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NATIONAL INSTITUTES OF HEALTH
DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL PRIMATE RESEARCH CENTERS (NPRC) PROGRAM
DIVISION OF COMPARATIVE MEDICINE
NATIONAL CENTER FOR RESEARCH RESOURCES

5P51RR000167-43

NATIONAL PRIMATE RESEARCH CENTER SUPPORT

Final

UNIVERSITY OF WISCONSIN-MADISON

ANNUAL PROGRESS REPORT

Reporting From: 05/01/2003

Reporting To: 04/29/2004

36.880% AIDS Related

J h W K 4/27/04

Signature Date

JOSEPH W KEMNITZ, PHD
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Patent or Copyright was not awarded this grant year.

MAY 1 9 2004

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RESEARCH SUBPROJECTS

NEUROBIOLOGY

PATHOLOGY

REPRODUCTION&DEVELOPMENT

PERSONNEL ROSTER

Core Doctoral Scientists

Name, Degree	Department	Non-Host Institution: State, Country
ABBOTT, DAVID H, PHD	WNPRC ASSAY SERVICES & OB/GYN	
BEAM, SHEREE, DVM	WNPRC PATHOLOGY SERVICES	
BOLTON, IRIS, DVM	WNPRC ANIMAL SERVICES	
BRUNNER, KEVIN G., DVM	WNPRC ANIMAL SERVICES	
COE, CHRISTOPHER L, PHD	WNPRC & PSYCHOLOGY	
COLMAN, RICKI J, PHD	WNPRC AGING	
FRIEDRICH, THOMAS, PHD	WNPRC WATKINS LAB & VIROLOGY	
GOLOS, THADDEUS G, PHD	WNPRC & OB/GYN	
HARKE, MICHELE, DVM	WNPRC ANIMAL SERVICES	
KEMNITZ, JOSEPH W, PHD	WNPRC DIRECTOR & PHYSIOLOGY	
KNABLE, STEVEN, MBA	WNPRC OPERATIONAL SERVICES	
KNABLE, STEVEN M, MBA	OPERATIONAL SERVICES/WNPRC	
[redacted]	WNPRC VIROLOGY SERVICES	
O'CONNOR, DAVID, PHD	WNPRC WATKINS LAB	
RAKASZ, EVA, PHD	WNPRC IMMUNOLOGY SERVICES	
ROBINSON, CYNTHIA, MLS	WNPRC LIBRARY/INFO SERV	
SCHOBERT, CHARLES, DVM	WNPRC ANIMAL SERVICES	
SCHRAMM, R DEE, PHD	WNPRC REPRO RES SERVICES	
SCHULTZ-DARKEN, NANCY, PHD	WNPRC ANIMAL SERVICES	
TERASAWA, EI, PHD	WNPRC ASSAY SERVICES & PEDS	
THOMSON, JAMES A, VMD, PHD	WNPRC STEM CELL RES & ANATOMY	
USBORNE, AMY, DVM	WNPRC RESEARCH SERVICES	
WATKINS, DAVID I, PHD	WNPRC & PATHLAB MED	
WEINDRUCH, RICHARD, PHD	WNPRC & MEDICINE & VA-GRECC	
WILSON, NANCY, PHD	WNPRC WATKINS LAB	
ZIEGLER, TONI E, PHD	WNPRC ASSAY SERV & PSYCHOLOGY	

Affiliated

Name, Degree	Department	Non-Host Institution: State, Country
[redacted]	ANIMAL HEALTH & BIOMEDICAL SCI	
[redacted]	WAISMAN CENTER	
[redacted]	BIOSTATISTICS	UNIVERSITY OF ALABAMA-BIRMINGHAM: AL, USA

Affiliated

Name, Degree	Department	Non-Host Institution: State, Country
[illegible]	MICROBIOLOGY & IMMUNOLOGY	EMORY UNIVERSITY: GA, USA
ALTMANN, JEANNE, PHD	ECOLOGY & EVOLUTIONARY BIOLOGY	PRINCETON UNIVERSITY: NJ, USA
[illegible]	PATHOBIOLOGY AND IMMUNOLOGY	OHSU & ONPRC: OR, USA
[illegible]	INST. REPROD & DEVELOPMENT	MONASH UNIV., AUSTRALIA
[illegible]	PHYSIOLOGY	
[illegible]	PSYCHIATRIC RESEARCH INSTITUTE	
BIRD, IAN, PHD	OB/GYN	
[illegible]	BEHAVIORAL NEUROSCIENCES	NIA GERONTOLOGY RESEARCH CTR.: MD, USA
[illegible]	DIRECTOR	NETHERLANDS PRIMATE RES CTR, NETHERLANDS
[illegible]	WNPRC GOLOS LAB	
[illegible]	WNPRC ABBOTT LAB	
BURTON, DENNIS, PHD	IMMUNOLOGY	SCRIPPS RESEARCH INST.: CA, USA
[illegible]	TRACER METHOD & CLINICAL NUTR	LOUISIANA STATE UNIVERSITY: LA, USA
[illegible]	REPROD SCI & NEUROSCIENCES	OHSU SCHOOL OF MEDICINE: OR, USA
[illegible]	HUMAN GENETICS	OXFORD UNIVERSITY, UK
[illegible]	SENIOR SCIENTIST	POPULATION COUNCIL: NY, USA
[illegible]	ANATOMIC PATHOLOGY	MARSHFIELD CLINIC: WI, USA
[illegible]	WAISMAN CTR	
[illegible]	NORC NATIONAL OPIN AND RES CTR	UNIVERSITY OF CHICAGO: IL, USA
[illegible]	WNPRC GOLOS LAB	
[illegible]	DEPARTMENT OF ZOOLOGY	UNIVERSIDAD SAN FRANCISCO DE QUITO, ECUADOR
[illegible]	MEDICAL PHYSICS	
[illegible]	GENETICS	
DEWHURST, STEPHEN, PHD	MICROBIOL/MMUNOL & ONCOLOGY	UNIVERSITY OF ROCHESTER MEDICAL CTR.: NY, USA
[illegible]	HUMAN IMMUNOLOGY	NIH VACCINE RESEARCH CENTER: MD, USA
[illegible]	MEDICINE	
DUMESIC, DANIEL A, MD	MEDICINE & OB/GYN	MAYO CLINIC: MN, USA
[illegible]	MEDICINE	NORTHWESTERN UNIVERSITY: IL, USA
[illegible]	PSYCHIATRY	VANDERBILT UNIVERSITY, NASHVILLE: TN, USA
EDWARDS, IRIS J, PHD	SCHOOL OF MEDICINE	WAKE FOREST UNIVERSITY: NC, USA
[illegible]	NEUROLOGICAL SCIENCES	RUSH UNIVERSITY: IL, USA

Affiliated

Name, Degree	Department	Non-Host Institution: State, Country
[illegible]	INSTITUTE OF BIOLOGY	NATIONAL UNIVERSITY OF MEXICO, MEXICO
FERRIS, CRAIG F., PHD	PSYCHIATRY	U MASS. MEDICAL SCHOOL: MA, USA
[illegible]	PSYCHOLOGY	UNIVERSITY OF TORONTO, CANADA
FOWLER, CYNTHIA, PHD	COMMUNICATIVE DISORDERS	
[illegible]	REPRODUCTION & DEVELOPMENT	IMPERIAL COLLEGE, LONDON, UK
FREEDMAN, ROBERT, PHD	PSYCHIATRY & OB/GYN	WAYNE STATE UNIVERSITY: MI, USA
[illegible]		POWDERJECT VACCINES: WI, USA
[illegible]	OPHTHALMOLOGY & VISUAL SCIENCE	
[illegible]	NEUROLOGY	
GARELL, CHARLES, MD	NEUROLOGICAL SURGERY	
[illegible]	NEUROSCIENCE	ONPRC: OR, USA
[illegible]	PHARMACOLOGY	
GORE, ANDREA C, PHD	PHARMACOLOGY & TOXICOLOGY	UNIVERSITY OF TEXAS AT AUSTIN: TX, USA
[illegible]	MICHAEL BEST & FRIEDRICH	
[illegible]	PHYSIOLOGY AND PHARMACOLOGY	TEL-AVIV UNIVERSITY, ISRAEL
GRUNEWALD, ALEXANDER, PHD	PSYCHOLOGY AND PHYSIOLOGY	
HAASE, ASHLEY T, MD	MICROBIOLOGY	UNIVERSITY OF MINNESOTA: MN, USA
[illegible]	OB/GYN	OXFORD UNIV., UK
[illegible]		BOYS TOWN NATL RESEARCH HOSPITAL: NE, USA
[illegible]	MICROBIOLOGY & IMMUNOLOGY	UNIVERSITY OF OKLAHOMA: OK, USA
[illegible]	MEDICAL PHYSICS	
[illegible]	NEUROLOGY	
[illegible]	BIOLOGICAL SCIENCES	INDIANA UNIVERSITY: IN, USA
[illegible]	SURGERY	
HUTZ, REINHOLD, PHD	BIOLOGICAL SCIENCES	UNIVERSITY OF WISCONSIN-MILWAUKEE: WI, USA
[illegible]	BEHAVIORAL NEUROSCIENCE	NIA GERONTOLOGY RESEARCH CTR.: MD, USA
[illegible]	MEDICINE & VA-GRECC	
KALIN, NED H, MD	PSYCHIATRY	
KAMP, TIMOTHY J, MD, PHD	CARDIOLOGY	
[illegible]	PATHOLOGY & COMPATIVE MEDICINE	WAKE FOREST UNIVERSITY: NC, USA
KARASOV, WILLIAM, PHD	WILDLIFE ECOLOGY	

Affiliated

Name, Degree	Department	Non-Host Institution: State, Country
KAUFMAN, PAUL L, MD	OPHTHALMOL & VISUAL SCIENCE	
	PATHOBIOLOGICAL SCI (VET SCH)	
KENNEDY, STEPHEN, PHD	OB/GYN	OXFORD UNIVERSITY, UK
	MICROBIOLOGY & IMMUNOLOGY	UNIVERSITY OF MELBOURNE, AUSTRALIA
	MICROBIOLOGY & IMMUNOLOGY	UNIVERSITY OF ROCHESTER MEDICAL CTR.: NY, USA
KIMBERLING, W.J., PHD		BOYS TOWN NATL RESEARCH HOSP: NE, USA
	PSYCHIATRY	U MASS. MEDICAL SCHOOL: MA, USA
KRAEMER, GARY W, PHD	KINESIOLOGY	
	CARDIOLOGY	
		ONPRC: OR, USA
LATHAM, KEITH, PHD	BIOCHEMISTRY	FELS INSTITUTE OF CANCER RESEARCH & TEMPLE U. SCH. OF MEDICINE, PHILADELPHIA: PA, USA
	NAT'L INST OF TOXICOLOGICAL RE	REPUBLIC OF SEOUL, KOREA
	ENDANGERED SPECIES RESEARCH	UNIVERSITY OF NEW ORLEANS AND AUDUBON CENTER: LA, USA
	WNPRC THOMSON LAB	
	NEUROBIOLOGY AND PHYSIOLOGY	NORTHWESTERN UNIVERSITY: IL, USA
	PSYCHOLOGY	
	DIVISION OF CLINICAL SCIENCES	UNIVERSITY OF TORONTO, CANADA
	ANTHROPOLOGY	
		CNPRC: CA, USA
MACDONALD, KELLY S, MD	DIVISION OF CLINICAL SCIENCES	UNIVERSITY OF TORONTO, CANADA
	NEPRC	HARVARD MEDICAL SCHOOL: MA, USA
MARLER, CATHERINE A, PHD	PSYCHOLOGY	
	PATHOLOGY & LABORATORY MED	
	WPRC WATKINS LAB	
	ANIMAL HLTH & BIOMED SCI	
	OB/GYN	UNIVERSITY OF EDINBURGH, UK
	MRC HUMAN REPRO SCI UNIT	U EDINBURGH, SCOTLAND
	CNPRC	UC-DAVIS: CA, USA
MONTGOMERY, ERWIN, MD	WPRC NEUROLOGY	
	PSYCHOLOGY	
	NEUROSCIENCE	ONPRC: OR, USA

Affiliated

Name, Degree	Department	Non-Host Institution: State, Country
[redacted]	MEDICAL PHYSICS & RADIOLOGY	
[redacted]		CIPHERGAN BIOSYSTEMS: CA, USA
ODORICO, JON, MD	SURGERY	
O'MALLEY, JAMES P, PHD		PFIZER, INC.: CT, USA
[redacted]		BOYS TOWN NATL RESEARCH HOSP: NE, USA
[redacted]	PEDIATRICS	UNIVERSITY OF MICHIGAN: MI, USA
[redacted]		STANFORD UNIVERSITY: CA, USA
[redacted]		UNIVERSITY OF ROCHESTER MEDICAL CTR.: MN, USA
[redacted]	NUTRIONAL SCIENCES	
PICKER, LOUIS, PHD		WASHINGTON UNIVERSITY, ST. LOUIS: MO, USA
[redacted]	PRIMATE INFORMATION CENTER	WANPRC: WA, USA
[redacted]		SWISS INSTITUTE OF TECHNOLOGY, SWITZERLAND
[redacted]	ANATOMY	UNIVERSITY OF CALIFORNIA-SAN FRANCISCO: CA, USA
[redacted]	MOLECULAR BIOSCI	UNIVERSITY OF CALIFORNIA-DAVIS: CA, USA
[redacted]	CHEMISTRY	MAHIDOL UNIVERSITY, BANGKOK, THAILAND
[redacted]	MEDICAL PHYSICS/PSYCHIATRY	
[redacted]	PEDIATRICS	UNIVERSITY OF CHICAGO: IL, USA
[redacted]	SCHOOL OF MEDICINE	WAKE FOREST UNIVERSITY: NC, USA
SALTZMAN, WENDY, PHD	BIOLOGY	UNIVERSITY OF CALIFORNIA-RIVERSIDE: CA, USA
SCHNEIDER, MARY, PHD	KINESIOLOGY	
[redacted]	NUTRITIONAL SCIENCES	
[redacted]		EPIMMUNE: CA, USA
[redacted]	PSYCHIATRY	
[redacted]	CORPORATE DEVELOPMENT	BRIDGE PHARMACEUTICALS, INC.: CA, USA
[redacted]	VETERINARY & BIOMED SCIENCES	UNIVERSITY OF MINNESOTA: MN, USA
SLUKVIN, IGOR I, MD, PHD	PATHOLOGY	
[redacted]	BEHAVIOR	SWNPRC: TX, USA
SNOWDON, CHARLES T., PHD	PSYCHOLOGY & ZOOLOGY	
SOLTIS, JOSEPH, PHD	COMPARATIVE ETHOLOGY	NIH: MD, USA
STRIER, KAREN B, PHD	ANTHROPOLOGY	

Affiliated

Name, Degree	Department	Non-Host Institution: State, Country
[redacted]	BIOTECHNOLOGY CENTER	
SVENDSEN, CLIVE, PHD	ANATOMY	
[redacted]		PFIZER RESEARCH LABORATORIES: CT, USA
[redacted]	WNPRC ABBOTT LAB	JOHNSON & JOHNSON ORTHO: NJ, USA
TANUMIHARDJO, SHERRY A, PHD	NUTRITIONAL SCIENCES	
[redacted]	CNPRC & PEDIATRICS	UNIVERSITY OF CALIFORNIA-DAVIS: CA, USA
[redacted]		SNPRC: AZ, USA
[redacted]	MEDICAL CENTER	DUKE UNIVERSITY: NC, USA
[redacted]	NORC OPIN AND RES CTR	UNIVERSITY OF CHICAGO: IL, USA
[redacted]	KINESIOLOGY	HARVARD UNIVERSITY: MA, USA
VAN DER HORST, VERONIQUE G J M, PHD	NEUROBIOLOGY	UNIV CALIF AT SAN FRANCISCO: CA, USA
[redacted]	KINESIOLOGY	
VANDEVOORT, CATHERINE A., PHD	PHYSIOLOGY	CALIFORNIA NATIONAL PRIMATE RESEARCH CENTER: CA, USA
[redacted]	OPTHALMOL & VISUAL SCI	UNIVERSITY OF MINNESOTA: MN, USA
VINYARD, CHRIS, PHD	COLLEGE OF MEDICINE	NORTHEASTERN OHIO UNIVERSITIES, ROOTSTOWN: OH, USA
[redacted]		BOYS TOWN NATL RESEARCH HOSPITAL: NE, USA
[redacted]	SCHOOL OF VET MED	
[redacted]	HUMAN GENETICS	UNIVERSITY OF PITTSBURGH: PA, USA
[redacted]		REGENERON PHARMAEUTICALS: NY, USA
[redacted]	REPRODUCTIVE SCIENCES	ONPRC & OREGON HEALTH SCIENCES UNIVERSITY: OR, USA
[redacted]	COMPREHENSIVE AIDS CENTER	NORTHWESTERN UNIVERSITY: IL, USA
[redacted]	BIOLOGICAL SCIENCES	U WISCONSIN WHITEWATER: WI, USA
[redacted]	CELL THERAPY CENTER	BEIJING INSTITUTE OF GERIATRICS, CAPITAL UNIVERSITY OF MED SCI, CHINA
ZHANG, SU-CHUN, MD, PHD	ANATOMY	
[redacted]	WNPRC ABBOTT LAB	
[redacted]	DIRECTOR	YNPRC: GA, USA
[redacted]	WELLCOME TRUST CTR HUMAN GEN.	UNIVERSITY OF OXFORD, UK
[redacted]	WNPRC THOMSON LAB	

Graduate Student/Postdoctoral Scientists

Name, Degree	Department	Non-Host Institution: State, Country
[redacted]	WNPRC TERASAWA LAB	
[redacted]	BIOSCIENCES	UNIVERSITY OF WISCONSIN-MILWAUKEE: WI, USA
[redacted]	WNPRC KEMNITZ LAB	
[redacted]	WNPRC ABBOTT LAB	
[redacted]	WNPRC GOLOS LAB	
[redacted]	WNPRC GOLOS LAB	
[redacted]	WNPRC GOLOS LAB	
[redacted]	WNPRC GOLOS LAB & OB/GYN	
[redacted]	PSYCHOLOGY	
[redacted]	WNPRC THOMSON LAB	
[redacted]	WNPRC GOLOS LAB	
[redacted]	WNPRC THOMSON LAB	
[redacted]	WILDLIFE ECOLOGY	
[redacted]	WNPRC TERASAWA LAB	
[redacted]	WNPRC TERASAWA LAB	
[redacted]	OB/GYN	
[redacted]	WNPRC GOLOS LAB	
[redacted]	WNPRC THOMSON LAB	
[redacted]	WNPRC THOMSON LAB	
[redacted]	WNPRC GOLOS LAB	
[redacted]	POPULATION HEALTH SCIENCES	
[redacted]	WNPRC THOMSON LAB	
[redacted]	WNPRC THOMSON LAB	
[redacted]	WNPRC GOLOS LAB	

SUBPROJECT DESCRIPTIONS

NPRC MANAGEMENT SUBPROJECTS

WNPRC DIRECTOR'S OFFICE (0184)

NPRC UNIT: ADMINISTRATIVE

%NPRC $: 0.500% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KEMNITZ, JOSEPH W	PHD	C	WNPRC DIRECTOR & PHYSIOLOGY	
L	DVM	C	WNPRC ANIMAL SERVICES	
names	MBA	C	OPERATIONAL SERVICES/WNPRC	
1	DVM	C	WNPRC RESEARCH SERVICES	

AXIS I CODES: 28(ADMINISTRATIVE) **AXIS II CODES:** 31, 92(ADMINISTRATIVE)

ABSTRACT

A narrative of the Director's Office appears in the Infrastructure Word document appended to this report.

Essential to the Director's Office but not categorized on the Personnel Roster are an executive assistant, quality assurance coordinator, public information officer/outreach coordinator, PIO/outreach assistant, and student assistants as needed.

FUNDING: NIH P51 RR000167

WNPRC AGING COLONY RESOURCE (0239)

NPRC UNIT: AGING & METABOLIC DISEASE

%NPRC $: 4.500%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
COLMAN, RICKI J	PHD	C	WNPRC AGING	
Lname, ...	PHD	C	WNPRC DIRECTOR & PHYSIOLOGY	

AXIS I CODES: 1 AXIS II CODES: 30, 46, 49, 55, 58

ABSTRACT

A narrative for the Aging Colony Resource appears in the Infrastructure Word document appended to this report.

Essential to the Colman lab and Aging Colony Resource but not categorized on the Personnel Roster are four research specialists and student lab assistants as needed.

FUNDING: NIH P51 RR000167

WNPRC VIROLOGY SERVICES UNIT (0230)

NPRC UNIT: AIDS COMPONENT

%NPRC $: 0.500% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
FRIEDRICH, THOMAS	PHD	C	WNPRC WATKINS LAB & VIROLOGY	
[name]	MS	C	WNPRC VIROLOGY SERVICES	

AXIS I CODES: 3 **AXIS II CODES:** 31

ABSTRACT

A narrative for the Virology Services Unit appears in the Infrastructure Word document appended to this report.

Essential to Virology Services but not categorized on the Personnel Roster are three research specialists and student lab assistants as needed.

FUNDING: NIH P51 RR000167

WNPRC IMMUNOLOGY SERVICES UNIT (0229)

NPRC UNIT: AIDS COMPONENT

%NPRC $: 0.500% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
RAKASZ, EVA	PHD	C	WNPRC IMMUNOLOGY SERVICES	
L	PHD	A	GENETICS	
names	PHD	A	PATHOLOGY & LABORATORY MED	
	PHD	A	WPRC WATKINS LAB	
	PHD	C	WNPRC & PATHLAB MED	
J	PHD	C	WNPRC WATKINS LAB	

AXIS I CODES: 1 **AXIS II CODES:** 31, 64, 66, 69, 77, 91

ABSTRACT

A narrative for the Immunology Services Unit appears in the Infrastructure Word document appended to this report.

Essential to Immunology Services but not categorized on the Personnel Roster are one researcher, two research specialists, and student assistants as needed.

FUNDING: NIH P51 RR000167

NOTE: Investigators other than Drs. Rakasz, Watkins, L names and Wilson listed on this SPID are not part of Immunology Services. These individuals did not submit SPIDS this year, but are described in the Infrastructure section of this report as using Immunology services, therefore they should remain on the Personnel Roster as active affiliates.

WNRPC GENETICS RESOURCES (0146)

NPRC UNIT: AIDS COMPONENT

%NPRC $: 2.000% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
WATKINS, DAVID I	PHD	C	WNPRC & PATHLAB MED	
	PHD	C	WNPRC WATKINS LAB & VIROLOGY	
	PHD	A	WPRC WATKINS LAB	
	DVM, PHD	A	CNPRC	UC-DAVIS, CA USA
	PHD	C	WNPRC WATKINS LAB	
	PHD	A		WASHINGTON UNIVERSITY, ST. LOUIS, MO USA
	PHD	C	WNPRC WATKINS LAB	

AXIS I CODES: 1A, 1D, 7B, 17, 19 **AXIS II CODES:** 31, 64, 66, 83, 91, 94

ABSTRACT

A narrative for Genetics Resources appears in the Infrastructure Word document appended to this report.

Essential to Genetics Resources but not categorized on the Personnel Roster are 21 technicians and other staff, in addition to many undergraduate student lab assistants.

FUNDING: NIH P51 RR000167

WNPRC ANIMAL SERVICES DIVISION (0214)

NPRC UNIT: ANIMAL SERVICES

%NPRC $: 1.000% AIDS RELATED RESEARCH

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
BOLTON, IRIS	DVM	C	WNPRC ANIMAL SERVICES	
L	DVM	C	WNPRC ANIMAL SERVICES	
names	DVM	C	WNPRC ANIMAL SERVICES	
J	DVM	C	WNPRC ANIMAL SERVICES	

AXIS I CODES: 1 AXIS II CODES: 30, 31, 58, 86

ABSTRACT

A narrative for the Animal Services Division appears in the Infrastructure Word document appended to this report.

Essential to Animal Services but not categorized on the Personnel Roster are two colony managers, 39 technicians and 8 students.

FUNDING: NIH P51 RR000167

WNPRC ASSAY SERVICES UNIT (0215)

NPRC UNIT: ASSAY SERVICES

%NPRC $: 1.500%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ABBOTT, DAVID H	PHD	C	WNPRC ASSAY SERVICES & OB/GYN	
L	MD	A	MEDICINE	
names	PHD	A	PATHOLOGY & COMPATIVE MEDICINE	WAKE FOREST UNIVERSITY, NC USA
	PHD	A		SNPRC, AZ USA
J	PHD	C	WNPRC ASSAY SERV & PSYCHOLOGY	

AXIS I CODES: 2, 3, 9, 15, 23 **AXIS II CODES:** 30, 36, 46, 49, 60, 69

ABSTRACT

A narrative for the Assay Services Unit appears in the Infrastructure Word document appended to this report.

Essential to Assay Services but not categorized on the Personnel Roster are two lab managers, a research specialist, and student lab assistants as needed.

FUNDING: NIH P51 RR000167

NOTE: Investigators other than Drs. Abbott and Ziegler listed on this SPID are not part of Assay Services. These individuals did not submit SPIDS this year, but are described in the Infrastructure section of this report as using Assay services', therefore they should remain on the Personnel Roster as active affiliates.

WNPRC LIBRARY AND INFORMATION SERVICES UNIT (0231)

NPRC UNIT: LIBRARY

%NPRC $: 0.250% AIDS RELATED RESEARCH

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ROBINSON, CYNTHIA	MLS	C	WNPRC LIBRARY/INFO SERV	
[name]	MLS	A	PRIMATE INFORMATION CENTER	WANPRC, WA USA

AXIS I CODES: 9 AXIS II CODES: 31, 51

ABSTRACT

A narrative for Library and Information Services appears in the Infrastructure Word document appended to this report.

Essential to Library and Information Services but not categorized on the Personnel Roster are three librarians and student assistants as needed.

FUNDING: NIH P51 RR000167

WNPRC OPERATIONAL SERVICES DIVISION (0189)

NPRC UNIT: OPERATIONAL SERVICES

%NPRC $: 0.500% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KNABLE, STEVEN M	MBA	C	OPERATIONAL SERVICES/WNPRC	

AXIS I CODES: 28(OPERATIONAL SERVICES) **AXIS II CODES:** 31, 92(OPERATIONAL SERVICES)

ABSTRACT

A narrative for the Operational Services Division appears in the Infrastructure Word document appended to this report.

