia for painful procedures is provided using injectable ketamine & xylazine, or isoflurane inhalation anesthesia that is induced by mask under manual restraint.

Anesthetic Monitoring and Recovery: During routine short anesthesia periods when ketamine and xylazine are used as the anesthetic agents, the animal's condition is monitored by close observation of its breathing pattern and the color of its mucus membranes, and auscultation of its heart and lung sounds. Major surgery requires use of an inhalation anesthetic agent and may include monitoring of blood pressure, electrocardiogram, anesthetic agent, oxygen saturation and other parameters. During the recovery period, animals are placed in lateral recumbency to allow drainage and prevent aspiration of secretions, and they are periodically observed until they are able to maintain a sitting posture.

Analgesia: A variety of oral and injectable analgesics, ranging in strength from nonprescription analgesics to potent narcotics, are available at the discretion of the clinical veterinarian. Buprenorphine is the most frequently used analgesic. In evaluating the need of analgesics, the guidelines from PHS policy "Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Education" are followed (Interagency Research Animal Committee, 1985). Specifically, "Unless the contrary is established, investigators should consider that procedures that cause pain or distress in human beings may cause pain or distress in other animals." In addition, close monitoring, coupled with knowledge of the normal behavior of the individual animal, is used to detect subtle signs of discomfort that indicate a need for analgesia.

Euthanasia Policy: Euthanasia is administered for humane reasons based upon the decision of the attending veterinarian. Methods of euthanasia are in compliance with the AVMA Guidelines for Euthanasia of Animals 2013 Edition Version 2013.0.1 (www.avma.org). Euthanasia, in instances when it becomes necessary, is carried out using a barbiturate administered intravenously.

References – Applied Research

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LETTERS OF COLLABORATION – Applied Research

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