Essential to Operational Services but not categorized on the Personnel Roster are a facilities manager, human resources manager, payroll and benefits specialist, three information processing consultants, programmer analyst, media specialist, grants manager, stores manager, two instrument makers (shop), five program assistants, and three financial specialists.

FUNDING: NIH P51 RR000167

WNPRC PATHOLOGY SERVICES UNIT (0190)

NPRC UNIT: PATHOLOGY

%NPRC $: 0.500% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
USBORNE, AMY	DVM	C	WNPRC RESEARCH SERVICES	
[name]	DVM	C	WNPRC PATHOLOGY SERVICES	

AXIS I CODES: 28(PATHOLOGY SERVICES) **AXIS II CODES:** 31, 92(PATHOLOGY SERVICES)

ABSTRACT

A narrative for Pathology Services appears in the Infrastructure section of this report.

Essential to Pathology Services but not categorized on the Personnel Roster are a health technologist, information processing consultant, and student assistants as needed.

FUNDING: NIH P51 RR000167

WNPRC RESEARCH SERVICES DIVISION (0340)

NPRC UNIT: RESEARCH SERVICES

%NPRC $: 0.010% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
USBORNE, AMY	DVM	C	WNPRC RESEARCH SERVICES	

AXIS I CODES: 1, 1A, 1D **AXIS II CODES:** 30, 31, 46, 60, 71, 72, 74, 77, 78, 91, 93

ABSTRACT

A narrative for the Research Services Division appears in the Infrastructure Word document appended to this report.

This division includes Assay, Immunology, Virology, Library and Pathology Services.

FUNDING: NIH P51 RR000167-43

RESEARCH SUBPROJECTS

C-REACTIVE PROTEIN LEVELS WITH DIETARY RESTRICTION (0287)

NPRC UNIT: AGING & METABOLIC DISEASE

%NPRC $: 2.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
COLMAN, RICKI J	PHD	C	WNPRC AGING	
	PHD	G	WNPRC KEMNITZ LAB	
	PHD	C	WNPRC DIRECTOR & PHYSIOLOGY	
	PHD	C	WNPRC & MEDICINE & VA-GRECC	

AXIS I CODES: 1A, 13 **AXIS II CODES:** 30, 64

ABSTRACT

OBJECTIVE: To determine the effect of caloric restriction on circulating c-reactive protein levels in adult male and female rhesus macaques.

RESULTS: The past decade has seen a major shift in our understanding of the pathogenesis of cardiovascular disease. Inflammatory mechanisms are now believed to play a central role in mediating all phases of atherosclerosis. Thus attention has recently focused on whether circulating levels of inflammation markers may help identify individuals at risk for future cardiovascular events. Among several potential markers of inflammation, the acute phase reactant, c-reactive protein, is the best validated and standardized as a marker of cardiovascular risk assessment. Therefore we have recently begun to measure CRP in our animals. Our initial results, lower CRP levels in DR compared to Control animals, are consistent with decreased cardiovascular risk in the Restricted animals.

FUNDING: NIH PO1 AG11915

REPRODUCTIVE HORMONES AND DIETARY RESTRICTION (0288)

NPRC UNIT: AGING & METABOLIC DISEASE

%NPRC $: 2.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
COLMAN, RICKI J	PHD	C	WNPRC AGING	
L	PHD	C	WNPRC ASSAY SERVICES & OB/GYN	
names	PHD	C	WNPRC DIRECTOR & PHYSIOLOGY	
	PHD	C	WNPRC & MEDICINE & VA-GRECC	
1	PHD	C	WNPRC ASSAY SERV & PSYCHOLOGY	

AXIS I CODES: 1A, 15, 23 AXIS II CODES: 30, 74E, 78

ABSTRACT

OBJECTIVE: To determine if caloric restriction effects reproductive function in adult females rhesus monkeys.

RESULTS: We collected urine 3 times per week over a three month period in our Control and Restricted female rhesus macaques. These samples were then assayed for metabolites of estrogen and progesterone allowing us to plot each individual animal's reproductive hormone cycles. There were no clear group differences in the number of either progesterone or estrogen peaks, or in the total levels of these metabolites. However, on average the intervals between progesterone peaks are longer in the Control compared to Restricted animals. This is suggestive of lengthening ovulatory cycles and possible reproductive function decline in the Control animals with maintenance in the Restricted animals.

FUNDING: NIH PO1 AG11915

MOTOR FUNCTION WITH DIETARY RESTRICTION (0289)

NPRC UNIT: AGING & METABOLIC DISEASE

%NPRC $: 2.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
COLMAN, RICKI J	PHD	C	WNPRC AGING	
L	PHD	A	MEDICINE & VA-GRECC	
names	PHD	C	WNPRC DIRECTOR & PHYSIOLOGY	
J	PHD	C	WNPRC & MEDICINE & VA-GRECC	

AXIS I CODES: 1A, 20, 21, 25D AXIS II CODES: 30, 36, 78

ABSTRACT

OBJECTIVE: To determine if caloric restriction effects motor function in adult male rhesus monkeys.

RESULTS: We utilized the Automated Movement Assessment Panel developed by [Graeme] at the University of Kentucky to assess three specific movement types, reaction time, fine motor speed and coarse motor speed in 10 Control and 10 Restricted male rhesus monkeys. The apparatus was placed on the cage front configured with one of the three difficulty levels. The time it takes the animal to place his arm through the armhole is reaction time, the time the animal keeps his hand in the reward receptacle is fine motor speed, and the entire time the animals hand is within the apparatus is the coarse motor speed. Reaction times were similar between groups until the most difficult level. Although fine motor speed was similar between groups at the easiest level, both fine and coarse motor speeds were faster in the Restricted animals compared to Controls at all other levels. This data possibly indicates declining motor function in the Control animals.

FUNDING: NIH PO1 AG11915

AUDITORY THRESHOLDS AND AGING (0253)

NPRC UNIT: AGING & METABOLIC DISEASE

%NPRC $: 2.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
FOWLER, CYNTHIA	PHD	A	COMMUNICATIVE DISORDERS	
L	PHD	C	WNPRC DIRECTOR & PHYSIOLOGY	
Names	PHD	G	POPULATION HEALTH SCIENCES	
J	PHD	C	WNPRC & MEDICINE & VA-GRECC	

AXIS I CODES: 1A, 21, 25A **AXIS II CODES:** 30, 45, 57, 74, 78, 94

ABSTRACT

OBJECTIVE: To determine noninvasively the effects of aging and reduced food intake on the neurological senstivity to sounds stimuli.

Progressive sensorneural hearing loss (presbycusis) beginning in middle age is typical in humans. The change predominantly affects high-frequency tones. Reduced caloric intake (CR) has been shown to have beneficial effects on aging in several models. This subproject was designed to assess the effects of moderate CR on auditory evoked potential in rhesus monkeys eating ad libitum a reduced food allotment. We found improved responses on early middle-aged monkeys compared to late middle-aged monkeys, as predicted. We also found more robust responsiveness in females compared to males, and in restricted monkeys compared to controls.

FUTURE DIRECTIONS: We plan to continue these assessments on the effects of age, sex and diet as the animals become elderly.

FUNDING: NIH P01 AG11915

MENOPAUSAL HOT FLASHES (0198)

NPRC UNIT: AGING & METABOLIC DISEASE

%NPRC $: 0.355%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
FREEDMAN, ROBERT	PHD	A	PSYCHIATRY & OB/GYN	WAYNE STATE UNIVERSITY , MI USA
L names	PHD	C	WNPRC ASSAY SERVICES & OB/GYN	
⊥	PHD	C	WNPRC DIRECTOR & PHYSIOLOGY	

AXIS I CODES: 5A **AXIS II CODES:** 30, 93

ABSTRACT

OBJECTIVE: To develop a primate model of menopausal hot flashes.

RESULTS: More than 30 million women in the U.S. suffer from menopausal hot flashes, which are associated with severe discomfort, sleep loss, fatigue and, possibly, depression. Although hormone replacement therapy is an effective treatment for hot flashes, most women do not receive it due to a fear of cancer. A better understanding of the causes of hot flashes will aid in the development of improved treatments.

We have shown that hot flashes are triggered by small fluctuations in body temperature acting on a thermostat which is too tightly regulated. Since the thermostat (hypothalamus) is located in the middle of the brain, it is not easily studied in humans.

We are conducting a study to see if human indicators of hot flashes, such as increased skin temperature and sweating, can be replicated in the rhesus monkey. This is being accomplished by first taking out the ovaries, to simulate menopause, to see if increased temperature and sweating occur. Then estrogen is being replaced using a small implant, to see if these indicators return to premenopausal levels.

FUNDING: $435,763

private funding source

HYPOTHALAMIC MECHANISMS CONTROLLING FEEDING AND METABOLISM IN RHESUS MONKEYS (0306)

NPRC UNIT: AGING & METABOLIC DISEASE

%NPRC $: 1.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
GARELL, CHARLES	MD	A	NEUROLOGICAL SURGERY	
[name]	PHD	C	WNPRC DIRECTOR & PHYSIOLOGY	

AXIS I CODES: 1A AXIS II CODES: 52, 74

ABSTRACT

OBJECTIVE: To evaluate feeding and metabolism in rhesus monkeys in response to chemical or electrical stimulation of the hypothalamus.

Morbid obesity is a major health problem that is suboptimally treated at present. Current procedures to control appetite and obesity suffer from either low efficacy or high morbidity and mortality. The hypothalamus plays a critical role in regulating appetite and energy balance. More specifically, the lateral hypothalamus appears to regulate hunger while the ventral medial hypothalamus (VMH) regulates satiety. This is supported by studies of the hypothalamus in laboratory animals and humans (Anand et al.,1951; Quaade et al., 1974; Ruffin et al., 1997). The exact mechanism of hypothalamic control of feeding is not known but likely involves neuroactive peptides and their receptors. Neuroactive peptides such as leptin and orexin have been shown to affect feeding and metabolism in laboratory animals (Finn at al., 2001; Larsen et al., 1999; Ramsey et al., 1998). Thus, our aim is to accumulate pilot data for a physiologic model of hypothalamic function in feeding, metabolism and weight. This will serve as an important foundation for future studies of feeding and metabolism.

FUNDING: Functional Neurosurgery Program, UW Department of Neurological Surgery.

WATER SOLUABLE NUTRIENT ABSORPTION BY NONHUMAN PRIMATES (0318)

NPRC UNIT: AGING & METABOLIC DISEASE

%NPRC $: 0.500%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KARASOV, WILLIAM	PHD	A	WILDLIFE ECOLOGY	
[name]	PHD	G	WILDLIFE ECOLOGY	

AXIS I CODES: 1A, 3, 16C AXIS II CODES: 74A, 77, 78

ABSTRACT

OBJECTIVE: To better understand the digestive physiology of non-human primates.

ASTRACT BODY: We are measuring the extent of passive absorption of water soluble nutrients. This project has important implications for understanding the digestive physiology of humans and non-human primates, and also for understanding vertebrate nutritional ecology and toxicology. Many nutrients, natural toxins and man-made toxins and drugs are hydrosoluble. Efficient transport of hydrosoluble chemicals across the vertebrate small intestine is generally thought to depend on membrane transport proteins (mediated transport), but some animals can efficiently transport these chemicals through the gaps between cells (i.e., by a passive, paracellular pathway). We use physiological and pharmacokinetic techniques to test the extent of passive absorption in primates. The differential absorption of carbohydrate probes, which range in size from 150 to 666 Daltons, are used to assess how the gap between cells restricts transport according to molecular size. Differences in the absorption of two forms of glucose (D- and L-glucose) provide information about the relative rates of glucose absorption by the mediated versus passive pathways.

RESULTS: This study began during in Fall 2003. We are using WNPRC facilities, equipment and Animal Services.

FUNDING: NSF grant IBN-0216709 to William H. Karasov, $127,307 in current budget year.

REGULATION OF FOOD INTAKE AND OBESITY (0255)

NPRC UNIT: AGING & METABOLIC DISEASE

%NPRC $: 0.500%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KEMNITZ, JOSEPH W	PHD	C	WNPRC DIRECTOR & PHYSIOLOGY	
L	PHD	A	BIOSTATISTICS	UNIVERSITY OF ALABAMA-BIRMINGHAM, AL USA
names	PHD	A	MOLECULAR BIOSCI	UNIVERSITY OF CALIFORNIA-DAVIS, CA USA
J	PHD	A		PFIZER RESEARCH LABORATORIES, CT USA

AXIS I CODES: 1A, 2, 15, 21 **AXIS II CODES:** 36, 49, 50, 57, 74, 78

ABSTRACT

OBJECTIVE: To identify peptides that modulate ingestive behavior in primates.

Obesity has reached epidemic proportions in developed countries and this is having a profoundly negative impact on health and health care systems. Several peptides have recently been identified that may regulate appetite and feeding behaviors. We are evaluating the effects of central administration of these substances and their antagonists in rhesus monkeys, with the long-term aim of reducing obesity and ameliorating its consequences.

FUNDING: E J

private funding

PRIMATE AGING DATABASE (0328)

NPRC UNIT: AGING & METABOLIC DISEASE

%NPRC $: 0.025%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KEMNITZ, JOSEPH W	PHD	C	WNPRC DIRECTOR & PHYSIOLOGY	
L	PHD	A	BEHAVIORAL NEUROSCIENCES	NIA GERONTOLOGY RESEARCH CTR., MD USA
	MS	A	NORC NATIONAL OPIN AND RES CTR	UNIVERSITY OF CHICAGO, IL USA
names	PHD	A	BEHAVIORAL NEUROSCIENCE	NIA GERONTOLOGY RESEARCH CTR., MD USA
	MBA	C	WNPRC OPERATIONAL SERVICES	
	PHD	A	BEHAVIOR	SWNPRC, TX USA
J	MBA	A	NORC OPIN AND RES CTR.	UNIVERSITY OF CHICAGO, IL USA

AXIS I CODES: 1A, 1D **AXIS II CODES:** 30, 42, 68

ABSTRACT

OBJECTIVE: To develop and manage a database of primate biomarkers of aging to improve collaborative research and treatment efforts related to diseases and disorders of aging.

ABSTRACT BODY: The Primate Aging Database (PAD) is a new multi-center, relational database of biological variables in aging, captive nonhuman primates. The NIA, National Center for Research Resources (NCRR), and National Primate Research Center, University of Wisconsin-Madison, have already organized more than 400,000 data points on 17 species at nine facilities. An invaluable research, veterinary and clinical resource, PAD now features biomarkers on body weight, blood chemistry and hematology. This will grow in terms of numbers of animals and biological endpoints, using support from the new contract.

FUNDING: NIH N01-AG-3-1014

AGE-RELATED DECLINE IN TESTOSTERONE BIOACTIVITY (0341)

NPRC UNIT: AGING & METABOLIC DISEASE

%NPRC $: 0.250%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
O'MALLEY, JAMES P	PHD	A		PFIZER, INC. , CT USA
Lname	PHD	C	WNPRC DIRECTOR & PHYSIOLOGY	

AXIS I CODES: I, 1A, 2, 15, 23 **AXIS II CODES:** 30, 50B, 73, 75

ABSTRACT

OBJECTIVE: To examine age-related changes in testosterone levels, control of testosterone secretion and testosterone metabolism in older rhesus monkeys.

ABSTRACT BODY: Many middle-aged and elderly men are taking testosterone, believing it can restore the vitality of youth, improve mood and memory and increase sexual drive. Approximately 1.75 million prescriptions were written in 2002. Staff at the National Institute on Aging expressed concern that the testosterone boom was a public health issue and wanted a large clinical trial. Those at the National Cancer Institute were concerned about giving healthy men testosterone in large clinical studies when it might fuel the growth of prostate cancer. But all agreed that research needed to be done. Limited studies demonstrate that many symptoms of aging (weakness, diminished sex drive, osteoporosis and sense of malaise) occur in young men who do not make testosterone. These symptoms are reversible by testosterone therapy. Also, it is known that testosterone levels gradually decline as men grow older. However, there are limited published studies of this nature and those have been conducted with relatively small numbers of subjects. This project, currently in its earlier phases, is designed to examine in more detail age-related changes in testosterone levels, control of testosterone secretion and testosterone metabolism, using older rhesus monkeys as an animal model.

FUNDING: [ ] private funding

ASSESSING HIGH DIETARY VITAMIN A (0272)

NPRC UNIT: AGING & METABOLIC DISEASE

%NPRC $: 0.025%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
TANUMIHARDJO, SHERRY A	PHD	A	NUTRITIONAL SCIENCES	
L name J	MS	A	NUTRIONAL SCIENCES	

AXIS I CODES: 1, 2, 5 **AXIS II CODES:** 54, 56, 71, 74, 78

ABSTRACT

OBJECTIVE: To further define the effects of chronically high dietary vitamin A, we analyzed lung and kidney tissues.

RESULTS: We found elevated concentrations of retinol, retinyl oleate, palmitate, and stearate, as well as several other unidentified esters in rhesus monkey tissue. Recent work in the determination of vitamin A requirements of rhesus monkeys (Macaca mulatta) used for biomedical research has revealed subtoxic to toxic hepatic vitamin A concentrations. Histological examination of liver showed hepatic stellate cell hypertrophy and hyperplasia, which in conjunction with findings of high serum retinyl esters in both the liver tissue and serum, provide sufficient justification for further study in this area. Meanwhile, the livers of marmoset monkeys (Callithrix jacchus), another common experimental animal, were also high in vitamin A, as was serum retinyl ester concentrations, although no evidence of stellate cell irregularities was apparent. Both species had consumed commonly used research diets providing vitamin A as preformed retinyl acetate that exceed National Research Council recommendations for vitamin A by as much as four times.

FUNDING: NIH NIDDK 61973. C Private funding J

DIETARY RESTRICTION AND AGING IN RHESUS MONKEYS (0160)

NPRC UNIT: AGING & METABOLIC DISEASE

%NPRC $: 2.500%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
WEINDRUCH, RICHARD	PHD	C	WNPRC & MEDICINE & VA-GRECC	
L	PHD	G	WNPRC KEMNITZ LAB	
names	PHD	C	WNPRC AGING	
	PHD	C	WNPRC DIRECTOR & PHYSIOLOGY	
	PHD	A	NUTRITIONAL SCIENCES	
J	PHD	C	WNPRC WATKINS LAB	

AXIS I CODES: 1A, 1D, 20, 26

AXIS II CODES: 30, 49, 58, 74A, 74C, 78

ABSTRACT

OJECTIVE: To explore the possibility that dietary restriction retards aging processes in a nonhuman primate species.

RESULTS: This Program Project has provided a wealth of new information about the biology of aging and how the manipulation of diet can influence the process of growing old. Rhesus monkeys eating 30 percent fewer calories of a nutritionally complete diet exhibit better health than study controls. Reduced caloric intake seems to slow basic aging processes and may extend the maximum life span in primates, as has been shown in rodents.

--Diabetes develops less frequently in monkeys on a restricted diet. Animals allowed to eat freely have a greater incidence of diabetic or pre-diabetic conditions.

--Fasting basal insulin and glucose concentrations are lower in monkeys on a restricted diet.

--Both fat mass and fat-free mass were lower in monkeys on a restricted diet.

--Monkeys on a reduced-caloric diet have fewer signs of spinal arthritis, a condition that manifests itself with age in both rhesus monkeys and humans.

--Results so far suggest that fewer calories may reduce the risk of vascular disease.

--Caloric restriction altered circulating LDL in a manner that may inhibit atherogenesis.

--Caloric restriction retards several age-dependent physiological and biochemical changes in skeletal muscle, including oxidative damage.

--Physical activity is about the same for both the restricted and control monkeys.

--Controlled caloric restriction has not disrupted menstrual cycles of female monkeys.

The next five years of the study should be even more insightful, as the oldest monkeys in the study enter late middle age. During this phase, age-related diseases and disorders appear more frequently, including adult-onset diabetes, osteoporosis, cancers, obesity, hypertension and the loss of skeletal muscle mass.

FUNDING: NIH P01 AG11915

DIETARY RESTRICTION AND SARCOPENIA IN AGING RHESUS MACAQUES (0266)

NPRC UNIT: AGING & METABOLIC DISEASE

%NPRC $: 0.500%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
WEINDRUCH, RICHARD	PHD	C	WNPRC & MEDICINE & VA-GRECC	
names	PHD	A	ANIMAL HEALTH & BIOMEDICAL SCI	
	PHD	A	ANIMAL HLTH & BIOMED SCI	

AXIS I CODES: 1D, 20 **AXIS II CODES:** 30, 78

ABSTRACT

OBJECTIVE: To determine whether sarcopenia is causally associated with mitochondrial DNA (mtDNA) deletion mutations and subsequent electron transport system (ETS) dysfunction, leading to oxidatively damaged muscle fibers that atrophy. Further, to determine whether dietary restriction affects these changes.

The loss of skeletal muscle mass with age (sarcopenia) contributes to deficits in strength and an overall increase in physical frailty in older individuals. Accordingly, saropenia is a geriatric process of huge public health significance.

RESULTS: During the past year we have continued collection and analysis of whole quadriceps muscles and heart tissue necropsy samples from aging rhesus macaques. We have also collected and analyzed 12-year vastus lateralis muscle biopsy samples from all control and dietary restricted Group I male rhesus monkeys and identified muscle fibers and cardiomyocytes with ETS abnormalities using both phenotypic and genotypic analysis. Our growing data set provides for the analysis of whole muscle weight and is beginning to indicate signficant muscle mass loss with age. Muscle weight values for animals in their 30s were lower than muscle weights for monkeys in their teens and 20s. The muscle mass loss in the vastus lateralis muscle is significant. Twenty-three Group I male rhesus monkeys remain in the dietary restriction study (12 control and 11 restricted). The previous year biopsies were completed on all Group I monkeys. Adult onset dietary restriction began on adult monkeys in 1990. The first biopsies were taken after 6 years (1996-1997) of restriction, the second at 9 years (1999-2000) and the third at 12 years (2002-2003). These samples are undergoing analysis for ETS abnormalities, fiber cross-sectional area, fibrosis, oxidative damage and numbers of neuro-muscular junctions to provide a longitudinal analysis of muscle mass loss with age in the rhesus macaque.

FUNDING: NIH PO1 AG 11915

LENTIVIRUS ATTENUATION THROUGH HIGH FIDELITY REPLICATION (0322)

NPRC UNIT: AIDS COMPONENT

%NPRC S: 2.500% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
DEWHURST, STEPHEN	PHD	A	MICROBIOL/MMUNOL & ONCOLOGY	UNIVERSITY OF ROCHESTER MEDICAL CTR., NY USA
L	PHD	A	MICROBIOLOGY & IMMUNOLOGY	UNIVERSITY OF ROCHESTER MEDICAL CTR., NY USA
MeMes	PHD	A		UNIVERSITY OF ROCHESTER MEDICAL CTR., MN USA
J	PHD	C	WNPRC & PATHLAB MED	

AXIS I CODES: 1A, 1D, 7B, 17, 19 **AXIS II CODES:** 31, 64, 66, 83, 91, 94

ABSTRACT

OBJECTIVE: To address the relationship of viral escape to viral pathogenesis in SIV, to provide insight into the potential utility of using high fidelity RT mutants to improve the safety of live-attenuated viruses.

ABSTRACT BODY: Human Immunodeficiency Virus type-1 (HIV-1) reverse transcriptase (RT) is a highly error-prone enzyme thought to be responsible for the generation of viral genetic diversity. This in turn might be essential to the virus' ability to evade host immune responses, and to establish a state of persistent, productive infection. We hypothesize that viruses with enhanced replicational fidelity will generate fewer mutants than wild-type viruses, and that such "high fidelity" viruses may be incapable of escaping from host immune pressure, due to their inability to spawn highly diverse quasispecies. If correct, this hypothesis could have important implication for the design of live-attenuated HIV vaccines. This represents a proof-of-concept study designed to test whether a high fidelity primate lentivirus is indeed attenuated in terms of the generation of new mutants and escape from immune pressure within a nonhuman primate host. We are using the Simian Immunodeficiency Virus (SIV)/macaque model system for these experiments. We will create SIVmac239 high-fidelity RT mutants and generate virus stocks (SIVmac239hifi). Clones with fitness similar to WT will be inoculated into macaques and the development of virus specific responses examined. We will monitor virus load and sequence to assess escape. This study aims to gain insight into using high-fidelity RT mutants to improve the safety of live-attenuated HIV vaccines.

RESULTS: None yet.

FUNDING: NIH R21-AI-049102

SIV T CELLS IN VIVO (0292)

NPRC UNIT: AIDS COMPONENT

%NPRC $: 1.500% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
HAASE, ASHLEY T	MD	A	MICROBIOLOGY	UNIVERSITY OF MINNESOTA, MN USA
[name]	PHD	A	VETERINARY & BIOMED SCIENCES	UNIVERSITY OF MINNESOTA, MN USA

AXIS I CODES: 1D, 9 **AXIS II CODES:** 31, 64, 66

ABSTRACT

OBJECTIVE: To study SIV specific CD8+ T cell function, localization, and association with SIV infected cells in vivo in vaccinated and non-vaccinated macaques in order to gain insights into SIV pathogenesis.

RESULTS: Studies of SIV infections in macaques serve as a corollary to HIV infections in humans. During the last year, we made much progress in our efforts to gain insights into SIV specific CD8+ T cell responses in vivo. We continue to receive tissues from macaques at the WNPRC, and still have projects underway with WNPRC monkeys. For each animal, we stained SIV specific CD8+ T cells in relevant tissues. We are determining the localization and abundance the SIV specific T cells in each tissue. We are comparing the virus specific CD8+ T cell response in vaccinated to non-vaccinated animals. We recently developed a method to visualize SIV infected cells and SIV specific CD8+ T cells simultaneously, and we developed a method to study the functional status of SIV specific CD8+ T cells in vivo.

FUNDING: Wisconsin National Primate Research Center Support: Immunology Base Grant -Haase Subcontract, NIH/NIAID, P51 RR000167-42, $50,582 (sub only)

36

PATHOGENESIS OF MUCOSAL TRANSMISSION/HIV ACUTE TRANSMISSION (0323)

NPRC UNIT: AIDS COMPONENT

%NPRC S: 1.500% AIDS RELATED RESEARCH

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
HAASE, ASHLEY T	MD	A	MICROBIOLOGY	UNIVERSITY OF MINNESOTA, MN USA
Lname_1	PHD	C	WNPRC & PATHLAB MED	

AXIS I CODES: 1D, 7B, 17, 19 AXIS II CODES: 31, 64, 66, 83, 91, 94

ABSTRACT

OBJECTIVE: To gain a deeper understanding of heterosexual transmission of HIV.

ABSTRACT BODY: Simian immunodeficiency virus (SIV) is an excellent animal model for HIV. Rhesus macaques will be infected with SIV intravaginally. Cells and tissue samples will be obtained. Tissues will be evaluated to discover which cell types are infected with virus using in situ hybridization and PCR-based techniques. The cellular immune response will also be evaluated. Virus-specific cytotoxic T cells (CTLs) will be identified and characterized. These studies will establish mechanisms and dynamics of viral propagation and dissemination and the immune response to the viral challenge.

FUNDING: NIH 1 R01 AI48484

CENTERS FOR AIDS RESEARCH NONHUMAN PRIMATE MODELS CORE RESOURCE (0333)

NPRC UNIT: AIDS COMPONENT

%NPRC $: 10.500% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KEMNITZ, JOSEPH W	PHD	C	WNPRC DIRECTOR & PHYSIOLOGY	
L	PHD	C	WNPRC IMMUNOLOGY SERVICES	
names	PHD	C	WNPRC & PATHLAB MED	
1	MD	A	COMPREHENSIVE AIDS CENTER	NORTHWESTERN UNIVERSITY, IL USA

AXIS I CODES: 1A, 1D, 19 **AXIS II CODES:** 31, 66, 77, 83, 91

ABSTRACT

OBJECTIVE: To conduct basic, clinical and animal models research on HIV transmission, pathogenesis, vaccination and therapy, in support of a multi-center quest to find a vaccine for HIV and stop the worldwide AIDS epidemic.

ABSTRACT BODY: The WNPRC manages the Nonhuman Primate Models Core Laboratory in support of the Great Lakes Regional Center for AIDS Research (CFAR), established through a $9 million NIH NAIDS grant in 1998. Participants include the Universities of Chicago, Michigan, Minnesota and Wisconsin.

CFARs provide a pool of shared resources, such as technical expertise, equipment and training; to local AIDS researchers. The centers also advance AIDS research by facilitating interdisciplinary and international collaborations, technology transfer through academic-industry collaborations, research dissemination activities and community outreach promotion.

RESULTS: The Nonhuman Primate Models Core Lab provides tissue and blood specimens from ongoing or archived studies of SIV or SHIV infection in rhesus macaques. In addition, the WNPRC has recently acquired colonies of vervets and cynomolgous macaques for use as models for researching AIDS. WNPRC AIDS researchers develop new experimental protocols to test concepts in disease prevention. These would include innovative approaches to gene therapy, and developmental and preclinical studies on vaccines. They also collect data on Major Histocompatibility Complex genotype of animals in treatment or prevention studies.

Since 1988, the national CFAR program has sponsored many advances in AIDS research, including identification of new co-receptors for HIV, the role of cytotoxic T-lymphocytes in early infection and in controlling virus replication, and the use of antiretroviral drugs as probes to understand the dynamics of HIV replication. The program also has developed community research laboratories with capabilities such as flow cytometry and DNA sequencing, and has made those resources available to AIDS researchers in many communities.

The centers are committed to addressing the particular concerns of minority communities. They explore ways to increase the number of minority scientists involved in AIDS research. They also handle problems related to enrollment and retention of women and minorities in AIDS clinical trials.

FUNDING: NIH NIAID CFAR (Center for AIDS Research)

CTL-BASED VACCINES FOR THE AIDS VIRUS (0147)

NPRC UNIT: AIDS COMPONENT

%NPRC $: 1.000% AIDS RELATED RESEARCH

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
WATKINS, DAVID I	PHD	C	WNPRC & PATHLAB MED	
	PHD	A	BIOSTATISTICS	UNIVERSITY OF ALABAMA-BIRMINGHAM, AL USA
	PHD	A	MICROBIOLOGY & IMMUNOLOGY	EMORY UNIVERSITY, GA USA
	PHD	A		POWDERJECT VACCINES , WI USA
	MD	A	MICROBIOLOGY	UNIVERSITY OF MINNESOTA, MN USA
	PHD	A	PATHOBIOLOGICAL SCI (VET SCH)	
	DVM, PHD	A	CNPRC	UC-DAVIS, CA USA
	MD	A	COMPREHENSIVE AIDS CENTER	NORTHWESTERN UNIVERSITY, IL USA

AXIS I CODES: 1A, 1D, 7B, 17, 19 AXIS II CODES: 31, 64, 66, 83, 91, 94

ABSTRACT

OBJECTIVE: To generate strong cytotoxic T lymphocytes (CTL) responses using several different vaccine approaches.

ABSTRACT BODY: We are determining the role of CTL in control of viral replication using the SIV-infected rhesus macaques as an animal model for HIV-infected humans. We are attempting to generate strong CTL responses in the absence of any other SIV-specific immune responses and challenge vaccinated animals with SIV. We are attempting to generate CTL against multiple epitopes in several different SIV proteins. We are inducing CTL at mucosal sites. This will allow us to test the hypothesis that CTL can ameliorate the course of disease after infection.

RESULTS: We observed robust immune responses after the first rMVA, which was given i.n. and i.d. However, mucosal markers were not observed on tetramer positive cells. After the second rMVA, robust immune responses were observed, the highest responses ever seen. All monkeys were challenged with high doses of SIVmac239 i.r. 16 weeks after the final rMVA boost. In vaccinated animals, the peak of viremia was significantly reduced by a log, but by three weeks post infection, there was no difference in viral load between vaccinated and control animals. Neutralizing antibodies were not observed to SIVmac239.

We identified two Mamu A*02 alleles, Gag71-79GY9 and Nef159-167YY9. The Nef159-167YY9 epitope is immunodominant, has high functional avidity and escapes rapidly.

Mamu-A*01+ -B*17+ animals survive longer than either allele alone. In a second study, we found that animals which bear the combination of Mamu A*01, Mamu B*17 and Mamu B*29 alleles are often able to control their infection.

In a new study, 8 A*01 animals were vaccinated with DNA encoding whole gag, tat, nef and rev. They will be given adenovirus encoding these same proteins in the same limb, then will be challenged with a low dose SIVmac239 to more realistically emulate sexual transmission in humans.

FUNDING: NIH AI46366

AIDS & DIETARY RESTRICTION AND AGING IN RHESUS MACAQUES (0324)

NPRC UNIT: AIDS COMPONENT

%NPRC $: 0.500% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
WEINDRUCH, RICHARD	PHD	C	WNPRC & MEDICINE & VA-GRECC	
L	PHD	C	WNPRC AGING	
names	PHD	C	WNPRC & PATHLAB MED	
J	MD	A	COMPREHENSIVE AIDS CENTER	NORTHWESTERN UNIVERSITY, IL USA

AXIS I CODES: 1A, 1D, 7B, 17, 19 **AXIS II CODES:** 30, 31, 64, 66, 91, 94

ABSTRACT

OBJECTIVE: To understand what is different about the aging immune system, we are vaccinating animals that are dietarily restricted or not with the well characterized SIV vaccination regimen. We will compare immune responses in old, dietary-restricted and young animals.

ABSTRACT BODY: Viral infections are important pathogens in the elderly. Immune responses play a major role in protecting individuals from lethal infection with viruses. Evidence suggests that T cell function is compromised in both old rodents and humans. Our hypothesis is that dietary restriction (DR) can prevent the deficiencies induced by aging. We will quantitate the cellular immune response to vaccination in young, control (old) and dietary restricted (DR) rhesus macaques. The unique cohort of animals provided by the core represents an invaluable resource of animals that will allow us to test hypotheses concerning the role of aging and DR on the immune response of primates in virus infection.

RESULTS: We observed a broad and robust immune response to the vaccine regimen. We observed no differences in the breadth or intensity of responses (number of epitopes responded to in an animal) or the magnitude of the response (percent of antigen specific CTL) between the three groups.

FUNDING: NIH AG11915

ALLOIMMUNIZATION AS AN ANTI-SIV IMMUNIZATION STRATEGY (0311)

NPRC UNIT: IMMUNOLOGY

%NPRC $: 1.500% AIDS RELATED RESEARCH

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
MACDONALD, KELLY S	MD	A	DIVISION OF CLINICAL SCIENCES	UNIVERSITY OF TORONTO, CANADA
L	PHD	A	DIVISION OF CLINICAL SCIENCES	UNIVERSITY OF TORONTO, CANADA
names	PHD	C	WNPRC IMMUNOLOGY SERVICES	
J	PHD	C	WNPRC & PATHLAB MED	

AXIS I CODES: 1A, 2, 3, 7B, 9, 19 AXIS II CODES: 31, 64, 66, 83, 91, 94

ABSTRACT

OBJECTIVE: To determine in an animal model (SIV in the Rhesus Macaque) whether vaccines to elicit immune responses to MHC molecules should be considered as HIV vaccine candidates in humans.

RESULTS: Simian Immunodeficiency Virus and Human Immunodeficiency Virus are envelope viruses that form at the surface of infected cells and that incorporate a portion of the host cell membrane. In addition to viral surface glycoproteins, host cell proteins are found in the viral envelope. The proteins of the major histocompatibility complex (MHC) are found in abundance, exceeding in density the major viral glycoprotein gp120. Immunization of Simian Macaques (Macaca Mulatta) with xenogeneic major histocompatibility complex class I and class II molecules has been shown to protect against an SIV challenge (Chan, W. L. et al. 1995. AIDS 9:223-8, Arthur, L. O. et al. 1995. J Virol. 69:3117-24). Antibody to xenogeneic (human) MHC on the challenge virus has been implicated (Gardner, M., et al. 1995. AIDS Res Hum Retroviruses. 11:843-54). Xenoimmunity, or immunity to MHC molecules of another species, is qualitatively different from alloimmunity, the immune response to MHC molecules of other individuals of the same species. The natural transmission of HIV, however, involves the acquisition of virus from another member of the same species. Thus a protective immunization in humans based on immunity to MHC molecules would involve alloimmunization. These experiments address that issue, by immunizing with allogeneic MHC followed by challenge with SIV bearing the same allogeneic molecules. During FY2003/2004, 16 immunized and challenged animals were monitored for AIDS pathogenesis.

For day-to-day animal handling we utilize the WNPRC Animal Care Unit, for viral challenge and virus detection we work closely with the Virology Unit, and to monitor pathogenesis and SIV specific immune responses we collaborate with the Immunology Core Laboratory.

FUNDING: L 3 ($222,397).

private funding source

IGG FC DOMAIN CONTAINING PROTEINS AS MUCOSAL VACCINATION VEHICLES (0337)

NPRC UNIT: IMMUNOLOGY

%NPRC S: 1.100% AIDS RELATED RESEARCH

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
RAKASZ, EVA	PHD	C	WNPRC IMMUNOLOGY SERVICES	

AXIS I CODES: 1D, 2, 3, 16C, 17 AXIS II CODES: 31, 64, 66, 77, 91

ABSTRACT

OBJECTIVE: To establish a model in rhesus macaques to utilize a transporter molecule for mucosal vaccination.

RESULTS: The prolonged expression of neonatal Fc receptor in humans may provide a novel mechanism for oral antigen administration in the form of chimeras of selected antigens and the IgG Fc domain. This new transportation mechanism might facilitate simple, inexpensive mucosal vaccination regimens, enabling the delivery of selected antigens to the mucosal compartment. Since it is now apparent that mucosal immune responses are crucial in the control of both SIV and HIV replication, this approach may be important in generating long-lasting protection from these immunodeficiency viruses. Our long-term goal is to establish mucosal vaccination regimens in humans that utilize fusion proteins of relevant HIV antigens and IgG Fc domains. Our short-term goal is to perform initial feasibility studies with human IgG (huIgG) in the rhesus macaque model system. In this pilot study we determine whether human immunoglobulins are bound by the neonatal Fc eceptor of rhesus macaques. We have performed RT-PCR on mRNA isolated from blood of adult rhesus macaques, using PCR primers designed on the basis of highly conserved genomic sequences between rodents, bovine and human FcRn heavy chain. We have sequenced the PCR product to confirm its identity. Furthermore we have constructed and expression vector to transfect human cell lines to perform in vitro binding experiments.

FUNDING: 0600 370 XAC1 504 (Nonhuman Primate Models Core through Northwestern University CFAR grant), NCI, CFDA# 93 397, $40,000

POPULATION CODING OF VISUAL MOTION AND BINOCULAR DISPARITY IN RHESUS MONKEYS (0237)

NPRC UNIT: NEUROBIOLOGY

%NPRC $: 0.500%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
GRUNEWALD, ALEXANDER	PHD	A	PSYCHOLOGY AND PHYSIOLOGY	

AXIS I CODES: 1A, 21, 25B

AXIS II CODES: 36, 41, 42, 52, 63C, 68, 84

ABSTRACT

OBJECTIVE: To study how populations of neurons represent visual information.

RESULTS: While it is known that populations of neurons jointly represent visual information, the mechanisms by which they do so are not well understood. To address this we are studying groups of neurons in the middle-temporal area (MT), a part of the brain that contains many neurons that respond selectively to the direction of motion and the binocular disparity of visual stimuli. The proposed experiments are designed to explore whether neuronal activity correlations between neurons enhance, hinder, or do not affect the ability of a population of neurons to represent information in comparison to the same neurons taken in isolation. This proposal has three specific aims. The first aim tests the hypothesis that for simple stimuli that contain a single direction of motion the information encoded by a population of neurons depends strongly on inter-neuronal correlations. The second aim tests the hypothesis that complex stimuli containing several movement directions are encoded in a similar fashion as simple stimuli. The third aim tests the hypothesis that correlations within a population of neurons are decoded to give rise to a percept. To study these aims, we are training animals to observe visual stimuli and to report what they see. At the same time we are collecting the activity of several MT neurons. We will subsequently analyze these neural data with advanced statistical techniques to determine the nature of correlations, and the information represented. Taken together, these research aims represent the first studies to directly explore the relevance of correlations for encoding and decoding of visual information by a population of neurons. These studies are essential to understand how the visual system functions in normal and diseased states.

This work used WNPRC Animal Services.

FUNDING: [illegible] $75,000 per year

private funding source

PRIMATE SLEEP AND THE AMYGDALA (0112)

NPRC UNIT: NEUROBIOLOGY

%NPRC $: 0.025%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KALIN, NED H	MD	A	PSYCHIATRY	
L	MD, PHD	A	PSYCHIATRIC RESEARCH INSTITUTE	
names 1	PSYD	A	PSYCHIATRY	

AXIS I CODES: 1A, 21 **AXIS II CODES:** 36, 72, 85

ABSTRACT

OBEJCTIVE: To perform preclinical studies to examine neural circuits and mechanisms underlying primate sleep

RESULTS: Increased daytime emotionality, anxiety, and depression are commonly associated with sleep alterations. Since the amygdala plays an important role in emotional processing and is connected to sleep regulating regions, we are examining the role of the primate amygdala in regulating sleep. These studies are of particular relevance since sleep patterns in rhesus monkeys are similar to those in humans.

This research used WNPRC Animal Services.

FUNDING: NIMH MH46729

CILIARY MUSCLE AGING AND PRESBYOPIA (0122)

NPRC UNIT: NEUROBIOLOGY

%NPRC $: 0.500%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KAUFMAN, PAUL L	MD	A	OPHTHALMOL & VISUAL SCIENCE	
[name]	MS	A	OPHTHALMOLOGY & VISUAL SCIENCE	

AXIS I CODES: 1A, 9, 21, 25B

AXIS II CODES: 30, 63H, 77, 92(PRESBYOPIA)

ABSTRACT

OBJECTIVE: To understand human presbyopia by studying the dynamics of accommodation and presbyopia in nonhuman primates.

RESULTS: Non-human primates are the preferred model for human presbyopia, the loss of ability to focus with age. We determined real-time dynamics of the intraocular structure involved in accommodation during midbrain electrical stimulation. These studies generated new information about the mechanisms of accommodation. Centrally stimulated maximum accommodative amplitude declined significantly with age, suggesting that such stimulation is valid for studying accommodation and presbyopia. The decline of accommodation vs age in the current study is similar to humans (adjusted for lifespan). The neurological pathway in the older monkey can function to induce ciliary muscle (CM) accommodative responses at least as well as in the young monkey. Lens centripetal movement decreased with age, possibly due to a loss of forward CM movement, which was more pronounced than the loss of centripetal CM movement. The space between the lens and CM declined with age and was significantly correlated with accommodation. This space does not impact accommodation directly, but may be an indicator of another presbyopia-related process or processes that impacts accommodation, such as the age-related loss of lens equator accommodative movement, diminished ciliary ring diameter or axial lens thickening. Intraocular lenses (IOL) were studied, which have the potential to restore accommodation in the presbyopic eye.

This research used WNPRC Pathology Services.

FUNDING: NIH EY10213, Shenasa Medical LLC (NIH subcontract to UW), [private funding]

EFFECTS OF COMPOUNDS ON CILIARY MUSCLE CONTRACTION IN VITRO (0218)

NPRC UNIT: NEUROBIOLOGY

%NPRC $: 0.500%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KAUFMAN, PAUL L	MD	A	OPHTHALMOL & VISUAL SCIENCE	
Lname_1	MS	A	OPHTHALMOLOGY & VISUAL SCIENCE	

AXIS I CODES: 1D, 25B AXIS II CODES: 50, 92(GLAUCOMA)

ABSTRACT

OBJECTIVE: To determine whether compounds which generate nitric oxide (NO) can relax carbachol contracted or resting ciliary muscle (CM) in vitro. This will indicate whether this class of compounds may be useful in enhancing uveoscleral outflow as an approach for lowering intraocular pressure in glaucoma.

RESULTS: Nitric Oxide (NO) donors such as SNP and ISDN were most effective in relaxing precontracted CM in vitro. The non-selective NO synthase inhibitor L-NAME induced further contraction, possibly suggesting some endogenous production of NO in the longitudinal CM. NO compounds have potential value in therapeutic areas where relaxation or contraction of the CM is desirable, such as the treatment of glaucoma.

This research used WNPRC Pathology Services.

FUNDING: NIH EY02698

EFFECTS OF COMPOUNDS ON OUTFLOW FACILITY IN ORGAN-CULTURED ANTERIOR SEGMENTS (0220)

NPRC UNIT: NEUROBIOLOGY

%NPRC $: 0.025%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KAUFMAN, PAUL L	MD	A	OPHTHALMOL & VISUAL SCIENCE	
[illegible]	MS	A	OPHTHALMOLOGY & VISUAL SCIENCE	

AXIS I CODES: 1D, 9, 25B AXIS II CODES: 50, 77, 92(GLAUCOMA)

ABSTRACT

OBJECTIVE: To determine the effects of potential glaucoma therapeutic agents on outflow through the trabecular meshwork in vitro.

RESULTS: H-7, a compound shown to increase outflow facility in monkey eyes in vivo, was also effective in increasing outflow facility in this system thus validating the technique. A viral vector containing a gene that alters the actin cytoskeleton was also found to be effective in increasing outflow facility in this system by targeting the trabecular meshwork outflow pathway.

This research used WNPRC Pathology Services.

FUNDING: NIH EY02698

USHER SYNDROME, RETINITIS PIGMENTOSA AND GENETIC MUTATIONS IN RHESUS MACAQUES (0330)

NPRC UNIT: NEUROBIOLOGY

%NPRC $: 0.025%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KIMBERLING, W.J.	PHD	A		BOYS TOWN NATL RESEARCH HOSP, NE USA
L	PHD	A	NEUROSCIENCE	ONPRC, OR USA
	PHD	A		BOYS TOWN NATL RESEARCH HOSPITAL, NE USA
	PHD	C	WNPRC DIRECTOR & PHYSIOLOGY	
names	PHD	A		ONPRC, OR USA
	PHD	A		CNPRC, CA USA
	PHD	A	NEUROSCIENCE	ONPRC, OR USA
	PHD	A		BOYS TOWN NATL RESEARCH HOSP, NE USA
J	PHD	A		BOYS TOWN NATL RESEARCH HOSPITAL, NE USA

AXIS I CODES: 1A, 21, 25A, 25B **AXIS II CODES:** 45, 46, 55, 58, 77

ABSTRACT

OBJECTIVE: To screen rhesus macaques for genetic material that may be a cause of retinitis pigmentosa (RP), a characteristic of Usher Syndrome.

ABSTRACT BODY: Usher Syndrome, a recessive disorder characterized by RP and sensorineural hearing loss, is the leading cause of combined hearing and vision loss among humans in the industrialized world, affecting 25,000-30,000 people in the United States. Mutations in the USH2A gene account for over half of Usher Syndrome cases and 25-50% of autosomal recessive RP cases, which affect about 67,000 people in the United States. Disparities in retina function indicate that rodents may not be ideal models for this type of RP. Based on the carrier rate for the average recessiv gene, we predict that screening about 500 macaques has about 95 percent probability of detecting a pathologic mutation. We are screening for macaque carriers of USH2A mutations because these mutations are a common genetic cause of RP in humans.

RESULTS: We found evidence of genetic mutations that indicate that a macaque model for RP will provide insights into pathologic mechanisms of RP and may be better suited than mice for testing new treatments that could reduce or prevent inherited blindness.

FUNDING: L private funding J; NIH NEI RO3EY013991-02, NIH NIDCD R21DC05472-02

DEEP BRAIN STIMULATION AND PARKINSON'S DISEASE (0320)

NPRC UNIT: NEUROBIOLOGY

%NPRC $: 0.010%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
MONTGOMERY, ERWIN	MD	A	WPRC NEUROLOGY	
names	MD	A	NEUROLOGICAL SURGERY	
	MS	A	NEUROLOGY	

AXIS I CODES: 1A, 9, 21 AXIS II CODES: 30, 46, 77

ABSTRACT

OBJECTIVE: To learn how the brain controls movement and what goes wrong in the brain with Parkinson's Disease.

We are studying how the brain responsed to deep brain stimulation (DBS) as a method for treating symptoms of Parkinson's Disease. DBS is proving effective in reversing the symptoms of Parkinson's Disease in some, but not all patients. The therapy involves implanting a modified electronic cardiac pacemaker into the chest, and connecting this stimulator to electrodes implanted deep within the brain. However, researchers are not certain why it works in some people and not in others. More knowledge gained from nonhuman primate studies using this electrical, versus pharmaceutical approach to treating Parkinson's may help doctors help more patients with this and other neurological conditions in the future.

RESULTS: None yet. Project is just starting and no animals have yet been assigned.

Preliminary work has used WNPRC Operational Services (Shop) to build special equipment necessary for this research to proceed.

FUNDING: Pending.

PARKINSON'S DISEASE (0327)

NPRC UNIT: NEUROBIOLOGY

%NPRC $: 0.500%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
MONTGOMERY, ERWIN	MD	A	WPRC NEUROLOGY	
L	PHD	C	WNPRC ASSAY SERVICES & OB/GYN	
	PHD	A	PHYSIOLOGY	
	PHD	A	MEDICAL PHYSICS	
	MD, PHD	A	NEUROLOGICAL SCIENCES	RUSH UNIVERSITY, IL USA
names	MD	A	NEUROLOGICAL SURGERY	
	PHD	A	MEDICAL PHYSICS	
	PHD	C	WNPRC DIRECTOR & PHYSIOLOGY	
	PHD	A		STANFORD UNIVERSITY, CA USA
	PHD	A	ANATOMY	
	PHD, VMD	C	WNPRC STEM CELL RES & ANATOMY	
J	MD, PHD	A	ANATOMY	

AXIS I CODES: 1, 1A, 1D **AXIS II CODES:** 30, 46, 77, 88

ABSTRACT

OBJECTIVE: To construct the infrastructure to facilitate a comprehensive program on Parkinson's disease (PD) using nonhuman primate models.

ABSTRACT BODY: Rhesus monkeys, cynomolgus monkeys and African Green monkeys will be studied, and the MPTP model of PD induction will be used. Therapeutic modalities including replacement of dopaminergic neurons with stem cells and neuroprogenitor cells, delivery of neurotrophic factors by genetic engineering of stem cells, and deep brain electrical stimulation are envisioned. Expertise in nonhuman primate models of PD, neuro-imaging, stem cell biology and clinical application of PD therapies is being assembled.

FUNDING[ ]NIH RR00167

private funding

THE MECHANISM OF LHRH PULSE GENERATION AND STEROID FEEDBACK (0223)

NPRC UNIT: NEUROBIOLOGY

%NPRC $: 0.250%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
TERASAWA, EI	PHD	C	WNPRC ASSAY SERVICES & PEDS	
L	PHD	C	WNPRC ASSAY SERVICES & OB/GYN	
names	PHD	G	WNPRC TERASAWA LAB	
J	PHD	A	NEUROBIOLOGY AND PHYSIOLOGY	NORTHWESTERN UNIVERSITY, IL USA

AXIS I CODES: 1A, 15, 21 AXIS II CODES: 60, 71, 74H, 93

ABSTRACT

OBJECTIVE: To understand the mechanism of LHRH pulse generation and the mechanism of steroid action on LHRH neurons in vitro.

ABSTRACT BODY: In vitro studies, LHRH neurons originating from the olfactory pit/placode region were cultured and examined for the cellular mechanism of LHRH pulse generation. Upon receipt of supplemental funding, we have established a patch-clamp recording set up. We have found: 1) with the cell attached patch configuration, monkey LHRH neurons show spontaneous rhythmic bursting action potentials (3-7 spikes/burst) with a periodicity of 5-20 sec, and depolarization with high extracellular potassium resulted in an increase in the frequency of action current; 2) With the perforated patch clamp technique the resting membrane potential of monkey LHRH neurons was –80 to –90 mV and the activation threshold was –39.2±0.3 mV inducing action potentials with an amplitude of 88.7±1.2 mV and duration of 1.39 ms at half-amplitude. Some of these characteristics in monkey LHRH neurons were similar to those described for mouse LHRH neurons and GT1 cells, but the resting membrane potentials in monkey LHRH neurons were lower and the periodicity of bursting action potentials was much slower than mouse LHRH neurons and GT1 cells. We also found that LHRH neurons respond to estrogen with a short latency (within several minutes) stimulating the frequency of intracellular calcium oscillations, the frequency of synchronization of intracellular calcium oscillations, and LHRH release. These findings are important for the development of contraceptive tools and treatment of infertility.

Not categorized on the Personnel Roster but essential to the Terasawa lab are two research specialists and several undergraduate students.

FUNDING: NIH HD15433-18 $202,500 and Supplement $25,016

HYPOTHALAMIC MECHANISM OF THE ONSET OF PUBERTY (0224)

NPRC UNIT: NEUROBIOLOGY

%NPRC $: 0.250%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
TERASAWA, EI	PHD	C	WNPRC ASSAY SERVICES & PEDS	

AXIS I CODES: 1A, 15, 21 **AXIS II CODES:** 60, 71, 74H, 93

ABSTRACT

OBJECTIVE: To investigate the role of ATP in puberty.

ABSTRACT: Evidence from other laboratories indicate that glia in the hypothalamus may be important for the mechanism of the onset of puberty. Because glia releases ATP, we investigated the possible role of ATP in the pubertal LHRH increase at the onset of puberty in female rhesus monkeys. Results suggest that 1) ATP stimulated LHRH release with prepubertal monkeys being more sensitive to ATP than pubertal monkeys and that 2) a high level of endogenous ATP in the stalk-median eminence region in pubertal monkeys interfered with ATP's effects, as apyrase's effects are larger in pubertal monkeys than in prepubertal monkeys. Our collateral study also indicates that adult ovariectomized monkeys were less sensitive to ATP than pubertal monkeys. Taken together, the present study indicates that ATP potentially plays an important role in the mechanism of the onset of puberty in non-human primates. The results are consistent with the hypothesis, and important for better understanding a current trend in precocious puberty in boys and girls.

FUNDING: NIH HD11355-21 $184,275

CHANGES IN LHRH RELEASE IN AGED MONKEYS (0225)

NPRC UNIT: NEUROBIOLOGY

%NPRC $: 0.250%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
TERASAWA, EI	PHD	C	WNPRC ASSAY SERVICES & PEDS	
[name]	PHD	A	PHARMACOLOGY & TOXICOLOGY	UNIVERSITY OF TEXAS AT AUSTIN , TX USA

AXIS I CODES: 1A, 15, 21 **AXIS II CODES:** 30, 74E, 74H, 93

ABSTRACT

OBJECTIVE: To examine the hypothesis that an increase in LHRH release occurs at menopause and the transitional stage to menopause.

Despite the fact that menopause is a critical event in women's lives, the mechanism leading to menopause is unclear. We investigated whether LHRH release in female rhesus monkeys at menopause and during the transitional stage prior to menopause differs from eugonadal young females. The results indicate that 1) LHRH release is pulsatile in both young and aged monkeys; 2) mean concentrations of LHRH increase during reproductive aging; and 3) LHRH pulse frequency does not change with aging. We conclude that not only do LHRH neurons have the continued capacity to release GnRH in a pulsatile manner, but its activity is enhanced in aged primates.

FUNDING: NIH AG16765 $32,000

AGING-RELATED CHANGES IN CONTROL OF GROWTH HORMONE RELEASE (0300)

NPRC UNIT: NEUROBIOLOGY

%NPRC $: 0.250%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
TERASAWA, EI	PHD	C	WNPRC ASSAY SERVICES & PEDS	
names	PHD	G	WNPRC TERASAWA LAB	
	DVM, PHD	G	WNPRC TERASAWA LAB	

AXIS I CODES: 1A, 15, 21 **AXIS II CODES:** 30, 74E, 74H, 93

ABSTRACT

OBJECTIVE: To examine the hypothesis that the decline of somatotropic function with aging is due to a decrease in growth hormone releasing hormone (GHRH) and an increase in somatostatin.

A physical decline with aging has been associated with a decrease in growth hormone (GH) release, which is controlled by stimulatory GHRH and inhibitory somatostatin. Because previously we have found that GH release decreases with aging and the rhesus monkey is an excellent model for studies of aging, we measured release of GHRH and somatostatin from the hypothalamus in vivo. Results suggest that both neuropeptides were released in a pulsatile manner, and the pulse amplitude and baseline levels of GHRH release greatly decreased whereas the pulse amplitude and baseline levels of somatostatin release increased with aging. The pulse frequencies of neither neurohormone changed. The finding is very important for future implication in human aging, such as development of effective agents for preventing and treating postmenopausal osteoporosis.

FUNDING: NIH AG14972 (1999-2002)

ENGINEERED TISSUE CONSTRUCTS: AN ARTIFICIAL LYMPH NODE (0342)

NPRC UNIT: PATHOLOGY

%NPRC $: 0.500%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
THOMSON, JAMES A	PHD, VMD	C	WNPRC STEM CELL RES & ANATOMY	

AXIS I CODES: 4, 6 AXIS II CODES: 60

ABSTRACT

OBJECTIVE: To differentiate human stem cells into multiple immune functions within an in vitro 3D culture system.

The goal of this research is to ultimately develop the technologies and science for efforts leading to the creation of a 3D ex vivo human immune system. This system would be used to test new vaccine constructs and immunomodulators that would provide superior protection against bioterrorism threat agents.

RESULTS: The results are confidential due to intellectual property issues.

FUNDING: DOD DARPA, [ ] $460,453 2002-2004.

private funding

PRENATAL ANDROGEN EXCESS IN FEMALES PROGRAMS FOR PCOS (0083)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 2.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ABBOTT, DAVID H	PHD	C	WNPRC ASSAY SERVICES & OB/GYN	
	PHD	C	WNPRC AGING	
	MD	A	MEDICINE & OB/GYN	MAYO CLINIC, MN USA
	MD	A	REPRODUCTION & DEVELOPMENT	IMPERIAL COLLEGE, LONDON, UK
	MD	A	PHARMACOLOGY	
	PHD	C	WNPRC DIRECTOR & PHYSIOLOGY	
	PHD	A	PEDIATRICS	UNIVERSITY OF MICHIGAN, MI USA
	PHD	C	WNPRC REPRO RES SERVICES	

AXIS I CODES: 1A, 15, 16E, 23

AXIS II CODES: 49, 60, 63A, 63H, 71, 74E, 77, 92(REPRODUCTION), 93

ABSTRACT

OBJECTIVE: To determine the role of insulin in the development of anovulation in a prenatally androgenized (PA) female rhesus monkey model for polycystic ovary syndrome (PCOS).

We found insulin resistance, impaired insulin secretion, hyperlipidemia and diabetes in adult female rhesus monkeys exposed to excess testosterone during early gestation. Fetal programming of such adult disease became demonstrable as the monkeys aged from ~15 to ~20 years old, during their mid- to late reproductive years. Daily treatment with an insulin sensitizer, pioglitazone, improved insulin secretion and action in PA females, and normalized their ovulatory frequency by decreasing follicular phase and lengthening luteal phase duration in PA females. This improvement in ovulatory function may be analogous to that observed in PCOS women when insulin sensitivity is improved by insulin sensitizer treatment or dietary restriction. Prenatal androgen excess may therefore provide a mechanism for fetal programming at least two obesity-related syndromes in women, PCOS and metabolic syndrome, and an opportunity for determining the cellular and molecular regulation of the physiological processes involved.

This research relied on the WNPRC Assay Services Unit.

FUNDING: NIH RR13635

PHYSIOLOGICAL MECHANISMS UNDERLYING DIABETES AND OBESITY (0084)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 2.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ABBOTT, DAVID H	PHD	C	WNPRC ASSAY SERVICES & OB/GYN	
	PHD	G	WNPRC ABBOTT LAB	
	MD	A	WNPRC ABBOTT LAB	
	PHD	C	WNPRC AGING	
	MD	A	MEDICINE & OB/GYN	MAYO CLINIC, MN USA
	MD	A	MEDICINE	NORTHWESTERN UNIVERSITY, IL USA
	MD	A	PHARMACOLOGY	
	PHD	C	WNPRC DIRECTOR & PHYSIOLOGY	

AXIS I CODES: 1A, 15, 16E, 23 AXIS II CODES: 49, 60, 63A, 63H, 71, 74E, 93

ABSTRACT

OBJECTIVE: To examine the physiological consequences of altered body composition in a nonhuman primate model for PCOS and their implications for the development of diabetes and obesity.

We initiated a study examining the circulating concentrations of leptin, free fatty acids and tryglycerides and their relationship to the onset of diabetes and preferential accumulation of visceral fat, as estimated by CT and DXA scan body composition analyses. Initial results suggest that prenatally androgenized females exposed to androgen excess during either early or late gestation exhibit increased abdominal adiposity.

This research relies on the WNPRC Assay Services Unit.

FUNDING: NIH RR13635

OVARIAN AND ADRENAL HYPERANDROGENISM IN A NONHUMAN PRIMATE MODEL FOR PCOS (0085)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 2.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ABBOTT, DAVID H	PHD	C	WNPRC ASSAY SERVICES & OB/GYN	
	PHD	A	OB/GYN	
	MD	A	MEDICINE & OB/GYN	MAYO CLINIC, MN USA
Nannes	DSC, PHD	A	OB/GYN	UNIVERSITY OF EDINBURGH, UK
	MD	A	PEDIATRICS	UNIVERSITY OF CHICAGO, IL USA
	PHD	C	WNPRC REPRO RES SERVICES	
	MD	A	WNPRC ABBOTT LAB	

AXIS I CODES: 1A, 15, 23 **AXIS II CODES:** 60, 62, 71, 74F, 77, 92(REPRODUCTION), 93

ABSTRACT

OBJECTIVE: To determine the basis of ovarian and adrenal hyperandrogenism exhibited by prenatally androgenized female rhesus monkeys.

We obtained initial endocrine evidence of functional ovarian and adrenocortical androgen excess in adult, prenatally androgenized female rhesus monkeys. We then commenced a series of endocrine challenges and molecular studies to identify intra-ovarian and intra-adrenal mechanisms. Initial results suggest that exposure to androgen excess during the second third of gestation may result in greater enhancement of androgen biosynthesis than exposure to androgen excess during the last third of gestation. Adrenal androgen excess also appears prevalent in adult, prenatally androgenized females that were exposed to androgen excess during the second third of gestation.

This research relied on the WNPRC Assay Services Unit.

FUNDING: NIH RR13635

FETAL AND NEONATAL BIOMARKERS OF PCOS (0282)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 2.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ABBOTT, DAVID H	PHD	C	WNPRC ASSAY SERVICES & OB/GYN	
[redacted]	PHD	G	WNPRC ABBOTT LAB	[redacted]
	MD	A	MEDICINE & OB/GYN	MAYO CLINIC, MN USA
	MD	A	MEDICINE	NORTHWESTERN UNIVERSITY, IL USA
names	MD	A	PHARMACOLOGY	
	PHD	C	WNPRC DIRECTOR & PHYSIOLOGY	
	PHD	A	PEDIATRICS	UNIVERSITY OF MICHIGAN, MI USA
[redacted]	PHD	A	CNPRC & PEDIATRICS	UNIVERSITY OF CALIFORNIA-DAVIS, CA USA

AXIS I CODES: 1A, 15, 16E, 23

AXIS II CODES: 49, 60, 63A, 63H, 71, 74E, 77, 92(REPRODUCTION), 93

ABSTRACT

OBJECTIVE: To determine fetal and neonatal markers for fetal programming of polycystic ovary syndrome (PCOS).

We initiated this project to determine fetal and neonatal consequences of exposing female rhesus monkey fetuses to androgen excess during early gestation. The results will provide the first direct evidence for fetal programming of PCOS.

This research relies on the WNPRC Assay Services Unit.

FUNDING: NIH P50 HD44405

EFFICACY OF AF2364 AS A NEW ORAL CONTRACEPTIVE FOR MALES (0284)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 2.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ABBOTT, DAVID H	PHD	C	WNPRC ASSAY SERVICES & OB/GYN	
[	PHD	A	SENIOR SCIENTIST	POPULATION COUNCIL, NY USA
names	PHD	A	CHEMISTRY	MAHIDOL UNIVERSITY, BANGKOK, THAILAND
]	PHD	A	WNPRC ABBOTT LAB	JOHNSON & JOHNSON ORTHO, NJ USA

AXIS I CODES: 1A, 2, 9, 15, 21, 23 **AXIS II CODES:** 36, 50B, 62, 73, 74E, 77

ABSTRACT

OBJECTIVE: To determine the efficacy of synthetic AF2364 as an oral, male contraceptive in marmoset monkeys.

AF2364 is an effective suppressor of spermatogenesis in adult male rats within 3-8 weeks. The treated males also failed to impregnate their regular female partners during this time. When removed from treatment, males rapidly recover motile, spermatogenic function and fertility. This study was initiated to determine whether AF2364 would be similarly effective in a nonhuman primate, the common marmoset.

This research relied on the WNPRC Assay Services Unit.

FUNDING: [ ] private funding

NEUROENDOCRINE REGULATION OF SOCIALLY-INDUCED ANOVULATION (0316)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 2.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ABBOTT, DAVID H	PHD	C	WNPRC ASSAY SERVICES & OB/GYN	
L	DSC, PHD	A	OB/GYN	UNIVERSITY OF EDINBURGH, UK
	PHD	A	BIOLOGY	UNIVERSITY OF CALIFORNIA-RIVERSIDE, CA USA
names	PHD	C	WNPRC ANIMAL SERVICES	
	PHD	A	WNPRC ABBOTT LAB	JOHNSON & JOHNSON ORTHO, NJ USA
	PHD	C	WNPRC ASSAY SERVICES & PEDS	
J	PHD	A	BIOLOGICAL SCIENCES	U WISCONSIN WHITEWATER, WI USA

AXIS I CODES: 1A, 15, 21, 23

AXIS II CODES: 36, 74E, 77, 92(REPRODUCTIVE NEUROENDOCRINOLOGY), 93

ABSTRACT

OBJECTIVE: To determine the neuroendocrine mechanism of hypogonadotropic anovulation in socially subordinate female marmoset monkeys.

We have shown that social subordinate status among female marmosets does not result in a physiologically stressed condition, however, subordinates reliably respond to low social rank by suppressing their ovulatory cycles. Our recent work, including culture of marmoset tissues, suggests that oxytocin may play a role in regulating gonadotropin-releasing hormone release.

This research relied on the WNPRC Assay Services Unit.

FUNDING: NIH MH60728.

GNRH II STIMULATION OF FEMALE MARMOSET SEXUAL BEHAVIOR (0317)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 2.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ABBOTT, DAVID H	PHD	C	WNPRC ASSAY SERVICES & OB/GYN	
L names	PHD	G	WNPRC ABBOTT LAB	
	PHD	A	MRC HUMAN REPRO SCI UNIT	U EDINBURGH, SCOTLAND

AXIS I CODES: 1A, 2, 15, 23 **AXIS II CODES:** 36, 63E, 93

ABSTRACT

OBJECTIVE: To improve our understanding of the neuroendocrine mechanisms that regulate the female sexual response in order to clarify the efficacy of GnRH peptides as non-estrogenic stimulators of female sexual behavior and aid in developing more appropriate clinical intervention for sexual dysfunction in women.

RESULTS: Sexual dysfunction affects and estimated 43% of women. Currently there are no approved drug therapies for female sexual inadequacy and increasing worries that hormonal treatment with estrogens and progestogens are not safe motivates the need for non-steroidal pharmacotherapy. The neuropeptide gonadotropin releasing hormone II has been shown to stimulate sexual behavior is a range of non-primates, but it role in humans and non human primates is unknown. A model system with female common marmosets has been developed to determine the behavioral responses to GnRH II. GnRH II increases nearly 4 fold the frequency of proceptive (sexual solicitation) behaviors (tongue flicking, proceptive stares and frozen postures) exhibited by females towards their pair-mates compared to vehicle. GnRH II increases sexual receptivity (females enabling male sexual behavior) by doubling the frequency of intromission by males compared to vehicle without affecting mount or mount attempt frequencies. GnRH II stimulation of sexual behavior is not estradiol dependent. These findings indicate a role for GnRH II in the regulation of primate sexual behavior and ongoing studies are investigating (1) if GnRH II stimulation is mediated through the cognate type II receptor and (2) if MicroPET brain imaging can be used to determine the areas of the brain activated by GnRH II.

This research relied on WNPRC Assay Services.

FUNDING: private funding

PHYSIOLOGY AND BEHAVIOR OF MATURATION IN WILD BABOONS (0331)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.010%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ALTMANN, JEANNE	PHD	A	ECOLOGY & EVOLUTIONARY BIOLOGY	PRINCETON UNIVERSITY, NJ USA
Learned	PHD	A	ANTHROPOLOGY	

AXIS I CODES: 1, 1A, 1D, 9, 15, 23 AXIS II CODES: 60

ABSTRACT

OBJECTIVE: To validate and refine techniques for sample collection, storage, extraction and assay of four classes of baboon steroid hormones.

ABSTRACT BODY: We achieved our objective partly with the assistance of WNPRC Assay Services, which has enabled us to proceed to the developmental project.

Social interactions and environment are increasingly recognized as potentially important influences on reproductive function, health, and well-being. Although data are not available for reproductive maturation in boys, social factors influence time of menarche in girls. Depending on circumstances, early puberty may be either an asset or detriment to the social and physical development of the individual or to its lifetime survival and reproduction. This pilot research will provide a first investigation into the physiological mechanisms underlying inter-individual variability in the timing of puberty and the length of adolescence in a wild population of non-human primates and into some of the social impacts on these mechanisms. We shall investigate the extent to which a sub-set of behavioral and social factors correlate with maturational measures and what the temporal relationship is between detectable physiological and behavioral differences. Our aim is to determine the extent to which dominance status and aggressive-submissive interactions among juveniles and the juveniles' social interactions with adults predict physiological patterns of puberty, maturation, and adult rank attainment in males and females. We hypothesize that this relationship is mediated via the hypothalamic-pituitary-gonadal (HPG) and HP-adrenal (HPA) axes. Social environment will be characterized by dominance rank and by variability in the specific behaviors that determine rank, such as, spatial displacements, aggression, and submission. We will measure fecal hormone concentrations of estrogens, androgens, progestins, and glucocorticoids and correlate these with behaviors exhibited during the transition between juvenescence to adolescence and adolescence to adulthood in males and females.

RESULTS: Experiments determined that common, broadly disseminated and utilized methods of sample storage did not result in metabolite stability. Methods for field storage and sample processing that do stabilize metabolites were determined and are now being applied in our laboratory. Results obtained through use of the earlier techniques were discarded.

This work used WNPRC Assay Services.

FUNDING: NIH 1 R03 MH 65294-01

ADRENOCORTICAL FUNCTION IN FEMALE MARMOSET MONKEYS (0281)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 1.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
BIRD, IAN	PHD	A	OB/GYN	
L	PHD	C	WNPRC ASSAY SERVICES & OB/GYN	
names	PHD	G	OB/GYN	
1	PHD	A	BIOLOGY	UNIVERSITY OF CALIFORNIA-RIVERSIDE, CA USA

AXIS I CODES: 1D, 15, 23 **AXIS II CODES:** 36, 72, 74E, 77, 92(REPRODUCTION), 93

ABSTRACT

OBJECTIVE: To characterize sex differences in steroid hormone biosynthetic pathways in the adrenal cortex and their regulation by gonadal hormones, as a model for human adrenocortical development, function and dysfunction.

RESULTS: We investigated possible differences in the steroidogenic pathway in female marmosets that would account for their elevated androgen levels measured in vivo. We used immunohistochemistry to a number of enzymes and cofactors involved in steroid biosynthesis in adrenals from cycling and ovariectomized female marmosets. Differences were found between males and females, and between cycling and ovariectomized females. We conclude that female marmoset adrenals express higher quantities of factors known to enhance steroidogenic enzyme activity, and therefore adrenal androgen production, than male adrenals, and this effect appears to be further enhanced by ovariectomy. These results will be instrumental in our characterization of the marmoset adrenal cortex and our development of the marmoset as an animal model for studies of adrenocortical function and dysfunction.

Resources used include WNPRC Animal Services (marmoset colony) and Pathology Services.

FUNDING: NIMH MH60728. Total budget for grant year: $234,630

INTESTINAL MICROFLORA IN INFANT RHESUS MONKEYS (0303)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 2.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
COE, CHRISTOPHER L	PHD	C	WNPRC & PSYCHOLOGY	
Lname_1	PHD	A	PSYCHOLOGY	

AXIS I CODES: 1A AXIS II CODES: 60, 64, 65

ABSTRACT

Objective: To evaluate the developmental profile of protective gut microflora in infant rhesus monkeys, and the possible influence of prior pregnancy conditions.

Results: Breast-milking facilitates the establishment of certain type of gut bacteria, Lactobacilli and Bifidobacter, which serve a protective function against pathogenic bacteria. This study characterized the profile of Lactobacilli and Bifidobacteria in infant rhesus monkeys during the nursing phase, and showed that monkeys born to mothers that had been undisturbed during their pregnancies had higher levels of both bacterial strains. Infants that evinced low levels of these natural gut flora were more likely to become infected with Shigella, a gram negative pathogen. These findings indicates that events begun in fetal life can help set the stage for a postnatal process of particular relevance for infant health. Gastrointestinal disorders remain a major source of morbidity and mortality in children throughout the world, and diarrheic illnesses can certainly be a major concern in animal husbandry.

This research used WNPRC Animal Services, Assay Services, and Library and Information Services.

FUNDING: NIAID AI46521 (Prenatal stress and immune responsiveness. $250,000 Direct)

GROWTH TRAJECTORY, MENARCHE AND FECUNDITY (0304)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 2.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
COE, CHRISTOPHER L	PHD	C	WNPRC & PSYCHOLOGY	

AXIS I CODES: 1A **AXIS II CODES:** 60, 65

ABSTRACT

OBJECTIVE: To determine the influence of birth weight on subsequent growth trajectory, age of menarche and first pregnancy in female rhesus monkeys.

RESULTS: Size of female monkeys at birth was highly correlated with subsequent growth across the first 3 years of life and this growth trajectory was a significant predictor of age at first delivery. Monkeys born small were delayed on average 6 months as compared to there counterparts who were large at birth. These results suggest that growth patterns started already in fetal life can have long-lasting influences on age at menarche and the initial reproductive success of the rhesus monkey.

This research used WNPRC Animal Services, Assay Services, and Library and Information Services.

FUNDING: NIAID AI46521, Total Direct: $1,150,00.

BRAIN IMAGING IN AWAKE NONHUMAN PRIMATES (0295)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.500%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
FERRIS, CRAIG F.	PHD	A	PSYCHIATRY	U MASS. MEDICAL SCHOOL, MA USA
L	PHD	A	PSYCHIATRY	U MASS. MEDICAL SCHOOL, MA USA
	PHD	C	WNPRC ANIMAL SERVICES	
names	PHD	A	PSYCHOLOGY & ZOOLOGY	
	PHD	A	WNPRC ABBOTT LAB	JOHNSON & JOHNSON ORTHO, NJ USA
	PHD	A	OPTHALMOL & VISUAL SCI	UNIVERSITY OF MINNESOTA, MN USA
J	PHD	C	WNPRC ASSAY SERV & PSYCHOLOGY	

AXIS I CODES: 1A, 9, 21, 25 **AXIS II CODES:** 36, 63C, 71

ABSTRACT

OBJECTIVE: To evaluate primate brain activity associated with sexual arousal.

Fully conscious male marmoset monkeys were brain imaged during presentation of odors that naturally elicit high levels of sexual activity and sexual motivation. Periovulatory odors from female marmosets significantly increased cortical activity : the striatum, hippocampus, septum,periaqueductal gray and cerebellum in comparison with odors from ovariectomized monkeys. Conversely, negative signals increased in the temporal cortex, cingulate cortex, putamen, hippocampus, substantia nigra, medial preoptic area, and crebellum with presentation of odos from ovariectomized marmosets as compared to perivulatory odors. These data suggest the odor-driven enhancement and suppression of sexual arousal affect neuronal activity in many of the same general brain areas. These areas included not only those associalted with sexual activity but also areas involved in emotional processing and reward.

FUNDING: NIH MH58700, NIH RR000167

PREGNANCY ESTABLISHMENT AND ROLE OF RHESUS MONKEY UTERINE IMMUNE CELLS (0256)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 5.000% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
GOLOS, THADDEUS G	PHD	C	WNPRC & OB/GYN	
L names	DVM, PHD	A	WNPRC GOLOS LAB	
	MD, PHD	A	PATHOLOGY	

AXIS I CODES: 1D, 23 **AXIS II CODES:** 31, 60, 64, 71

ABSTRACT

OBJECTIVE: To define the phenotype and function of rhesus monkey uterine immune cells.

RESULTS: Humans and nonhuman primates share many unique characteristics of the female reproductive tract. We have shown that a majority of the lymphocytes from the uterine endometrium of the pregnant rhesus monkey have phenotypic and functional characterization of a unique population of uterine natural killer cells. In addition, there are significant numbers of macrophages and macrophage-related cells which have a distinctly different distribution with relation to the placenta and whose gene expression patterns have been shown to change within days of embryo implantation. We are defining the receptors expressed on these cells, their functional response to the presence of placental immune regulatory molecules, and their role in establishing an appropriate environment for successful pregnancy.

This research used WNPRC Animal Services.

FUNDING: NIH R01 HD37120

PRIMATE GENE TRANSFER STRATEGIES FOR WOMEN'S HEALTH (0257)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.500%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
GOLOS, THADDEUS G	PHD	C	WNPRC & OB/GYN	
	MD, PHD	G	WNPRC GOLOS LAB	
	DVM, PHD	A	WNPRC GOLOS LAB	
	PHD	G	WNPRC GOLOS LAB	
	PHD	A	WNPRC GOLOS LAB	
	MD	G	WNPRC GOLOS LAB	
	MS	G	WNPRC GOLOS LAB & OB/GYN	
	PHD	G	WNPRC GOLOS LAB	
	MS	G	WNPRC GOLOS LAB	
	MS	G	WNPRC GOLOS LAB	
	MD	G	WNPRC GOLOS LAB	

AXIS I CODES: 1D, 23 AXIS II CODES: 60, 64, 71

ABSTRACT

OBJECTIVE: To develop gene transfer techniques targeting the primate female reproductive tract.

RESULTS: Transgenic mice have provided invaluable information about gene function and regulation. However, due to marked differences between rodents and primates, some areas of human biology such as early embryonic development, female reproductive tract biology, and maternal-fetal interactions would best be studied in a nonhuman primate model. We have previously shown that gene transfer into rhesus monkey preimplantation embryos gives rise to transgenic placentas that express a reporter transgene (eGFP). This approach also provides a system for achieving primate transgenesis.

We are adapting the tools used in this work to develop approaches for achieving gene therapy of the reproductive tract and maternal-fetal interface. This technology would have relevance for research in infertility, menstrual cycle abnormalities, uterine cancer, placental insufficiency and fetal growth restriction, and maternal-fetal immune tolerance.

This research used WNPRC Animal Services.

FUNDING: NIH R24 RR14040

Note: This SPID lists most of the Golos Lab at the WNPRC. Not categorized on the Personnel Roster but essential to the lab are three technicians and student assistants as needed.

TEMPERATURE AND OVULATION IN NONHUMAN PRIMATES (0298)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.250%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
HARKE, MICHELE	DVM	C	WNPRC ANIMAL SERVICES	

AXIS I CODES: 1A, 23 **AXIS II CODES:** 60

ABSTRACT

OBJECTIVE: To discover if core body temperature is linked to ovulation in non-human primates.

RESULTS: Experiment begun in 2004. If we can link temperature to ovulation, monitoring body temperature would be a minimally invasive way to follow reproductive cycles in our animals. We could then provide more precise conception dates and estimated due dates, to improve our animal services in support of Center research. We also plan to include Chlorocebus aethiops, 10 estimated, and Callithrix jacchus, 10 animals estimated, in this project.

FUNDING: NIH R000167

OVARY DIOXIN BINDING AND REPRODUCTIVE DISRUPTION (0264)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.025%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
HUTZ, REINHOLD	PHD	A	BIOLOGICAL SCIENCES	UNIVERSITY OF WISCONSIN-MILWAUKEE, WI USA
[illegible]	MS	G	BIOSCIENCES	UNIVERSITY OF WISCONSIN-MILWAUKEE, WI USA

AXIS I CODES: 1D, 2, 3, 15, 23 AXIS II CODES: 54A, 63G, 74, 93

ABSTRACT

OBJECTIVE: To localize autoradiographically dioxin binding to specific compartments within the monkey ovary as a potentail mechanism of reproductive disruption in women.

2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD, dioxin) is a persistent and highly toxic by-product of many manufacturing processes and has been implicated in reproductive dysfunction, but the locus of effect is unknown. Here we show for the first time that radiolabeled TCDD binds ovarian follicles in rhesus monkey ovaries. Ovaries collected at necropsy were frozen and sectioned with a crysotat. Sections were incubated with either control vehicle, 3H-TCDD, or 3H-TCDD plus alpha-naphthoflavone, a known AHR receptor antagonist. We show specific binding of TCDD to antral follicles of rhesus monkey ovaries, and this is drastically reduced with competitive antagonist; additionally, the areas of binding are similar to where we have previously localized ER-alpha in rhesus monkey ovaries. The present findings support the hypothesis that dioxins directly affect primate ovarian function via receptors in ovarian follicles, possibly via ER modulation.

FUNDING: NIH ES011569.

ENDOMETRIOSIS IN RHESUS MACAQUES (0329)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.250%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KENNEDY, STEPHEN	PHD	A	OB/GYN	OXFORD UNIVERSITY, UK
	PHD	A	HUMAN GENETICS	OXFORD UNIVERSITY, UK
	PHD	C	WNPRC & PSYCHOLOGY	
	PHD	C	WNPRC AGING	
	PHD	A	OB/GYN	OXFORD UNIV., UK
	PHD	C	WNPRC DIRECTOR & PHYSIOLOGY	
	PHD	A	HUMAN GENETICS	UNIVERSITY OF PITTSBURGH, PA USA
	PHD	A	WELLCOME TRUST CTR HUMAN GEN.	UNIVERSITY OF OXFORD, UK

AXIS I CODES: 1, 1A, 1D, 23 **AXIS II CODES:** 60, 93

ABSTRACT

OBJECTIVE: To investigate the prevalence and familial aggregation of endometriosis in rhesus macaques.

ABSTRACT BODY: Endometriosis occurs in several non-human primate species that have menstrual cycles. Between 1978 and 2001, 142 animals with endometriosis were identified from necropsy and surgical records and through the use of magnetic resonance imaging (MRI) at the WNPRC. All cases were used to build one large multigenerational pedigree and nine nuclear families comprising 1,602 females in total. By 2002, the pedigrees contained 124 cases diagnosed at necropsy, 17 at surgery and three at MRI. Female animals that had died aged 10 years without endometriosis had both ovaries until at least 1 year prior to death, had a full necropsy, and were considered unaffected. The prevalence of endometriosis among necropsied animals aged 10 years in the colony was 31.4% [95% confidence interval (CI) 26.9-35.9%]; prevalence increased with rising age and calendar age at death. Familial aggregation of endometriosis was strongly suggested by a significantly higher average kinship coefficient among affected animals compared with those unaffected (P 0.001), and a higher recurrence risk for full sibs (0.75; 95% CI 0.45-1.0) compared with maternal half sibs (0.26; 95% CI 0.1-0.41) and paternal half sibs (0.18; 95% CI 0.02-0.34). The segregation ratio among affected mothers (44.2%) was not significantly higher compared with unaffected mothers (36.6%).

RESULTS: The results support familial aggregation of endometriosis in the rhesus macaque, and indicate that this is a promising animal model for investigating the mode of inheritance, the location of potential genetic susceptibility loci and the influence of environmental factors.

FUNDING: private funding

EFFECTS OF JUVENILE EXPERIENCE ON MATERNAL PSYCHOBIOLOGY (0116)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.025%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KRAEMER, GARY W	PHD	A	KINESIOLOGY	
[illegible]	PHD	C	WNPRC ASSAY SERVICES & OB/GYN	[illegible]
names	MD	A	PSYCHIATRY	VANDERBILT UNIVERSITY, NASHVILLE, TN USA
	PHD	A	PSYCHOLOGY	UNIVERSITY OF TORONTO, CANADA
[illegible]	PHD	A		SWISS INSTITUTE OF TECHNOLOGY, SWITZERLAND

AXIS I CODES: 1A, 2, 15, 21, 25 AXIS II CODES: 36, 41, 60, 71, 77

ABSTRACT

OBJECTIVES: To determine how early experiences of caregiving as a juvenile alter brain neurotransmitter, neuroendocrine, and sensory mechanisms so that maternal recognition of offspring and responsiveness to them is augmented in adulthood.

ABSTRACT: In many species of nonhuman primates the successful maternal care of first-born offspring appears to depend on experiences that the mother had while she was growing up. If juvenile and adolescent marmosets have the experience of carrying younger siblings, then the probability is about 80% that they will care for their first-born as adults. By comparison, if new marmoset mothers do not have such earlier experience with siblings, then the probability is only about 20% that they will care for their first-born. It has been assumed that the experiences that young nonhuman primates have with younger offspring allow them to "learn" about how to care for babies. Now, however, there is a considerable body of data suggesting that early experiences with offspring affect sensory, neurotransmitter, and neuroendocrine mechanisms that determine whether the new mother responds positively to her new babies, or is fearful, neglectful, or even aggressive towards them. Marmosets are a "bi-parental" species, so we will also be examining the effects of early rearing experiences on paternal behavior. Studies of this nature may provide a greater understanding of the psychobiological foundations of child neglect and abuse in humans, and help to identify avenues by which this can be reduced through prevention or intervention.

RESULTS: This is a longitudinal cross-generational study in which the first generation are adolescents or young adults. Initial results clearly indicate that marmosets that do not have the experience of caring for younger siblings exhibit persistently altered social behavior toward their parents and like-aged siblings. This may form part of the basis for altered parental behavior later on.

FUNDING: NIH MH60318

NEUROENDOCRINOLOGY OF AGGRESSIVE AND PATERNAL BEHAVIOR (0312)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.500%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
MARLER, CATHERINE A	PHD	A	PSYCHOLOGY	
Marler	PHD	A	KINESIOLOGY	HARVARD UNIVERSITY, MA USA

AXIS I CODES: 1A, 1D AXIS II CODES: 36

ABSTRACT

OBJECTIVE: To examine the social and neuroendocrine mechanisms underlying variation in aggression and paternal behavior in Peromyscus mice.

Using WNPRC Assay Laboratory facilities, we examined hormonal changes occurring in response to social experiences. The rapid but transient increases in male androgens following a single encounter occurs in a many species, but the function is unknown. We show that transient T increases have long lasting effects on aggression in the California mouse. T injections given to castrated males, but not saline injections, following a win in an aggressive encounter increased aggression in a test the following day. This effect is androgen based, as treatment with an aromatase inhibitor did not block T mediated plasticity in aggression. Instead aromatase inhibition increased aggression independently of previous experience, and aromatase was positively correlated with aggression (1). The challenge effect has rarely been investigated in females. We report a decrease in progesterone (P) in females, but no change in testosterone (T), after an aggressive encounter in female California mice (2). In response to the birth of their pups, male California mice become highly paternal. This behavior is positively associated with T (reviewed in 3). The onset of paternal behavior is also associated with increased aromatase activity in the medial preoptic area (MPOA), further suggesting that T alters paternal behavior when it is converted to estradiol via aromatase 4). P also changes with reproductive experience and is negatively correlated with aromatase in the MPOA, suggesting that P may contribute to the onset of paternal behavior (4). Finally, T baseline levels were compared among six species of Peromyscus with different levels of paternal behavior. We found no evidence suggesting that males in highly paternal species have low baseline T levels and baseline T levels were more likely explained by phylogenetic or ecological constraints (3).

This work relied on WNPRC Assay Services.

FUNDING: NIMH NRSA F31 MH64328, NIMH NRSA MH64280, NSF IBN-0110625

74

MECHANISMS OF PSYCHOSOCIAL SUPPRESSION OF CORTISOL (0126)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.500%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
SALTZMAN, WENDY	PHD	A	BIOLOGY	UNIVERSITY OF CALIFORNIA-RIVERSIDE, CA USA
[illegible]	PHD	C	WNPRC ASSAY SERVICES & OB/GYN	
[illegible]	PHD	A	OB/GYN	

AXIS I CODES: 1A, 15, 23 AXIS II CODES: 36, 72, 74E, 77, 92(REPRODUCTION), 93

ABSTRACT

OBJECTIVE: To identify the endocrine mechanisms that mediate the psychosocially induced suppression of the stress hormone cortisol in socially subordinate, reproductively suppressed female marmosets, as a model for understanding chronic endocrine dysregulation associated with a variety of human neuropsychiatric disorders, especially in women.

RESULTS: We are examining the roles of the reproductive hormones estrogen and luteinizing hormone (LH) in regulating adrenocortical function in female marmosets. We have established for the first time that the gonadotropin-releasing hormone (GnRH) agonist leuprolide successfully and reversibly supresses both baseline and GnRH-stimulated LH secretion in this species. Contrary to our hypothesis, however, suppression of LH in ovary-intact and ovariectomized females did not inhibit adrenocortical function. Moreover, chronic treatment with estradiol did not alter adrenocortical activity in subordinate or ovariectomized females. These results have improved our understanding of the interactions between reproductive and adrenocortical hormones in primates and may advance our understanding of chronic adrenocortical dysregulation in human psychopathology.

Resources used include the WNPRC marmoset colony and Assay Services laboratories.

FUNDING: NIMH MH60728. Total budget for grant year: $234,630

NEURAL MECHANISMS OF CORTISOL SUPPRESSION IN MARMOSETS (0336)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.250%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
SALTZMAN, WENDY	PHD	A	BIOLOGY	UNIVERSITY OF CALIFORNIA-RIVERSIDE, CA USA
[name]	PHD	C	WNPRC ASSAY SERVICES & OB/GYN	

AXIS I CODES: 1A, 15, 21, 23 AXIS II CODES: 36, 72, 74E, 77, 93

ABSTRACT

OBJECTIVE: To determine whether psychosocially induced suppression of cortisol in socially subordinate female marmosets is mediated, in part, by endocrine inhibition at the level of the brain or pituitary, as a model for understanding chronic endocrine dysregulation associated with a variety of human neuropsychiatric disorders.

RESULTS: We have conducted preliminary tests to optimize the use of two drugs, metyrapone and ovine corticotropin-releasing hormone (CRH), which we will use to characterize hypothalamic-pituitary activity in dominant and subordinate female marmosets in the absence of the confounding influences of differential negative feedback from cortisol. We are now completing these pilot tests and will soon begin data collection.

Resources used include WNPRC Animal Services (marmoset colony) and Assay Services.

FUNDING: NIMH MH60728. Total budget for grant year: $234,630

FETAL ALCOHOL EFFECTS IN MONKEYS: DOPAMINE AND BEHAVIOR (0250)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.025%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
SCHNEIDER, MARY	PHD	A	KINESIOLOGY	
	PHD	A	MEDICAL PHYSICS	
names	PHD	A	MEDICAL PHYSICS	
	PHD	A	PSYCHOLOGY	
	PHD	A	MEDICAL PHYSICS & RADIOLOGY	

AXIS I CODES: 1D, 21 AXIS II CODES: 36, 60, 71, 77

ABSTRACT

OBJECTIVE: To study fetal alcohol effects and prenatal stress in monkeys.

RESULTS: Fetal alcohol syndrome (FAS) is the leading known cause of mental retardation today and currently represents an enormous problem for our society. The central question addressed by this proposal is whether moderate alcohol exposure, alone, or in combination with prenatal stress constitutes a danger to the developing offspring. To address this issue, we characterize dopamine D2 receptor densities in striata of offspring using in vivo PET imaging techniques, characterize dopamine synthesis in these same cohorts, also using PET imaging, and uncouple presynaptic synthesis of dopamine from postsynaptic receptor binding availability. Subjects from prenatal stress conditions (prenatal stress alone and in combination wtih fetal alcohol exposure) showed an increase in the ratio of striatal dopamine D2 receptor binding potential and DA synthesis compared to controls. An increase in the ratio of radiotracer distribution volume ratios (DVR), used to evaluate the balance between striatal dopamine synthesis and receptor availability respectively, was significantly correlated with less behavioral inhibition. The latter supports a hypothesis linking striatal function to behavioral inhibitory control.

This work relied on WNPRC Assay Services, Pathology Services and Operational Services.

FUNDING: NIH NIAAA 12277 ($377,302.00)

MODERATE LEVEL PRENATAL ALCOHOL EXPOSURE IN PRIMATES (0313)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.025%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
SCHNEIDER, MARY	PHD	A	KINESIOLOGY	
	PHD	A	MEDICAL PHYSICS	
	PHD	A	KINESIOLOGY	
	PHD	A	PSYCHOLOGY	
	PHD	A	MEDICAL PHYSICS & RADIOLOGY	
	PHD	A	MEDICAL PHYSICS/PSYCHIATRY	

AXIS I CODES: 1D, 21 AXIS II CODES: 36, 60, 71, 77

ABSTRACT

OBJECTIVE: To assess the effect of gestational timing of prenatal alcohol exposure on cognition, social behavior, and stress reactivity and to determine the effect of gestational timing of prenatal alcohol exposure on offspring dopamine D2 receptor binding availability and dopamine synthesis in striata.

RESULTS: Early gestation alcohol exposure was related to reductions in infant orientation and motor maturity, while mid-late gestation reduced motor maturity but did not affect overall neurobehavioral performance in multivariate tests. Mid-late gestation exposure to a relatively moderate dose of alcohol reduced striatal dopaminergic system function.

This work used WNPRC Assays Services, Pathology Services and Operational Services.

FUNDING: NIH NIAA 10079. ($1,398,586 total funds for 5 years)

STRATEGIES FOR PRODUCTION OF MHC-DEFINED AND GENETICALLY IDENTICAL MONKEYS (0127)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 4.000% AIDS RELATED RESEARCH

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
SCHRAMM, R DEE	PHD	C	WNPRC REPRO RES SERVICES	
L names	PHD	C	WNPRC & PATHLAB MED	
1	PHD	A	REPRODUCTIVE SCIENCES	ONPRC & OREGON HEALTH SCIENCES UNIVERSITY, OR USA

AXIS I CODES: 1A, 1D, 9, 23 AXIS II CODES: 31, 77, 92(GAMETE/EMBRYO BIOLOGY)

ABSTRACT

OBJECTIVE: To 1) develop strategies for creating genetically identical monkeys using blastomere separation and 2) propagate a family of MHC-defined monkeys using assisted reproductive technologies. Genetically identical and MHC-defined monkeys would be extremely valuable models for biomedical studies of human disease.

RESULTS: Aggregation of one 4-cell and four 16-cell stage blastomeres enhanced (p 0.05) blastocyst formation (69.2%) compared to that obtained with one 4-cell stage blastomere alone (28.7%) to a level equivalent to nonmanipulated control embryos (66.9%). However, neither blastocyst development nor total cell numbers in resulting blastocysts differed between aggregate chimeras and those derived from embryos comprised of four 16-cell blastomeres alone. Blastocysts resulting from the aggregate chimeras were derived strictly from the 16-cell stage blastomeres, with complete exclusion of the 4-cell stage blastomeres. In contrast to blastocysts derived from 4-cell stage blastomeres, those derived from 16-cell stage blastomeres exhibited little or no inner cell mass development. In conclusion, due to exclusion of the less advanced cells, aggregation of developmentally asynchronous blastomeres did not improve the developmental competence or cell numbers of split rhesus embryos. Transfer of 5 pairs of split embryos derived from aggregation of diploid and tetraploid blastomeres resulted a singleton pregnancy that was lost between days 30 and 40 of pregnancy.

Efforts to produce MHC-defined monkeys have been seriously impacted by the lack of suitable recipient animals for embryo transfer at the WNPRC. Thus, as of October, 2003, MHC-defined embryos produced by in vitro fertilization have been sent to the Oregon National Primate Research Center for cryopreservation and future transfer. These efforts will continue for the remainder of the grant period.

WNPRC resources used for these studies: Animal Services (Veterinary Services, Surgical Services) and Assay Services (hormone assays).

FUNDING: NIH RR000167, NIH RR15193-01 (Total costs for current budget period: $560,606)

DECIDUAL MACROPHAGES IN PRIMATE PREGNANCY (0270)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.025%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
SLUKVIN, IGOR I	MD, PHD	A	PATHOLOGY	
[illegible] J	PHD	C	WNPRC & OB/GYN	

AXIS I CODES: 1D, 19, 23 **AXIS II CODES:** 64, 71

ABSTRACT

OBJECTIVE: To evaluate mechanisms of macrophage-trophoblast interactions in establishing primate pregnancy and to understand their potential role in human pregnancy pathology.

RESULTS: We are testing the hypothesis that the nonclassical MHC class I molecule Mamu-AG can protect invading cytotrophoblasts from destruction by macrophages through interaction with immunoglobulin-like transcripts (ILT) ILT2 and ILT4 receptors. We demonstrated that in the rhesus monkey placenta, macrophages are in close association with invading extravillous trophoblasts, which express non-classical MHC class I molecule Mamu-AG (analog of human HLA-G). We demonstrated the presence of ILT-4 transcripts in rhesus decidua. These findings suggest the possibility of Mamu-AG interaction with inhibitory ILT2 and ILT4 receptors on macrophages. This work brings us closer to understanding the role the placenta plays in promoting maternal immune system tolerance of the fetus, and thus early pregnancy success or failure.

FUNDING: NIH K08 HD44067

PROLACTIN LEVELS PREDICT RELATIONSHIP QUALITY IN COTTON-TOP TAMARINS (0307)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.250%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
SNOWDON, CHARLES T.	PHD	A	PSYCHOLOGY & ZOOLOGY	
Harned	PHD	C	WNPRC ASSAY SERV & PSYCHOLOGY	

AXIS I CODES: 1A, 15, 23 AXIS II CODES: 36, 74E

ABSTRACT

OBJECTIVE: To assess whether prolactin, commonly thought to be important in parent-offspring relationships is also important in relationships between mates.

RESULTS: Prolactin is necessary for successful nursing in mammals, and also regulates maternal behavior. In some biparental species of birds and mammals prolactin levels are elevated in fathers, and there is some evidence that prolactin may be important for quality male care of infants. Prolactin, thus, is often thought of as a "parental" hormone. Are there other conditions where elevated prolactin might be important? Parental care represents just one type of social relationship, and prolactin might, therefore, be important in other social relationships. We investigated the role of prolactin in 11 paired female cotton-top tamarins (3 mothers after the end of nursing and 8 non-reproducing females housed with a male mate). We collected urine samples noninvasively two days a week for four weeks, and four 20-min behavioral observations were made each week, two in the morning and two in the afternoon. Results indicated significant positive correlations between prolactin levels and affiliative behavior (huddle, groom), sexual behavior and aggression. Females that were engaged in more social interactions with their mates had higher prolactin levels. Surprisingly, the lowest levels of both prolactin and social interaction were found in mothers after the weaning of their infants. Prolactin may not simply be related to parental care but may play an important role in pairbonding and other social relationships.

This work relied on the WNPRC Assay Services Unit.

FUNDING: USPHS MH 35215 ($225,000);

COOPERATIVE COGNITION IN COOPERATIVELY BREEDING TAMARINS (0308)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.250%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
SNOWDON, CHARLES T.	PHD	A	PSYCHOLOGY & ZOOLOGY	

AXIS I CODES: 1A, 25A, 25B **AXIS II CODES:** 36, 40, 41

ABSTRACT

OBJECTIVE: To study the nature and mechanisms of social transfer of information in a cooperatively breeding species.

RESULTS: Cooperatively breeding primates must divide effort between infant care, vigilance, group defense, and foraging. Individuals within groups engage in each of these roles. Successful coordination of within group behavior for successful infant care requires clear communication and attention to others. Does this behavioral coordination lead to social facilitation of cognitive skills as well? In cotton-top tamarins (Saguinus oedipus) we have shown that monkeys attend to vocal and visual signals to avoid a highly preferred familiar food suddenly made noxious with the addition of white pepper, providing one of the few demonstrations of social learning to avoid foods in primates. Furthermore, tamarins in the presence of their mate learn a novel task to find food significantly faster than individual learners acquire the task. Tamarins rapidly demonstrated cooperation when the simultaneous actions of two monkeys were needed to solve a task, but when tested alone, they inhibited responses suggesting an understanding of the cooperative task. A longitudinal study on the relationship between food offering, tolerated begging and infant skill level with foods that are either familiar or novel to the infant addresses the issue of whether caretakers adjust their food-sharing behavior according to the knowledge that infants have. Collectively, these studies suggest an impressive ability for social learning and information transfer in Callitrichids comparable to or even beyond that of great apes. The evolutionary forces leading to cooperative care of infants appear to be linked with cooperative cognition.

This work relied on the WNPRC Library and Information Services.

FUNDING: USPHS MH29775 ($200,000)

VOCAL COMMUNICATION IN WILD PYGMY MARMOSETS (0309)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.250%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
SNOWDON, CHARLES T.	PHD	A	PSYCHOLOGY & ZOOLOGY	
Lname 1	PHD	A	DEPARTMENT OF ZOOLOGY	UNIVERSIDAD SAN FRANCISCO DE QUITO, ECUADOR

AXIS I CODES: 1A, 8, 25B AXIS II CODES: 36, 40, 41

ABSTRACT

OBJECTIVE: To study population differences in vocal communication and vocal development in wild pygmy marmosets.

RESULTS: There has been little evidence of vocal plasticity in calls of nonhuman primates. However, studies of vocal communication in wild primates have rarely studied more than one population and thus potential differences in vocalization may not be evident. We are studying four populations of pygmy marmosets in the upper Amazon basin in Eastern Ecuador. We are finding significant differences in the structure of long calls and "J-calls" in each population, after correcting for individual differences. This is the first evidence of variability in vocal structure in non-provisioned monkeys (ruling out human intervention as a source of change). We have also made detailed measurements of environmental noise and how sounds are degraded in each of the habitats and find some of the differences in call structure can be related to habitat differences. We have also found population variation in the species of trees used for exudate feeding. In addition we are studying the "babbling" of young infant marmosets to learn more about vocal development, and we are studying predator alarm calls.

This work used WNPRC Library and Information Services.

FUNDING: USPHS MH29775 ($200,000)

PARENTING AND VOCAL COMMUNICATION IN SQUIRREL MONKEYS (0338)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.025%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
SOLTIS, JOSEPH	PHD	A	COMPARATIVE ETHOLOGY	NIH, MD USA

AXIS I CODES: 1A, 20, 23 **AXIS II CODES:** 40, 60

ABSTRACT

OBJECTIVE: To study endocrinology and parenting in squirrel monkeys.

RESULTS: We found that immature offspring can have a disruptive influence on adult squirrel monkeys living in captivity. Adults in groups with immature offspring received an average of 18 play attempts per hour, experienced a five-fold decrease in affiliation with other adults, and presented higher urinary cortisol values, compared to adults in groups without immature offspring.

This research used WNPRC Assay Services.

FUNDING: NIH Intramural Research Training Award

MATING AND CONCEPTION IN FREE-RANGING MURIQUI MONKEYS (0297)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.250%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
STRIER, KAREN B	PHD	A	ANTHROPOLOGY	
[name illegible]	PHD	C	WNPRC ASSAY SERV & PSYCHOLOGY	

AXIS I CODES: 1A, 2, 9, 15, 23 AXIS II CODES: 36, 71, 74E

ABSTRACT

OBJECTIVE: To understand reproduction in free-ranging monkeys.

RESULTS: We examined the hormonal and behavioral changes in wild male and female northern muriquis (Brachyteles arachnoides hypoxanthus) during a 6-month period that encompassed the onset of the 1998-1999 mating and conception seasons. Individual females resumed mating with the resumption of ovarian cycling, which was not synchronized among them or related to their cortisol levels. Females experienced two to seven cycles prior to conceiving, and the first conception occurred two months after the onset of the group's mating season. There were no differences in female cortisol levels across their premating, mating, and conception conditions. Cortisol levels were significantly higher in females than in males prior to the conception season, consistent with the prediction that energy reserves may be associated with breeding readiness in females, but not males, in this species. The sustained elevation in male cortisol occurred after the peak in their sexual activity, which resulted in the first conception of the year. Male cortisol levels were positively correlated between years that were similar in rainfall, but differed in the timing of sexual and reproductive events. The timing of cortisol elevations in males appears to be generally regulated by environmental cues, but is responsive to fine tuning by social and behavioral cues related to the unpredictable timing of reproductive opportunities within their extended mating season.

This research relied on WNPRC Assay Services.

FUNDING: [illegible] and NIH RR000167.

MALE MARMOSET RESPONSE TO PERIOVULATORY CUES (0293)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.250%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ZIEGLER, TONI E	PHD	C	WNPRC ASSAY SERV & PSYCHOLOGY	
L	PHD	A	PSYCHIATRY	U MASS. MEDICAL SCHOOL, MA USA
names	PHD	C	WNPRC ANIMAL SERVICES	
	PHD	A	PSYCHOLOGY & ZOOLOGY	

AXIS I CODES: 1A, 2, 9, 15, 23 **AXIS II CODES:** 36, 71, 74E

ABSTRACT

OBJECTIVE: To understand the processing of sexually relevant chemical cues in male primates.

RESULTS: We delivered periovulatory scents-- collected from scent markers--to male common marmosets, both when they were in their own cages with their families (or paired females) removed, and when they were confined in small cages for 10 minutes. Behaviorally, the males showed increased investigative and arousal behaviors to the periovulatory scent compared to the control scent. Five out seven males showed an increase in testosterone to the periovulatory scent. When males were tested in a confined space to mimic fMRI brain imaging, eight of the twelve males showed an increase in testosterone. However, when the males were grouped by their present social housing, there were significant differences in testosterone response to the periovulatory scent. Males living in families had the lowest response, males living singly had the highest response, paired males responded in the middle range. These results suggest that social conditions can influence how a male responds to sexually relevant cues.

This research relied on WNPRC Assay Services.

FUNDING: NIMH 58700 to C.F. Ferris.

ANDROGENS AND MATING IN COTTONTOP TAMARINS (0294)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.250%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ZIEGLER, TONI E	PHD	C	WNPRC ASSAY SERV & PSYCHOLOGY	
names	PHD	A	PSYCHOLOGY & ZOOLOGY	
	PHD	A	SCHOOL OF VET MED	

AXIS I CODES: 1A, 2, 9, 15, 23 AXIS II CODES: 36, 71, 74E

ABSTRACT

OBJECTIVE: To investigate chemical cues of mating in primates

RESULTS: We examined: 1) whether male tamarins showed an androgen response to their female's postpartum ovulation; 2) whether an androgen response would be stimulated by follicular changes, and 3) whether males would alter their parenting behavior during the mate's receptive period. We found that male tamarins do show an increase in urinary testosteron, DHT, and estradiol around the timing of the female's periovulatory peak. The onset of the androgen increases began prior to the female's ovulation and occurs at the time females are beginning their follicular phase. Therefore, androgens are elevated by the time the female ovulates ensuring that males are at their optimal fertility simultaneously with the female. Male tamarins showed large variability in their infant carrying patterns with no significant carrying response to the female's fertile period.

This research relied on WNPRC Assay Services.

FUNDING: NIH MH00177

IMPORTANCE OF PATERNAL CARE IN PRIMATES (0296)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC S: 0.250%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ZIEGLER, TONI E	PHD	C	WNPRC ASSAY SERV & PSYCHOLOGY	
names	PHD	A	PSYCHOLOGY & ZOOLOGY	
	PHD	A	SCHOOL OF VET MED	

AXIS I CODES: 1A, 2, 9, 15, 23 **AXIS II CODES:** 36, 71, 74E

ABSTRACT

OBJECTIVE: To understand the role of fathers in a primate species where paternal care is critical to the survival of the offspring.

We examined urinary hormonal levels in expectant experienced and less experienced fathers during their mates' pregnancies. Fathers that had experienced several previous births showed significant changes in urinary estrogens, androgens, prolactin and cortisol in the last two months prior to birth whereas less experienced fathers did not. The females' midpregnancy rises in glucocorticoids were followed within one to two weeks by peaks of cortisol and corticosterone in their paired males in 70% of all males and 100% of all experienced males. Examination of behavioral interactions between the pairs did not reveal changes in rates of interactions between the experienced pairs over pregnancy. However, the less experienced pairs had significantly higher levels of affiliative and sexual interactions. Therefore, behavioral communication between the pairs did not appear to account for the hormonal changes occurring within the experienced fathers. The midpregnancy rise of glucocorticoids in females may stimulate a glucocorticoid response in male tamarins and thereby activate other hormonal changes in males to prepare them for their parenting role.

This research relied on WNPRC Assay Services.

FUNDING: NIH MH35215

TROPHOBLAST DIFFERENTIATION AND PLACENTAL MORPHOGENESIS (0285)

NPRC UNIT: STEM CELL

%NPRC $: 1.500%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
GOLOS, THADDEUS G	PHD	C	WNPRC & OB/GYN	
	MD	G	WNPRC GOLOS LAB	
	MS	G	WNPRC GOLOS LAB & OB/GYN	
	PHD, VMD	C	WNPRC STEM CELL RES & ANATOMY	

names

AXIS I CODES: 1D, 9, 13, 16E, 17, 21, 23 AXIS II CODES: 30, 38, 39, 46, 49, 50A, 55, 60, 73, 81

ABSTRACT

OBJECTIVE: To better understand the process of trophoblast differentiation and placental morphogenesis.

Trophoblast differentiation and placental morphogenesis are the earliest events in mammalian development, yet are virtually impossible to study in humans. Human embryonic stem (hES) cells have captured the public imagination as a source of cells for regenerative medicine and reconstitution of diseased organs. Human ES cells also provide an unprecedented opportunity to improve our understanding of basic processes of early human development. We have evaluated the expression of trophoblast markers in differentiating ES cells. Trophoblast differentiation is initiated during embryoid body formation, as demonstrated by secretion of chorionic gonadotropin, progesterone and estrogen, as well as the expression of the nonpolymorphic MHC class I trophoblast marker HLA-G. Human ES in vitro differentiation systems such as the formation of embryoid bodies will allow investigation of factors and regulatory pathways that direct both trophoblast differentiation and placental morphogenesis.

This research used federally approved hES cell line H1.

FUNDING: NIH 34215

private funding

RHESUS HEART REGENERATION WITH EMBRYONIC STEM CELLS (0286)

NPRC UNIT: STEM CELL

%NPRC $: 0.025%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KAMP, TIMOTHY J	MD, PHD	A	CARDIOLOGY	
Lname_1	PHD	A	CARDIOLOGY	

AXIS I CODES: 1D, 13

AXIS II CODES: 46, 88

ABSTRACT

OBJECTIVE: To address the major cause of death in the United States, heart disease, we will test a new form of cell-based therapy to regenerate diseased or damaged myocardium. We aim to test the ability of rhesus embryonic stems (ES) cells to regenerate heart muscle following myocardial infarction.

RESULTS: Efforts to date have optimized the rhesus myocardial infarction model. We evaluated this model using echocardiography and MRI imaging. We used pathological studies to corroborate the imaging results. Secondly, we produced a rhesus ES cell line expressing a marker protein, green fluorescent protein, which will allow us to track transplanted cells in the animal. Two control monkeys are also involved in the study. We anticipate treating an additional 2-3 animals with ES cells and studying the results this year.

This work used WNPRC Animal Services.

FUNDING: NIH R21 HL72089-01

PANCREATIC ISLET DIFFERENTIATION FROM RHESUS ES CELLS AND TRANSPLANTATION (0280)

NPRC UNIT: STEM CELL

%NPRC $: 0.025%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ODORICO, JON	MD	A	SURGERY	
L names	PHD	A	SURGERY	
	PHD, VMD	C	WNPRC STEM CELL RES & ANATOMY	

AXIS I CODES: 1D, 2, 4, 15, 16 AXIS II CODES: 49, 88, 95

ABSTRACT

OBJECTIVE: To develop a preclinical model of ES cell- derived islet tissue for transplantation based on Rhesus ES cells.

RESULTS: Rhesus ES cells differentiating in culture begin de novo to express genes for islet endocrine hormones and islet-restricted transcription factors. Insulin immunostaining cells also appear in small clusters as a rare cell population in late stage ES cell cultures that have been differentiated first as embryoid bodies for 2 weeks and then grown in serum containing medium. When transplanted to SCID mice, Rhesus ES cells develop into teratomas some of which express insulin mRNA and mRNA for other islet hormone genes such as somatostatin, glucagon, islet amyloid polypeptide and pdx1, the pancreatic and duodenal homeobox factor, expressed in the early foregut epithelium fated to become pancreas and adult beta and delta cells. These studies indicate the potential of Rhesus ES cells for pancreatic lineage differentiation.

WNPRC resources used include Stem Cell Resources and Pathology Services.

FUNDING: R2, NCRR DK58919-02, initial grant funding period of 2 years is over, it is in a no cost extension with a budget balance of ~$5,000. Total budget for 2 years was $288,000.

NATIONAL STEM CELL CENTER (0139)

NPRC UNIT: STEM CELL

%NPRC $: 2.500%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
THOMSON, JAMES A	PHD, VMD	C	WNPRC STEM CELL RES & ANATOMY	

AXIS I CODES: 1D, 9 AXIS II CODES: 54A, 60

ABSTRACT

OBJECTIVE: To develop a protocol for the proliferation of rhesus ES cells that will improve viability and promote uniformity, consistency and ease of use. This will be accomplished in part by 1) eliminating undefined media components, and 2) optimizing the physiochemical environment.

RESULTS: 1) Eliminating undefined media components. To eliminate the need for serum and fibroblast feeder layers, specific growth factors are very likely to be required to supplement the medium. Addition of specific growth factors to standard culture media may improve attachment, cell growth and proliferation, and reduce the need for fibroblast feeder layers or media conditioning. However, the cost and number of known growth factors that could be used to supplement primate ES cell basal medium, demands a rational method for selecting individual growth factors for testing. During our last budget cycle we developed a quantitative method to examine the impact of culture conditions on stem cell viability, differentiation and self-renewal using human ES cells with an EGFP reporter gene under control of the endogenous Oct4 (a marker of pluripotency) promoter regulatory region. Because the assay for evaluation of rhesus ES cell viability and proliferation is more cumbersome and qualitative than the human assay, we are using the human assay to initially screen growth factors prior to testing them in the rhesus model. Using this method, only those factors that show promise for increasing human ES cell proliferation and self-renewal are then tested on non-human primate ES cells. Using this method of prescreening allows us to significantly increase the number of factors that can be tested in a given period of time. To date we have screened more then 81 growth factors on human ES cells, and have identified 12 that show promise for increasing primate ES cell proliferation and self-renewal. Studies are currently underway to test those factors using the more involved and qualitative rhesus ES cell proliferation and self-renewal assay.

2) Optimizing the physiochemical environment. We are continuing experiments working toward optimization of the physiochemical culture environment. Recently completed studies demonstrate that a reduction in the environmental pH significantly reduces spontaneous differentiation and increases the cloning efficiency of rhesus ES cells. Additionally, studies currently underway suggest that altering the osmolarity of culture medium may also have a significant affect on the undifferentiated proliferation of rhesus ES cells.

FUNDING: AGR DTD 12/21/00 Agency, DHHS, PHS, NIH Subcontract from ATCC ($200,000)

IMPROVED LENTIVIRAL VECTORS FOR PRIMATE EMBRYONIC STEM CELLS (0275)

NPRC UNIT: STEM CELL

%NPRC $: 0.500%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
THOMSON, JAMES A	PHD, VMD	C	WNPRC STEM CELL RES & ANATOMY	

AXIS I CODES: 1D, 7B, 9 AXIS II CODES: 39, 49, 50A, 55, 77

ABSTRACT

OBJECTIVE: To generate lentiviral particles with improved long term, site dependent expression in primate ES cells and their derivates and to test specific genetic markers for their role in self renewal.

We are using a functional ES cell screen to isolate novel genomic DNA fragments that promote long term, integration site dependent expression of lentiviral vectors. We are using lentiviral vectors to test the role of specific genes involved in the self-renewal of the other stem cells (b-catenin, ID1, notch STAT3) in promoting the self-renewal of primate ES cells. We will use a lentiviral cDNA expression cloning strategy to identify novel genes produced by fibroblasts and by the ES cells themselves that promote ES cell self-renewal.

RESULTS: B-catenin and ECFP (enhanced cyan fluorescent protein) have been sucessfully expressed in primate ES cells and lentiviral construction has been further optimized. The full lentiviral vector has been sequenced and modified to increase the efficiency of cloning into the vectors. cDNA expression cloning and library construction is currently underway.

This research used federally approved hES cell lines H1, H7, H9, H13, and H14.

FUNDING: DHHS, PHS, NIH. LC92 1 R24 RR16209-01 document # R4RR16209A ($424,808.00)

OPTIMIZE EMBRYONIC STEM CELL CULTURE MEDIA (0276)

NPRC UNIT: STEM CELL

%NPRC $: 1.500%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
THOMSON, JAMES A	PHD, VMD	C	WNPRC STEM CELL RES & ANATOMY	
[name]	PHD	G	WNPRC THOMSON LAB	

AXIS I CODES: 1D, 4, 9 AXIS II CODES: 54A, 60

ABSTRACT

OBJECTIVE: To develop a media formulation and protocol for the human ES cell culture that will improve human ES cell viability and promote uniformity, consistency and ease of use across a variety of users in different locations. Some of the specific objectives necessary to accomplish this goal are to: 1) optimize the physiochemical environment, 2) optimize the basal media formulation and 3) eliminate undefined media components.

RESULTS: Optimizing the culture of primate ES cells is more difficult than optimizing the culture of most cells, because more parameters must be examined than just cell growth. If cell growth alone were examined, culture conditions that favor differentiation at the expense of self-renewal might be selected. During our last budget cycle we developed a quantitative method to examine the impact of culture conditions on stem cell viability, differentiation and self-renewal using human ES cells with an EGFP reporter gene under control of the endogenous Oct4 (a marker of pluripotency) promoter regulatory region. This year, we have utilized this quantitative assay to continue our work optimizing the physiochemical environment for human ES cells. We have determined that both media pH and osmolarity have a significant impact on human ES cell proliferation and self-renewal, and minor alteration in these parameters can significantly improve human ES cell culture. Work on the effects of oxygen tension on human ES cell viability are ongoing, but initial studies suggest that gas atmosphere may also have a significant impact on ES cell proliferation and self-renewal.

We have also made significant progress in the elimination of undefined media components from human ES cell culture medium. Currently, human ES cell culture relies on the presence of serum or serum substitute (Gibco knockout Serum Replacer iKOSRi) to maintain undifferentiated proliferation. While KOSR supports ES cell proliferation equivalent to serum in culture, it contains iAlbumax,i a poorly defined, lipid-rich bovine serum albumin preparation. For this reason, consistency, while better than that of serum alone, is still a major concern with this product. Additionally, continued spontaneous differentiation in culture suggests that further optimization of the serum replacer additive may be appropriate. Because the formulation of KOSR is now in the public domain, we have used it as a starting point for serum alternative media supplement optimization. We have recreated the formulation that includes Albumax in our laboratory with success, and are now focusing on replacing this component with more defined material. Modifications of our supplement, which reduce complexity and replace protein sources, have been tested in our laboratory. As the protein source used has become increasingly defined, it seems clear that the addition of growth factors to this serum substitute may increase attachment, promote proliferation, and aid in increasing self-renewal and cell competence. We have currently tested more than 30 individual growth factors to determine their affect on human ES cell culture, and have identified no fewer than 12 that have a positive impact on human ES cell proliferation and self-renewal.

This research used federally approved hES cell lines H1, H7, H9, H13, and H14.

FUNDING: AFR DTD 07/31/02 Agency, DHHS, PHS, NIH ($160,000 total costs)

WNPRC STEM CELL RESOURCES (0277)

NPRC UNIT: STEM CELL

%NPRC $: 5.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
THOMSON, JAMES A	PHD, VMD	C	WNPRC STEM CELL RES & ANATOMY	
	PHD	G	WNPRC THOMSON LAB	
	PHD	A	WNPRC THOMSON LAB	
	PHD	G	WNPRC THOMSON LAB	
	PHD	G	WNPRC THOMSON LAB	
	PHD	G	WNPRC THOMSON LAB	
	PHD	G	WNPRC THOMSON LAB	
	MD	A	WNPRC THOMSON LAB	

AXIS I CODES: 1D, 9, 13, 17, 21, 23 AXIS II CODES: 30, 60, 77, 88

ABSTRACT

A narrative for Stem Cell Resources appears in the Infrastructure section of this report.

Post-docs and graduate students in the Thomson lab at the WNPRC are listed on this SPID. Essential to Stem Cell Resources but not categorized on the Personnel Roster are a lab manager, six research specialists, and student assistants as needed.

FUNDING: NIH P51 RR000167

PILOT SUBPROJECTS

RHESUS MONKEY PARKINSON MODEL FOR STEM CELL TRANSPLANTATION (0227)

NPRC UNIT: STEM CELL

%NPRC $: 0.010%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
TERASAWA, EI	PHD	C	WNPRC ASSAY SERVICES & PEDS	
	PHD	A	WAISMAN CENTER	
	PHD	A	WAISMAN CTR	
	PHD	A	MEDICAL PHYSICS	
	PHD	A	NEUROLOGY	
	PHD	A	MEDICAL PHYSICS & RADIOLOGY	
	PHD, VMD	C	WNPRC STEM CELL RES & ANATOMY	
	MD, PHD	A	ANATOMY	

AXIS I CODES: 1A, 21 **AXIS II CODES:** 46, 63C, 63E, 77, 88

ABSTRACT

OBJECTIVE: To test the hypothesis that transplantation of neuroprogenitor cells differentiated from rhesus embryonic stem cells into the striatum of rhesus monkeys alleviates Parkinsonian symptoms induced by treatments with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP).

ABSTRACT BODY: All 4 monkeys treated with MPTP exhibited clear Parkinsonian symptoms in the side contra-lateral to the MPTP injection. The first monkey was sacrificed. Histological examinations in the animal indicated that there was a substantial loss of dopamine neurons in the substantia nigra of the MPTP injected side. Three monkeys received transplantation of either neuroprogenitor cells differentiated from rhesus embryonic stem cells into the striatum or sham surgery. Results suggested that neuroprogenitor cell transplantation moderately alleviates Parkinsonian symptoms.

FUNDING: Anonymous Foundation $30,000

COLLABORATIVE SUBPROJECTS

WNPRC SCIENTIFIC VISITORS (0321)

NPRC UNIT: ADMINISTRATIVE

%NPRC $: 0.010% AIDS RELATED RESEARCH

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KEMNITZ, JOSEPH W	PHD	C	WNPRC DIRECTOR & PHYSIOLOGY	
L	PHD	A	INST. REPROD & DEVELOPMENT	MONASH UNIV., AUSTRALIA
	PHD	A	REPROD SCI & NEUROSCIENCES	OHSU SCHOOL OF MEDICINE, OR USA
	MD	A	ANATOMIC PATHOLOGY	MARSHFIELD CLINIC, WI USA
	MD, PHD	A	NEUROLOGICAL SCIENCES	RUSH UNIVERSITY, IL USA
names	PHD	A	INSTITUTE OF BIOLOGY	NATIONAL UNIVERSITY OF MEXICO, MEXICO
	PHD	A	PSYCHIATRY & OB/GYN	WAYNE STATE UNIVERSITY , MI USA
	MD	A	MICROBIOLOGY & IMMUNOLOGY	UNIVERSITY OF MELBOURNE, AUSTRALIA
	MD	A	NAT'L INST OF TOXICOLOGICAL RE	REPUBLIC OF SEOUL, KOREA
	MD	A	WPRC NEUROLOGY	
	PHD	A		CIPHERGAN BIOSYSTEMS, CA USA
	PHD	A	CORPORATE DEVELOPMENT	BRIDGE PHARMACEUTICALS, INC., CA USA
	PHD	A	BIOTECHNOLOGY CENTER	
	PHD	A		REGENERON PHARMAEUTICALS, NY USA
	PHD	A	CELL THERAPY CENTER	BEIJING INSTITUTE OF GERIATRICS, CAPITAL UNIVERSITY OF MED SCI, CHINA
J	PHD	A	DIRECTOR	YNPRC, GA USA

AXIS I CODES: 1A, 1D, 9, 15, 19, 20, 21, 23 AXIS II CODES: 30, 31, 36, 46, 58, 60, 66, 77, 83, 88, 91, 93

ABSTRACT

OBJECTIVE: To directly introduce the WNPRC's resources and expertise to scientists and visitors from around the nation and world; with the goals of enhancing scientific collaboration, recruiting top investigators, increasing use of Center services and resources, and increasing funding for Center research and supporting activities.

The WNPRC hosts many scientific visitors. Some have projects using Center resources. Others are looking into conducting research through the Center. Many visit to consult with Center staff and scientists, present seminars or otherwise share their expertise, receive training or train their students, or use the Library, Assay Services, or other Center resources and services while they are on site. Scientific visitors to the WNPRC in FY2003-2004 are listed as "co-investigators" on this SPID so that they may remain on the WNPRC personnel roster as active, contributing affiliates of the Center. These individuals' involvement with the Center is detailed in the Director's Office Narrative of the Infrastructure section of this report.

CALORIE RESTRICTION AND PLASMA LIPIDS IN NON-HUMAN PRIMATES (0197)

NPRC UNIT: AGING & METABOLIC DISEASE

%NPRC $: 0.010%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
EDWARDS, IRIS J	PHD	A	SCHOOL OF MEDICINE	WAKE FOREST UNIVERSITY , NC USA
[illegible]	PHD	C	WNPRC DIRECTOR & PHYSIOLOGY	
names	PHD	A	SCHOOL OF MEDICINE	WAKE FOREST UNIVERSITY , NC USA
[illegible]	PHD	C	WNPRC & MEDICINE & VA-GRECC	

AXIS I CODES: 1D, 2, 13, 15, 16D **AXIS II CODES:** 30, 49, 74F, 74H, 78

ABSTRACT

OBJECTIVE: To determine the effects of calorie restriction on plasma lipids and clarify mechanisms of how this may alter the risk profile in relation to human heart disease.

ABSTRACT BODY: Cardiovascular disease is the leading cause of death in Western society. The risk of a cardiovascular event increases with age but the reason for this association is unknown. One potential link is age-associated changes in plasma lipids, a major risk factor for human cardiovascular disease. Caloric restriction (CR) is an intervention shown to retard aging processes and extend lifespan in many species. Our studies are investigating the effects of CR on plasma lipids of rhesus monkeys, to determine if CR may retard age-related changes in lipoproteins, the lipid carriers in the bloodstream. Studies to date have shown a significant benefit of CR in lowering in plasma triglycerides. In addition, CR-induced changes have been observed in the composition of and structure of LDL, the lipoprotein species positively associated with human coronary heart disease. Importantly, CR modified properties of LDL related to imparting increased coronary heart disease susceptibility. Another lipoprotein particle Lp(a) that is an independent risk factor for human coronary heart disease and resistant to current standard lipid lowering therapies, was also modified by CR. Studies are presently focusing on the mechanism of this finding. It is also apparent that the response to CR in lipoprotein metabolism is different in male and female animals, with a greater response measured in males in a number of parameters.

FUNDING: NIH AG11915

COOPERATIVE HUMORAL & CELLULAR IMMUNITY AGAINST HIV/SIV (0278)

NPRC UNIT: AIDS COMPONENT

%NPRC $: 1.000% AIDS RELATED RESEARCH

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
BURTON, DENNIS	PHD	A	IMMUNOLOGY	SCRIPPS RESEARCH INST., CA USA
[name]	PHD	C	WNPRC & PATHLAB MED	

AXIS I CODES: 1A, 2, 3, 7B, 9, 19 AXIS II CODES: 31, 64, 66, 77, 83, 91

ABSTRACT

OBJECTIVE: To determine to what degree or under what circumstances cellular and humoral immunity can act cooperatively in clearing or controlling HIV-1 infection.

RESULTS: In these studies we investigate the ability of combined cellular and humoral immunity to protect against HIV infection by providing, prior to viral challenge, a cellular response through vaccination and neutralizing antibodies by passive administration. We refer to this approach as "active T cell/passive antibody". We evaluate the approach in SIVmac239 challenge of macaques. We use vaccination protocols already established to elicit vigorous T cell responses to SIV proteins and a recombinant CD4-IgG2 antibody. CD4-IgG2 have been shown to be highly effective in neutralizing this generally resistant virus. SIVmac239 is chosen because it is considered as one of the most appropriate model for HIV-1 infection. CD4-IgG2 is chosen because it behaves in key respects as a conventional monoclonal antibody, but has particularly potent activity against SIVmac239. We have finished the first set of experiments, which aimed at finding an CD4-IgG2 administration regimen that provides protection against intrarectal SIVmac239 challenge. We are set to start the second set of experiments with an aim of finding a CD4-IgG2 dosage that will provide a subprotective plasma level of this recombinant protein.

For day-to-day animal handling we utilize the WNPRC Animal Care Unit, for viral challenge and virus detection we work closely with the Virology Unit, and to monitor pathogenesis and SIV specific immune responses we collaborate with the Immunology Core Laboratory.

FUNDING: NIH R01 AI 52057, a total amount of $367,528.00 for FY2003/2004.

ROLE OF MEMORY T CELL DYNAMICS IN SIV INFECTION (0268)

NPRC UNIT: AIDS COMPONENT

%NPRC $: 0.010% AIDS RELATED RESEARCH

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
PICKER, LOUIS	PHD	A		WASHINGTON UNIVERSITY, ST. LOUIS, MO USA
	DVM, PHD	A	PATHOBIOLOGY AND IMMUNOLOGY	OHSU & ONPRC, OR USA
	MD, PHD	A	HUMAN IMMUNOLOGY	NIH VACCINE RESEARCH CENTER, MD USA
	PHD	A	PHYSIOLOGY AND PHARMACOLOGY	TEL-AVIV UNIVERSITY, ISRAEL
	PHD	C	WNPRC & PATHLAB MED	

AXIS I CODES: 1A, 1D, 7B, 19 **AXIS II CODES:** 31, 64, 66, 91

ABSTRACT

OBJECTIVE: To characterize the nature and regulation of T cell turnover in various stages of Simian Immunodeficiency Viris (SIV) infection, and to ascertain the impact of this regulation on viral dynamics and disease progression.

RESULTS: The mechanisms linking replication of HIV-1 to the progressive cellular immunodeficiency of AIDS are controversial, particularly the relative contribution of CD4+ T cell destruction to the disease process. Indeed, in the rhesus macaque model, progressive disease can occur in the absence of significant CD4+ lymphopenia, suggesting that mechanisms other than direct or indirect CD4+ destruction play a role. In the past year's work, we used new approaches for delineation of systemic CD4+ T cell dynamics to determine the extent to which CD4+ T cell insufficiency underlies rapid disease progression.

This research used the nonhuman primate MHC typing laboratory at the WNPRC.

FUNDING: NIH NIAID 1 R01 AI54292-02 ($112,545)

MHC-BOUND, SIV-DERIVED, CTL AND HTL EPITOPES (0152)

NPRC UNIT: AIDS COMPONENT

%NPRC $: 1.000% AIDS RELATED RESEARCH

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
WATKINS, DAVID I	PHD	C	WNPRC & PATHLAB MED	
L	PHD	A	MICROBIOLOGY & IMMUNOLOGY	EMORY UNIVERSITY, GA USA
	PHD	A	DIRECTOR	NETHERLANDS PRIMATE RES CTR, NETHERLANDS
names	PHD	A	MICROBIOLOGY & IMMUNOLOGY	UNIVERSITY OF OKLAHOMA, OK USA
	PHD	A	BIOLOGICAL SCIENCES	INDIANA UNIVERSITY, IN USA
	PHD	A	WPRC WATKINS LAB	
	PHD	A		WASHINGTON UNIVERSITY, ST. LOUIS, MO USA
	PHD	C	WNPRC REPRO RES SERVICES	
J	PHD	A		EPIMMUNE, CA USA

AXIS I CODES: 1D, 7B, 17, 19 AXIS II CODES: 31, 64, 66, 83, 91, 94

ABSTRACT

OBJECTIVE: To work on developing a vaccine for HIV, we are identifying additional epitopes for cytotoxic and helper T cells.

ABSTRACT: Five pairs of animals are egg and sperm donors for our IVF program and constitute the founding animals for our MHC-defined breeding program. MHC-defined males produce offspring with a single defined haplotype. Father/daughter IVF produce MHC homozygotes. We aim to define the MHC class I and II molecules, and infect the offspring of these five pairs of macaques with SIV to define the cellular immune response to the virus. This will enable us to synthesize both MHC class I and II tetramers.

RESULTS: Given the binding motif for Mamu A*02, L J name determined that 220 potential SIV peptides fit this binding motif, 75 peptides actually bound with high affinity. These 75 peptides were tested in Mamu A*02 animals infected with SIVmac239 and 19 responses were observed. Mamu A*02 tetramers were loaded with 8 of these peptides.

Given the binding motif for Mamu A*11, 462 possible SIV peptides fit the binding motif, 152 bind with high affinity. These 152 peptides were tested in Mamu A*11 animals infected with SIVmac239 and 14 responses were observed. We have not made tetramers using these peptides, because we have not been able to achieve good expression of Mamu A*11 monomers in the .221 transferent expression system.

We developed CD4 HTL cell lines to each of these peptides (Rev9-23ET15, Rev11-27RY15, Gag101-115KT15, Nef138-152RI15) to which responses are made in long term non-progressors. Despite extensive characterization, no alleles could be found that were common amongst all the animals. We postulate that these peptides may bind to DP alleles. Further typing of DPB in additional animals will confirm or deny this. Once restricting alleles are determined, we can proceed to generate tetramers for these peptides.

FUNDING: NIH RR15371

COORDINATED INFORMATION SERVICES (CIS) AMONG NPRCS (0211)

NPRC UNIT: LIBRARY

%NPRC $: 0.010%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ROBINSON, CYNTHIA	MLS	C	WNPRC LIBRARY/INFO SERV	

AXIS I CODES: 28(28) AXIS II CODES: 92(92)

ABSTRACT

OBJECTIVE: To support the coordination of information services among the NPRCs as well as service and outreach to the national and international primatological communities.

RESULTS: Current status: 1) The NPRC staff menu has been folded into Primate Info Net (PIN) under the new title Federally Funded Primate Research. The site provides links to NCRR and NPRC web pages as well as the ability to perform web searches for government information related to primate research. A series of pre-configured searches covering areas such as AIDS, gene therapy and Parkinson's disease are provided. 2) The WPRC Library continues to provide document delivery services to scientists and researchers at the various NPRCs and the Caribbean PRC. Over the past year approximately 12,500 requests have been handled. Because of the continued growth in document delivery the library has expanded and redesigned the space available to this unit. 3) PrimateLit (1940-present) is freely available as an NCRR resource via the Web. Current enhancements under development include the ability to download citations to bibliographic software and migration to a newer more robust version of the SiteSearch Database (version 4.2.2). 4) Primate Info Net (PIN) is undergoing a major redesign that includes a new more up-to-date look, a dynamic front page, a reorganization of the file structure, the use of XHTML and cascading style sheets, database driven link access and maintenance, more intuitive pathways to identify location within the site and additional content. 5) New projects included Primates in the News and access to a variety of primate newsletters converted to digital format and made available through the PrimateLit bibliographic database and Primate Info Net. Subcontractors on the grant are the Primate Information Center, WaNPRC, Seattle, providing indexing, and the UW Madison Libraries providing technical support for the PrimateLit database.

FUNDING: NIH P40 RR015311

AFFECTIVE STYLE: SOCIAL AND PSYCHOBIOLOGICAL SUBSTRATES (0113)

NPRC UNIT: NEUROBIOLOGY

%NPRC $: 0.025%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KALIN, NED H	MD	A	PSYCHIATRY	
[redacted]	PSYD	A	PSYCHIATRY	

AXIS I CODES: 1A, 2, 15, 21 AXIS II CODES: 36, 62, 72

ABSTRACT

OBEJCTIVE: To use the rhesus monkey as a model to further characterize the behavioral and physiological correlates of extreme behavioral inhibition and to investigate the brain mechanisms underlying this trait.

RESULTS: Behavioral inhibition (BI) or, in its extreme form, freezing, is an adaptive response which individuals engage in when confronted with threatening situations. Clinical research has demonstrated that in its excessive form BI is a trait marker for children who are very shy and develop into overly fearful adolescents and adults. Later in life, these individuals have an increased likelihood of developing clinically significant anxiety and depression suggesting that extreme behavioral inhibition may be an early marker for later development of psychopathology. Because of its potential clinical importance, we have developed a paradigm in rhesus monkeys to assess BI. We have characterized the biological correlates of extreme BI and found that these animals have relative right frontal electrical activity and elevated basal cortisol levels. These findings further characterize the endocrinology phenotype of fearful temperaments and point to mechanistic studies to further understand the biology of fear related psychopathology.

This research used WNPRC Animal Services.

FUNDING: NIH MH52354

DEVELOPMENT AND REGULATION OF EMOTION IN PRIMATES (0114)

NPRC UNIT: NEUROBIOLOGY

%NPRC $: 0.025%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KALIN, NED H	MD	A	PSYCHIATRY	
[redacted]	PSYD	A	PSYCHIATRY	

AXIS I CODES: 1A, 2, 15, 21 **AXIS II CODES:** 36, 62, 63C, 72

ABSTRACT

OBEJCTIVE: To understand the neural system underlying the expression of emotion in primates.

RESULTS: We used sophisticated behavioral measures to address mechanisms underlying emotional processing in primates. Results demonstrate an important role for the amygdala in the processing of acutely fearful stimuli. The findings from these studies will be highly relevant to humans, addressing the role of amygdala-orbitofrontal interactions in mediating normal emotion and psychopathology.

This work used WNPRC Animal Services.

FUNDING: NIH MH46729

SOCIAL STRESS IN PRIMATES: VULNERABILITY AND RESILIENCE (0115)

NPRC UNIT: NEUROBIOLOGY

%NPRC $: 0.010%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KALIN, NED H	MD	A	PSYCHIATRY	
[redacted]	PSYD	A	PSYCHIATRY	

AXIS I CODES: 1A, 2, 15, 21 AXIS II CODES: 36, 62, 72

ABSTRACT

OBJECTIVE: To demonstrate that individuals with positive disposition compared to those with negative dispositions have lower levels of stress-related hormones, better immune function, and are more likely to survive stressful social and physiological insults.

RESULTS: Evidence for a link between negative affect and disease progression exists. In humans, social stress is ubiquitous and often leads to psychological and physical disability. It appears that it is the interaction between stressful events and an individual's temperament that determines how individuals perceive and cope with stress. For example, a recent study demonstrated that the presence of depression greatly increased the risk of death in individuals who recently suffered heart attacks. To begin to understand the interaction among the factors involved in survival, researchers from the WNPRC have combined efforts and expertise with researchers at the Caribbean Primate Center in Cayo Santiago Puerto Rico to exploit the unique opportunity provided by the free ranging colony and its inherent naturalistic stressors. The overall purpose is to understand the biological factors associated with different dispositions, the biological similarities and differences associated with the constructs of emotional style and social status, and the effects these dispositions have on health, social functioning, and the ability to effectively deal with potentially stressful situations.

This work used WNPRC Animal Services.

FUNDING: NIH MH61083

NON-HOST INST: University of Puerto Rico Recinto Ciencias Medicas-Caribbean Primate Research Center.

MARMOSET AND TAMARIN MODELS FOR BIOMEDICAL RESEARCH (0326)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 5.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ABBOTT, DAVID H	PHD	C	WNPRC ASSAY SERVICES & OB/GYN	
L	PHD	A	NEPRC	HARVARD MEDICAL SCHOOL, MA USA
names	PHD	C	WNPRC ANIMAL SERVICES	
d	PHD	A		SNPRC, AZ USA

AXIS I CODES: 1A, 1D, 23 **AXIS II CODES:** 36, 77

ABSTRACT

OBJECTIVE: To evaluate the current use of marmosets and tamarins in biomedical research, and identify new areas where these animals might prove to be invaluable research models.

ABSTRACT BODY: Three National Primate Research Centers, those with colonies of common marmosets (Callithrix jacchus) and/or Cottontop tamarins (Saguinus oedipus), have formed a research consortium to research this topic.

RESULTS: None yet.

PARACRINE DYSREGULATION OF OOCYTE COMPETENCE IN PCOS (0310)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.010%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
DUMESIC, DANIEL A	MD	A	MEDICINE & OB/GYN	MAYO CLINIC, MN USA
[redacted]	PHD	C	WNPRC ASSAY SERVICES & OB/GYN	
	PHD	C	WNPRC REPRO RES SERVICES	

AXIS I CODES: 1D, 4 AXIS II CODES: 74

ABSTRACT

OBJECTIVE: To further develop the prenatally androgenized (PA) female rhesus monkey as a model for PCOS.

RESULTS: Polycystic ovary syndrome (PCOS) in women is characterized by anovulation, LH hypersecretion, hyperandrogenism and insulin resistance. As the most common endocrinopathy in females, affecting 4-7% of reproductive-aged women, and as a frequent cause of infertility, accounting for 75% of anovulation, PCOS has staggering adverse physiological, psychological and financial consequence on reproduction in women. During gonadotropin stimulation for in vitro fertilization (IVF), PCOS women experience decreased fecundity and increased pregnancy loss. Since experimental investigation of oocyte and embryo development in humans is limited by ethical constraints, we have developed the prenatally androgenized (PA) female rhesus monkey as a model for PCOS. PA female monkeys undergoing follicle stimulating hormone (FSH) therapy for IVF exhibit LH hypersecretion, circulating insulin excess, an exaggerated shift in intrafollicular steroidogenesis from estradiol (E2) and androstenedione (A4) to progesterone (P4), and impaired embryo development beginning with embryonic genome activation.

FUTURE DIRECTIONS: Because insulin enhances FSH-induced granulosa cell differentiation, leading to LH-induced P4 production, we hypothesize that a) premature follicle luteinization and b) impaired oocyte developmental competence in PA monkeys are caused by adverse effects of hyperinsulinemia on follicle maturation. We predict that such abnormalities in PA monkeys are reversed by improved insulin sensitivity from weight loss through dietary restriction and will test our prediction in Specific Aims 1 and 2. Based upon data from our recognized nonhuman primate model of PCOS, we also hypothesize that c) premature follicle luteinization is a cause of poor oocyte developmental competence in PCOS women undergoing FSH therapy for IVF. We predict that granulosa cell dysregulation of LH receptor, insulin receptor (IR) and growth differentiation factor-9 (GDF-9) transcription from premature follicle luteinization causes poor cumulus cell proliferation in PCOS women (Specific Aim 3). We further hypothesize that d) meiotically-competent and meiotically-incompetent oocytes of PCOS patients are impaired in expression of GDF-9 and other developmentally relevant messenger ribonucleic acids (mRNAs) (Specific Aim 4). The long-term objectives of this proposal are to 1) define molecular markers of oocyte developmental competence that enhance IVF pregnancy outcome by improving rates of embryo cleavage and blastocyst formation; while minimizing pregnancy loss in women with PCOS and other insulin resistant states, such as obesity and Type II diabetes, and 2) to provide additional, unique, insight into the transgenerational effect of PCOS.

FUNDING: NIH U01 HD02-018

POST-MENOPAUSAL CHANGES IN PULSATILE GNRH IN THE RHESUS MONKEY (0199)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.010%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
GORE, ANDREA C	PHD	A	PHARMACOLOGY & TOXICOLOGY	UNIVERSITY OF TEXAS AT AUSTIN , TX USA
[redacted]	PHD	C	WNPRC ASSAY SERVICES & PEDS	[redacted]

AXIS I CODES: 1A, 23 AXIS II CODES: 60

ABSTRACT

OBJECTIVE: To understand how the release of the brain hormone, gonadotropin-releasing hormone (GnRH) changes in menopause in a non-human primate.

The reproductive axis of rhesus monkeys is virtually identical to that of humans, and these animals are an ideal model for understanding both normal and dysfunctional reproductive processes. The results of these studies are anticipated to provide novel information as to the role of the brain in the menopausal process in both human and nonhuman primates.

The control of reproductive function is quite complex. It involves all the levels of the reproductive axis, which comprises: 1) the hypothalamus in the brain; 2) the anterior pituitary gland; and 3) the gonads (ovary in females, testis in males). The primary regulatory level of the reproductive axis is the hypothalamus, containing neurons that synthesize and release gonadotropin-releasing hormone (GnRH). GnRH is released in a pulsatile manner into the portal capillary system leading to the pituitary gland. There, GnRH stimulates cells in the pituitary gland to release its hormones (lutcinizing hormone and follicle-stimulating hormone), which in turn travel through the general circulation to stimulate the gonads to produce the sex steroid hormones, estrogen and progesterone in females, and testosterone in males. Thus, changes in GnRH across the reproductive life cycle are responsible for activation of the reproductive axis and the attainment of adult reproductive function, and for senescent changes and possibly menopause during aging.

The proposed experiments are designed to test how GnRH release changes during reproductive aging in a non-human primate model of menopause in humans. Young adult female rhesus monkeys have 28-day menstrual cycles that are similar to those in women. During reproductive aging, these cycles become irregular and cease at menopause. Nevertheless, many of the mechanisms that are responsible for this transition are unknown. The proposed experiments will test the role of hypothalamic GnRH neurons in menopause. For these studies, pulsatile GnRH release will be measured and compared between young premenopausal, and old postmenopausal female monkeys. Studies are being conducted at the WRPRC in a collaboration with Mount Sinai School of Medicine in New York.

All experimentation (push-pull perfusion, surgeries, radioimmunoassays) were performed at the WNPRC. The results will determine, for the first time, whether GnRH neurons change during reproductive aging in a non-human primate, and should be extremely relevant to the menopausal process in humans.

FUNDING: NIH AG16765

NONHUMAN PRIMATE EMBRYO GENE EXPRESSION RESOURCE (0263)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.010%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
LATHAM, KEITH	PHD	A	BIOCHEMISTRY	FELS INSTITUTE OF CANCER RESEARCH & TEMPLE U. SCH. OF MEDICINE, PHILADELPHIA, PA USA
[illegible]	PHD	C	WNPRC REPRO RES SERVICES	

AXIS I CODES: 1A, 1D, 23, 28(OOCYTE/EMBRYO BIOLOGY)

AXIS II CODES: 39, 59, 77

ABSTRACT

OBJECTIVE: To develop the Primate Embryo Gene Expression Resource (PREGER), which is a cDNA-based resource for gene expression analysis in rhesus monkey oocytes and preimplantation embryos, and to utilize the PREGER to evaluate developmentally regulated genes to better understand the genetic regulation of primate embryogenesis.

RESULTS: During this budget period, we have obtained the remainder of the samples required to complete the primary PREGER sample set. The sample set now includes over 160 samples of oocytes and preimplantation stage embryos. Included are in vivo matured oocytes, in vitro matured oocytes from hormone primed and nonstimulated monkeys, and all stages of preimplantation embryos derived from in vivo and in vitro matured oocytes, or flushed from the uterus of naturally mated monkeys (blastocysts). Embryos derived from in vivo matured oocytes were cultured in two different embryo culture media. Samples of inner cell mass and trophectoderm cells were also obtained from hatched blastocysts. The PREGER was used to determine expression patterns of various "housekeeping" genes, transcription factors, and chromatin regulatory factors during oocyte maturation and preimplantation embryogenesis, and how they differ among in vitro and in vivo produced oocytes and embryos. Results demonstrate the utility of the PREGER as a novel resource for gene expression studies in nonhuman primate oocytes and embryos.

This research used WNPRC Animal Services (Veterinary Services, Surgical Services).

FUNDING: NIH RR000167; NIH RR15253 (Total costs for subcontract - current budget period: $100,000)

MONOSYNAPTIC CONNECTIONS BETWEEN THE BRAINSTEM AND SPINAL CORD AND ESTROGEN (0141)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.010%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
VAN DER HORST, VERONIQUE G J M	PHD	A	NEUROBIOLOGY	UNIV CALIF AT SAN FRANCISCO, CA USA
[redacted]	PHD	A	ANATOMY	UNIVERSITY OF CALIFORNIA-SAN FRANCISCO, CA USA
[redacted]	PHD	C	WNPRC ASSAY SERVICES & PEDS	

L names ⌟

AXIS I CODES: 1A, 20, 21 **AXIS II CODES:** 36, 46, 60, 77, 82, 90, 93

ABSTRACT

OBJECTIVE: To identify monosynaptic connections between the brainstem and the lumbosacral cord and determine the effects of estrogen.

ABSTRACT BODY: Neurons in the lateral periaqueductal gray contain estrogen receptor alpha, but it is unclear whether projections from the lateral periaqueductal gray to the nucleus retroambiguus that control vocalization and reproductive behavior, are estrogen sensitive. Track tracing with immunocytochemistry indicated that only a few estrogen immunoreactive neurons in the periaqueductal gray projected to the nucleus retroambiguus and the majority of projections were non-estrogen containing neurons. This finding is quite different from that observed in other mammalian species, in which aboundant estrogen containing neurons in periaqueductal gray project to the nucleus retroambiguus. The findings are parallel to the modest effects of estrogen on mating-related behavior in primates as compared to most other mammalian species.

FUNDING: Supplemental funding to RR000167 (1997-1998)

CAUSES OF DEVELOPMENTAL FAILURE OF IN VITRO MATURED RHESUS MONKEY OOCYTES (0262)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.010%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
VANDEVOORT, CATHERINE A.	PHD	A	PHYSIOLOGY	CALIFORNIA NATIONAL PRIMATE RESEARCH CENTER, CA USA
[redacted]	PHD	A	ENDANGERED SPECIES RESEARCH	UNIVERSITY OF NEW ORLEANS AND AUDUBON CENTER , LA USA
[redacted]	PHD	C	WNPRC REPRO RES SERVICES	
[redacted]	PHD	A	CNPRC & PEDIATRICS	UNIVERSITY OF CALIFORNIA-DAVIS, CA USA

AXIS I CODES: 1A, 1D, 23 AXIS II CODES: 59, 92(GAMETE/EMBRYO BIOLOGY)

ABSTRACT

OBJECTIVE: To develop strategies for using cytoplasm transfer to improve the developmental competence of in vitro matured (IVM) oocytes. Understanding the causes of developmental failure of embryos derived from IVM oocytes will lead to improvements in protocols for in vitro maturation of oocytes that would be extremely valuable for treatment of infertility, especially for women with polycystic ovarian syndrome and cancer patients undergoing radio- or chemo-therapy.

RESULTS: During this budget period, we have focused on developing strategies for transfer of cytoplasm from in vivo to in vitro matured oocytes. Bovine oocytes were used to assess the developmental competence of oocytes from which 0%, 25%, or 50% of the cytoplasm was removed. Blastocyst development was negatively correlated with the amount of cytoplasm removed. Therefore, in a second series of experiments, mature zona-free oocytes were fused to enucleated cytoplasts to form "giant eggs". Fusion rates were approximately 75% for both bovine and rhesus. Zona-free rhesus monkey zygotes were cultured in microdrops and developed into blastocysts at an equivalent rate to zona-intact control embryos. The goal during the next budget period will be to fuse in vivo matured rhesus cytoplasts to in vitro matured rhesus oocytes approximately 3 hours after insemination and evaluate their developmental competence compared to that of nonmanipulated in vivo and in vitro matured rhesus oocytes. Parallel studies have been initiated to determine the whether developmental failure of IVM oocytes is associated with impairments in the initiation of mRNA synthesis, rRNA synthesis, or both, among individual blastomeres of 8-cell stage embryos.

WNPRC resources used for these studies: Animal Services (Veterinary Services, Surgical Services.)

FUNDING: NIH R01 RR13439 (Total costs for subcontact - current budget period: $89,913)

MUSCLE ANATOMY AND JAW GAPES IN TREE GOUGING VERSUS NON-GOUGING CALLITRICHIDS (0267)

NPRC UNIT: REPRODUCTION&DEVELOPMENT

%NPRC $: 0.010%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
VINYARD, CHRIS	PHD	A	COLLEGE OF MEDICINE	NORTHEASTERN OHIO UNIVERSITIES, ROOTSTOWN, OH USA
[redacted]	PHD	A	MEDICAL CENTER	DUKE UNIVERSITY, NC USA

AXIS I CODES: 1A, 20, 22 AXIS II CODES: 34, 92(ORGANISMAL BIOLOGY)

ABSTRACT

OBJECTIVE: To understand the evolution of head form in tree-gouging marmosets.

ABSTRACT BODY: We are studying the muscle's position in the skull, basic anatomy and fiber architecture in marmosets and tamarins. Such insights into the basic biology of these small callitrichids will provide conservation biologists with further information for making management decisions in critically endangered South American callitrichids.

We are investigating and comparing the jaw-muscles of three South American monkey species. We are examining the overall morphology and position of these muscles as well as their structure, fiber length and physiological cross-sectional area. The three species are the common marmoset (Callithrix jacchus), the saddle-back tamarin (Saguinus fuscicollis), and the squirrel monkey (Saimiri sciureus). C. jacchus habitually gouges trees for food, that is, it elicits gums from trees by mechanically damaging them with its anterior teeth. This tree gouging is hypothesized to require relatively large gapes. The two comparative taxa, S. fuscicollis and S. sciureus, both feed on insects, fruits and gums, but do not gouge trees. We are testing whether the jaw muscles of C. jacchus are positioned in a way that allows larger gapes (i.e., reduces the amount of stretching on them during jaw opening) as compared to S. fuscicollis and S. sciureus. We also are looking at whether C. jacchus has relatively longer muscle fiber lengths to facilitate these larger gapes, as compared to S. fuscicollis and S. sciureus. Finally, we are determining if these three species are able to produce comparable jaw forces across a range of gapes using the data on physiological cross-sectional area. This work complements comparative functional analyses of skull form in these species and on-going field and lab work on tree gouging in common marmosets.

This research relied on WNPRC Animal Services.

FUNDING: NSF 7173-0 $6,870.00

DERIVATION OF VERVET EMBRYONIC STEM CELLS FOR STUDYING PARKINSON'S DISEASE (0319)

NPRC UNIT: STEM CELL
%NPRC $: 0.010%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
SVENDSEN, CLIVE	PHD	A	ANATOMY	
[names]	DVM	C	WNPRC ANIMAL SERVICES	
	PHD	C	WNPRC DIRECTOR & PHYSIOLOGY	

AXIS I CODES: 1D, 9, 21, 23 **AXIS II CODES:** 30, 46, 77

ABSTRACT

OBJECTIVE: To derive embryonic stem (ES) cell lines from vervet (African Green) monkeys and attempt to direct into dopaminergic neurons for treating Parkinson's Disease in a nonhuman primate model.

RESULTS: None yet. Project funded January 2004.

This work involves the use of WNPRC Animal Services and Stem Cell Resources.

FUNDING: [ ] awarded January 2004.

private funding

INDUCTION OF DOPAMINE NEURONS FROM RHESUS STEM CELLS (0196)

NPRC UNIT: STEM CELL

%NPRC $: 0.010%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ZHANG, SU-CHUN	MD, PHD	A	ANATOMY	
[redacted]	PHD, VMD	C	WNPRC STEM CELL RES & ANATOMY	

AXIS I CODES: 1A, 4 AXIS II CODES: 88

ABSTRACT

OBJECTIVE: To explore the possibility of generating dopamine neurons from an unlimited source of monkey embryonic stem (ES) cells for potential cell replacement therapy in Parkinson's disease.

ABSTRACT BODY: We have established a strategy that directs the pluripotent stem cells to a neural fate. This process entails aggregation and culture of ES cells in suspension, followed by differentiation of the ES cell aggregates in an adherent condition with a cocktail containing fibroblast growth factor 2 (FGF2) for 5-7 days. Neural precursor cells displayed a characteristic columnar morphology, organized into neural tube-like rosette formations, and expressed neuroepithelial marker, nestin and NCAM. These neural precursor cells were separated from surrounding non-neural cells to 95% purity by differential enzymatic response and differential adhesion. The isolated neural precursor cells differentiated into neurons and glial cells after withdraw of FGF2 in vitro. Ongoing study is to guide the ES-derived neural precursors further to dopamine neurons and examine the function of the dopamine neurons in a rat model of Parkinson's disease.

FUNDING: NIH R21 RR016588

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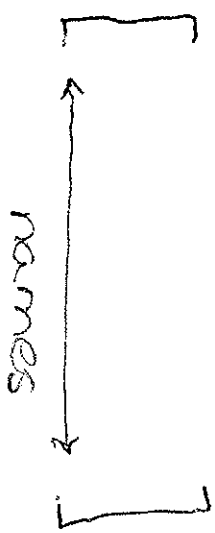
RESEARCH SERVICES

NAME	NON-HOST INSTITUTION: STATE, COUNTRY	# SPECIES: SPECIMEN
[redacted]		5 MACACA MULATTA: ORGANS
		1 MACACA MULATTA: TISSUES
		23 MACACA MULATTA: ORGANS
		11 MACACA MULATTA: ORGANS
	PATHOLOGY ASSOCIATES: MA	20 MACACA MULATTA: TISSUES
	PATHOLOGY ASSOCIATES: MA	
		29 MACACA MULATTA: TISSUES
		35 MACACA MULATTA: ORGANS
		29 MACACA MULATTA: OTHERS
		35 CALLITHRIX JACCHUS: ORGANS
		1 CALLITHRIX JACCHUS: TISSUES
		1 MACACA MULATTA: TISSUES
		17 MACACA MULATTA: ORGANS
	PATHOLOGY ASSOCIATES: MA	1 MACACA MULATTA: OTHERS
	LDS: MN	21 MACACA MULATTA: ORGANS
		20 MACACA MULATTA: ORGANS
		1 MACACA MULATTA: ORGANS
		6 MACACA MULATTA: TISSUES
	MARSHFIELD LABORATORIES: WI	
		2 CALLITHRIX JACCHUS: WHOLE
		44 MACACA MULATTA: ORGANS
		1 MACACA MULATTA: TISSUES
		22 CALLITHRIX JACCHUS: ORGANS
		1 CALLITHRIX JACCHUS: TISSUES
	UNIVERSITY OF WASHINGTON: WA	7 CALLITHRIX JACCHUS: ORGANS
	UNIVERSITY OF WASHINGTON: WA	
	UNIVERSITY OF WISCONSIN - MILWAUKEE: WI	4 MACACA MULATTA: WHOLE
	UNIVERSITY OF WISCONSIN MILWAUKEE: WI	12 CALLITHRIX JACCHUS: ORGANS
		2 MACACA MULATTA: ORGANS
		2 MACACA MULATTA: OTHERS
		50 MACACA MULATTA: ORGANS
		3 MACACA MULATTA: TISSUES
	PPL THERAPUTICS, INC.: VA	1 MACACA MULATTA: OTHERS
	PPL THERAPUTICS, INC.: VA	9 MACACA MULATTA: WHOLE
	VA HOSPITAL; UW-MADISON: WI	10 MACACA MULATTA: TISSUES
		11 MACACA MULATTA: OTHERS
		12 MACACA MULATTA: ORGANS
		1 MACACA MULATTA: ORGANS
	SLIPPERY ROCK UNIVERSITY: PA	40 CALLITHRIX JACCHUS: OTHERS
	VA HOSPITAL; UW-MADISON: WI	1 CALLITHRIX JACCHUS: ORGANS
[redacted]		2 MACACA MULATTA: TISSUES



	4 MACACA MULATTA: OTHERS
	9 MACACA MULATTA: ORGANS
	17 CALLITHRIX JACCHUS: ORGANS
	1 CALLITHRIX JACCHUS: TISSUES
	6 MACACA MULATTA: TISSUES
	12 MACACA MULATTA: ORGANS
MILLENNIUM PHARMACEUTICALS, INC.: MA	
MILLENNIUM PHARMACEUTICALS, INC.: MA	1 MACACA MULATTA: TISSUES
DUKE UNIVERSITY: NC	6 CALLITHRIX JACCHUS: WHOLE
	1 MACACA MULATTA: TISSUES
	10 MACACA MULATTA: OTHERS
	7 CALLITHRIX JACCHUS: OTHERS
	1 MACACA MULATTA: OTHERS
	1 MACACA MULATTA: TISSUES

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‡ NPRC Cited *NPRC Personnel

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ZWICK, MICHAEL B;KELLEHER, ROBERT;JENSEN, RICHARD;LABRIJN, ARAN F;WANG, MENG;QUINNAN, GERALD V JR;PARREN, PAUL W H I;BURTON, DENNIS R* A novel human antibody against human immunodeficiency virus type 1 gp120is V1, V2, and V3 loop dependent and helps delimit the epitope of thebroadly neutralizing antibody immunoglobulin G1 b12. J Virol 77 6965-78 2003

SPIDs Unknown Reference

1. PUBLICATIONS NOTE: Most papers cite the Wisconsin National Primate Research Center, Wisconsin Primate Research Center, or some other variant on the center's name. There is no practical way for the APR editor to search for the required citation text "RR" using the PubMed database; therefore, these publications, although they used center resources, are not marked as cited as required by this system's definition.

2. PUBLICATIONS NOTE: SPIDs are linked to published, peer-reviewed journal articles, books, and book chapters (chapters appear in the books category) on this list. SPIDs are not linked to abstracts for the purposes of this report

0211, 0231

3. PUBLICATIONS NOTE: Many publications each year involve the use of the WNPRC's world-renowned Library and Information Services in their preparation. Because these services include the Internet-based Primate Info Net, with its 10 million hits per year, publications not citing the WNPRC but involving use of the WNPRC Library and Information Services are too numerous to practically search and list in this report. For some examples of publications that involved the use of this resource, please contact WNPRC Library and Information Services at robinson@primate.wisc.edu

IN PRESS: ABSTRACTS, BOOKS & JOURNALS

‡ NPRC Cited *NPRC Personnel

SPIDs	Reference
Abstracts	
Books	
0295	
0215	
0313, 0250	
Journals	
0083	
0160	
0160	
0304	
0230, 0229, 0147	
0237	
0114	
0215	
0160	
0083	

in-press publications

0313, 0250

0313, 0250

In press publications

0312

0267

0293

Unknown

NOTE: NCRR cannot search Medline/PubMed for citations on in-press papers. Most in-press papers cite either the WNPRC, or both the WNPRC and the Base Grant, however there is no practical way to search for exact citation text at this time

SOURCE OF INVESTIGATORS' SUPPORT

NON-FEDERAL

FOUNDATION

INVESTIGATOR ORGANIZATION	GRANT/CONTRACT	TOTAL FUNDING	SPID
ABBOTT, DAVID H			
private funding	CIG-02-78	$ 207,510	0284
GOLOS, THADDEUS G			
private funding	FY00-164	$ 49,482	0285
GRUNEWALD, ALEXANDER			
private funding		$ 75,000	0237
private funding		$ 5,000	0330
SVENDSEN, CLIVE			
Private funding		$ 500,000	0319
TERASAWA, EI			
Private funding		$ 30,000	0227
VINYARD, CHRIS			
private funding	7173-0	$ 6,870	0267
private funding	TITLE	$ 8,000	0267
	FOUNDATION	$881,862	

INDUSTRY

INVESTIGATOR ORGANIZATION	GRANT/CONTRACT	TOTAL FUNDING	SPID
ABBOTT, DAVID H			
private funding		$ 224,478	0317
FREEDMAN, ROBERT			
Private funding		$ 435,763	0198
KAUFMAN, PAUL L			
private funding		$ 16,047	0122
KEMNITZ, JOSEPH W			
private		$ 40,482	0341
funding		$ 113,600	0255
KENNEDY, STEPHEN			
Private funding		$ 3,000	0329
MACDONALD, KELLY S			
Private funding		$ 222,397	0311
	INDUSTRY	$1,055,767	

FEDERAL

INVESTIGATOR ORGANIZATION	GRANT/CONTRACT	TOTAL FUNDING	SPID
FEDERAL - NON PHS			
KARASOV, WILLIAM			
NSF	IBN-0216709	$ 127,307	0318

MARLER, CATHERINE A NSF	IBN-0110625		0312
THOMSON, JAMES A DOD	DOD ARPA LM74 DRP5-UWM	$ 460,453	0342
VINYARD, CHRIS NSF	BCS0094666	$ 0	0267
	FEDERAL - NON PHS	$ 587,760	
FEDERAL - PHS			
NIH	5R01AG017543-05	$ 194,757	
NIH	5R01AG011604-08	$ 291,000	
NIH	5P30DK056336-04	$ 810,000	
NIH	5R01DK056366-05	$ 93,261	
NIH	1T32HL072757-01	$ 109,881	
NIH	5R01AI042373-06	$ 320,000	
ALTMANN, JEANNE NIH	5R03MH065294-02	$ 79,000	0331
NIH	5U24RR018107-02	$ 1,316,833	
NIH	5U42RR016025-04	$ 1,097,716	
NIH	5R01EY013692-02	$ 289,021	
NIH	5R01MH060338-04	$ 288,000	
NIH	5R01MH052226-09	$ 407,602	
BIRD, IAN NIH	5R01HL064601-03	$ 218,250	
BURTON, DENNIS NIH	5R01AI052057-02	$ 774,821	0278
NIH	5U01AI048494-04	$ 368,686	
NIH	5R01AI048053-04	$ 310,275	
NIH	5R37AI033292-12	$ 498,748	
NIH	1R01AI055332-01	$ 771,584	
NIH	5R01MH062568-02	$ 551,478	
NIH	1R01MH062568-01A2	$ 560,593	
DEWHURST, STEPHEN NIH	5R21AI049102	$ 350,000	0322
NIH	2R01AR027032-23A2	$ 311,543	
DUMESIC, DANIEL A NIH	1U01HD044650-01	$ 346,083	0310
NIH	5P50HD044405-02	$ 1,059,743	0282

NIH	5R01NS040578-04	$ 286,000	
FREEDMAN, ROBERT			
NIH	5R01MH063089-03	$ 332,310	
NIH	5R37AG005233-16	$ 391,661	
GOLOS, THADDEUS G			
NIH	3R01HD034215-06S1	$ 109,125	
NIH	5R01HD034215-06	$ 448,663	0285
NIH	5R24RR014040-04	$ 492,140	0257
NIH	5R01HD037120-05	$ 262,806	0256
GORE, ANDREA C			
NIH	1R21ES012272-01	$ 139,650	
NIH	5R01MH065723-04	$ 323,735	
KALIN, NED H			
NIH	5R01MH046729-12	$ 454,402	0112,0114
NIH	2R01MH040855-14A1	$ 487,460	
KAMP, TIMOTHY J			
NIH	5R21HL072089-02	$ 217,268	0286
KAUFMAN, PAUL L			
NIH	5R01EY010213-07	$ 288,000	0122
NIH	5R01EY002698-25	$ 664,880	0218,0220
NIH	2R01AI044386-06	$ 395,457	
NIH	5R01AI047446-04	$ 594,500	
NIH	1R21AI055625-01	$ 291,000	
NIH	1R01AI055519-01	$ 165,807	
NIH	5R01AI044386-05	$ 319,200	
KEMNITZ, JOSEPH W			
NIH	N01AG31014	$ 291,205	0328
NIH	5P30CA7945802	$ 0	
NIH	5R01AI049781-02	$ 275,625	
KIMBERLING, W.J.			
NIH	5R03EY013991-02	$ 100,000	0330
LATHAM, KEITH			
NIH	5R01HD041440-02	$ 304,763	
NIH	5R01HD038381-04	$ 254,512	
NIH	1R01HD043092-01A1	$ 304,763	
NIH	5R01HD020677-14	$ 279,215	
NIH	5T32HD007068-25	$ 224,764	
NIH	5U42RR016020-04	$ 130,309	
NIH	5P01DK055510-04	$ 1,079,923	
NIH	5R01EY013199-03	$ 278,250	

NIH	5R21DC005472-02	$ 50,000	0330
NIH	5R01HD041098-03	$ 377,500	
NIH	5R21NS045015-02	$ 152,682	
NIH	1R01NS045113-01A1	$ 377,200	
NIH	1R21NS045015-01	$ 151,301	
NIH	5R01AG017902-04	$179,155	
NIH	1R03AG17696-1	$ 0	
ROBINSON, CYNTHIA			
NIH	5P40RR015311-04	$ 503,223	0211
SALTZMAN, WENDY			
NIH	5R01MH060728-05	$ 234,630	0126,0281,03 16,0336
SCHNEIDER, MARY			
NIH	5R01AA012277-03	$ 388,620	0250
NIH	5R01AA010079-08	$ 366,100	0313
NIH	5R01DK030031-18	$ 307,369	
NIH	5R01AI056268-02	$ 845,827	
SLUKVIN, IGOR I			
NIH	1K08HD044067-01	$ 91,800	0270
SNOWDON, CHARLES T.			
NIH	5R01MH035215-20	$ 327,375	0296,0307
NIH	5R01MH029775-24	$ 291,000	0308,0309
TANUMIHARDJO, SHERRY A			
NIH	5R01DK061973-02	$ 134,315	0272
NIH	5U01HL069748-03	$ 562,169	
NIH	3U01HL069748-03S1	$ 59,650	
NIH	1R01HL073220-01	$ 323,250	
NIH	1R13HL072168-01	$ 20,000	
TERASAWA, EI			
NIH	3R01HD015433-18	$ 202,500	0223
NIH	3R01HD015433-19S1	$ 25,016	
NIH	5R01HD015433-20	$ 251,100	
NIH	5R01HD011355-22	$ 228,501	0224
THOMSON, JAMES A			
NIH	1P20GM069981-01	$ 669,175	0139,0276
NIH	5R24RR016209-02	$ 430,987	0275
NIH	5R01NS043317-02	$ 241,894	
NIH	1R01NS043317-01A1	$ 319,628	
VANDEVOORT, CATHERINE A.			
NIH	5R01RR013439-06	$ 551,925	0262
WATKINS, DAVID I			

NIH	5R24RR016038-03	$ 490,135	
NIH	5R24RR015371-04	$ 551,851	0152
NIH	5R01AI049120-03	$ 931,391	
NIH	5R01AI046366-05	$ 440,507	
NIH	1R01AI052056-01A1	$ 661,445	
NIH	R01DA12324-02	$ 0	0146
NIH	5R01AI46366-02	$ 0	0147
NIH	5R01AI41913-03	$ 0	0146
NIH	5D43TW006180-02	$ 356,329	
NIH	5R01MH064205-06	$ 375,367	
NIH	5T32MH020053-04	$ 86,497	
WEINDRUCH, RICHARD			
NIH	1P20CA103697-01	$ 586,000	
NIH	5R01AG018922-03	$ 372,081	
NIH	5P01AG011915-10	$ 1,416,472	0160,0197,0253,0266,0287,0288,0289,0324
NIH	5T32AG000213-13	$ 385,144	
NIH	1R13RR018799-01	$ 46,334	
NIH	5R01RR016030-03	$ 412,007	
NIH	5R01NS044330-02	$ 600,864	
ZHANG, SU-CHUN			
NIH	5R21RR016588-02	$ 145,500	0196
NIH	1U01NS046587-01	$ 308,820	
NIH	1R01NS045926-01	$ 337,339	
NIH	1G20RR018323-01	$ 695,449	
	FEDERAL - PHS	$ 39,469,692	
	FEDERAL	$40,057,452	
TOTAL FUNDING:		**$41,995,081**	

RESOURCE SUMMARY: SUBPROJECTS

The following only includes information associated with subprojects.

	Mgmt. A	Research B	Pilot C	Collab. D	Total (excludes
Number of Subprojects	11	74	1	18	104
Number of Investigators	27	148	8	54	199
Number of Published	24	41	0	9	55
Number In Press	3	14	0	2	18
%AIDS of NPRC Dollars	5.760%	29.100%	0.000%	2.020%	36.880%
%Non-AIDS of NPRC Dollars	6.000%	51.950%	0.010%	5.160%	63.120%
Total Percent of NPRC Funds Awarded	11.760%	81.050%	0.010%	7.180%	100.000%

RESOURCE SUMMARY: ADMINISTRATIVE

PERSONNEL		On Subprojects	Not On Subprojects
Core Personnel			
DOCTORAL LEVEL SCIENTISTS (C)		26	0
	Core Personnel	26	0
Non-Core Personnel			
AFFILIATED (A)		151	3
GRADUATE STUDENT/POST DOCTORAL SCIENTIST (G)		22	2
	Non-Core Personnel	173	5
Personnel Total:		199	5

ACCESS BY NON-NPRC PERSONNEL

GEOGRAPHICAL USAGE BY INVESTIGATORS AT NON-HOST INSTITUTIONS

Foreign Investigators by Country	20
AUSTRALIA	2
CANADA	3
CHINA	1
ECUADOR	1
ISRAEL	1
KOREA	1
MEXICO	1
NETHERLANDS	1
SCOTLAND	1
SWITZERLAND	1
THAILAND	1
UK	6
USA Investigators by State	78
AL	1
AZ	1
CA	13
CT	2
GA	2
IL	7
IN	1
LA	2
MA	4
MD	4
MI	2
MN	5
MO	1
NC	4
NE	4
NJ	2
NY	4
OH	1
OK	1
OR	6
PA	2
TN	1
TX	2
WA	1
WI	5
Total Investigators at Non Host Institutions:	98

RESEARCH SERVICES

Scientists Provided with Services	31
Services Provided	622

RESEARCH SERVICES BY COUNTRY

Research Services to USA Investigators by State	12
MA	3
MN	1
NC	1
PA	1
VA	1
WA	1
WI	4
Research Services to Host Investigators	19
Total Research Services:	31

INFRASTRUCTURE TABLE

GRANT REPORTED UNITS		**%NPRC USE**
ADMINISTRATIVE		5.750%
AGING & METABOLIC DISEASE		0.700%
AIDS COMPONENT		12.000%
ANIMAL SERVICES		22.000%
ASSAY SERVICES		3.500%
IMMUNOLOGY		9.000%
LIBRARY		5.000%
NEUROBIOLOGY		2.500%
OPERATIONAL SERVICES		16.550%
PATHOLOGY		5.000%
REPRODUCTION&DEVELOPMENT		2.000%
RESEARCH SERVICES		10.000%
STEM CELL		6.000%
	TOTAL NPRC:	**100.00%**

RESEARCH TABLE

UNITS GENERATED BY SUBPROJECTS		**%NPRC USE**
ADMINISTRATIVE		0.510%
AGING & METABOLIC DISEASE		18.165%
AIDS COMPONENT		22.510%
ANIMAL SERVICES		1.000%
ASSAY SERVICES		1.500%
IMMUNOLOGY		2.600%
LIBRARY		0.260%
NEUROBIOLOGY		3.145%
OPERATIONAL SERVICES		0.500%
PATHOLOGY		1.000%
REPRODUCTION&DEVELOPMENT		37.720%
RESEARCH SERVICES		0.010%
STEM CELL		11.080%
	TOTAL NPRC:	**100.000%**

RESOURCE SUMMARY: PUBLICATION/SUPPORT

PUBLICATIONS

	Cited	Not Cited	Total
Published			
Abstracts	0	36	36
Books	0	5	5
Journals	14	91	105
Unknown	0	3	3
In Press			
Abstracts	1	1	2
Books	2	3	5
Journals	4	15	19
Unknown	0	1	1
Total	21	155	176

INVESTIGATOR SUPPORT

NON-FEDERAL		
FOUNDATION		$881,862
INDUSTRY		$1,055,767
	NON-FEDERAL	**$ 1,937,629**
FEDERAL		
NON-PHS		
DOD		$460,453
NSF		$127,307
	NON-PHS	**$ 587,760**
PHS		
AA		$754,720
AG		$3,521,475
AI		$8,314,873
AR		$311,543
CA		$586,000
DA		$0
DC		$50,000
DK		$2,424,868
ES		$139,650
EY		$1,620,151
GM		$669,175
HD		$4,770,854
HL		$1,510,468
MH		$4,799,449
NS		$2,775,728
RR		$6,864,409
TW		$356,329

PHS	$ 39,469,692
TOTAL SUPPORT	$41,995,081

COLONY STATISTICS

Research Colony Only

Note: These animals are supported by NCRR Comparative Medicine.

1Genus Species	May-03	2Live Births	3Other Additions	Exper. Use	4Other Reduct.	5Sold or Trans.	6Trans. in Center	Apr-0
CALLITHRIX JACCHUS								
Adult Females	109	0	53	1	32	34	0	95
Adult Males	122	0	68	1	28	57	0	104
Infants/Juveniles	104	100	0	0	28	0	121	55
CHLOROCEBUS AETHIOPS								
Adult Females	0	0	10	0	0	0	0	10
Adult Males	0	0	10	0	1	0	0	9
MACACA FASCICULARIS								
Adult Females	20	0	10	0	0	0	0	30
Adult Males	20	0	10	0	0	0	0	30
Infants/Juveniles	0	0	0	0	0	0	0	0
MACACA MULATTA								
Adult Females	0	0	371	25	35	1	0	310
Adult Males	0	0	244	20	16	6	0	202
Infants/Juveniles	0	159	0	0	16	0	0	143
Gender Undetermined	0	0	0	0	0	0	0	0
MACACA MULATTA (SPF)								
Adult Females(SPF)	535	0	0	0	0	0	365	170
Adult Males(SPF)	305	0	0	0	0	0	244	61
Infants/Juveniles(SPF)	299	0	0	0	0	0	137	162
Gender Undetermined(SPF)	0	0	0	0	0	0	0	0
	1,514	**259**	**776**	**47**	**156**	**98**	**867**	**1,381**

1 - Animals that are known free of SIV, STLV, SRV/D and Herpes B

2 - Live birth defined as inflated lungs

3 - Purchased from outside Center or transferred from another colony within the Center

4 - Includes deaths due to intercurrent diseases and other causes

5 - Permanent transfer or sale to outside the Center

6 - Transferred to another colony within the Center

RESEARCH HIGHLIGHTS

AGING MONKEYS ON RESTRICTED DIETS SHOW HEALTH BENEFITS

SPID(s): 0160

(From WNPRC Centerline newsletter, spring/summer 2003)

Now in its 15th year, the Wisconsin National Primate Research Center's study on caloric restriction (CR) and aging has resulted in many health benefits to aging monkeys. These include better glucoregulation, which results in a lower risk for diabetes, a decreased rates of both osteoarthritis and cardiovascular disease, and less arthritis.

CR reliably causes reduced body weight and body fat. Although originally, this was thought to be the mechanism of CR's life extending actions, the researchers believe that the beneficial effects of CR are not conferred simply from weight reduction.

There are five possible explanations for how CR may be imparting its health benefits, and they are not mutually exclusive of one another:
--Decreases in oxidative stress and damage.
--Decrease in glycation or glycoxidation.
--Decrease in body temperature associated with a hypometabolic state.
--Alterations in gene expression and protein degradation.
--Neuroendocrine changes.

Among other reasons, CR helps us investigate diseases of aging and the normal aging process in the hope of understanding, treating and preventing age-related diseases. Additionally, since humans, on a widespread scale, are not likely to practice the strict dietary control necessary to successfully carry out CR, the identification and development of CR mimetics is a possible goal of these studies.

Publications:

Wang C, Weindruch R, Fernández JR, Patel P, Allison DB. Caloric restriction and body weight independently affect longevity in Wistar rats. Int. J. Obes. Relat. Metab. Disord. 28:357-62, 2004

Barger JL, Walford RL, Weindruch R: The retardation of aging by caloric restriction: its significance in the transgenic era. Exp Gerontol. 38:1343-51, 2003

Higami Y, Pugh TD, Page G, Allison DB, Prolla TA, Weindruch R: Adipose tissue energy metabolism: altered gene expression profile of mice subjected to long-term caloric restriction. FASEB J. 18:415-7, 2004

Bevilacqua L, Ramsey JJ, Hagopian K, Weindruch R, Harper, ME. Effects of Short-and Medium-Term Caloric Restriction on Muscle Mitochondrial Proton Leak and Reactive Oxygen Species Production. Am J Physiol Endocrinol Metab. [Epub ahead of print] Jan 21 2004

Page GP, Edwards JW, Barnes S, Weindruch R, Alison DB. A design and statistical perspective on microarray gene expression studies in nutrition: the need for playful creativity and scientific hard-mindedness, Nutrition. 19(11-12): 997-1000 Nov-Dec 2003

Weindruch R, Caloric restriction, gene expression, and aging. Alzheimer Dis Assoc Disord. 17 Suppl 2:S58-9. Review. Apr-Jun 2003

Atwood CS, Barzilai N, Bowen RL, Brown-Borg HM, Jarrard DF, Fu VX, Heilbronn LK, Ingram DK, Ravussin E, Schwartz RS, Weindruch R, Pennington scientific symposium on mechanisms and retardation of aging. Exp Gerontol. 38(10): 1217-26 Oct. 2003

Ramsey JJ, Hagopian K, Kenny TM, Koomson EK, Bevilaqua L, Weindruch R, Harper ME. Proton Leak and hydrogen peroxide production in the liver mitochondria from energy-restricted rats. Am J Physio Endocrinol Metab. 286(1): E31-40 Jan 2004

HIGH VITAMIN A LEVELS ENLARGE LIVER CELLS IN RHESUS MACAQUES

SPID(s): 0272

(From WNPRC Centerline newsletter, Fall/Winter 2003)

Sherry Tanumihardjo and Kristina Penniston, UW Department of Nutritional Sciences, have found elevated vitamin A concentrations and enlarged cells in rhesus monkey livers. While marmoset livers studied were also high in vitamin A, they did not show cell irregularities.

The monkeys ate widely used commercial diets. The researchers found that the diets contained vitamin A concentrations as great as four times higher than National Research Council recommendations for human vitamin A intake.

To further characterize the effects of high dietary vitamin A from preformed sources, the researchers analyzed serum from both rhesus monkeys and marmosets for vitamin A metabolites. They found total serum vitamin A within expected limits for both species, but high serum vitamin A esters (vitamin A attached to fat in the blood). Normal serum vitamin A concentrations were found for both species when compared with published normal values.

Publications:

PENNISTON, KRISTINA L;THAYER, JULIE C;TANUMIHARDJO, SHERRY A* Serum vitamin A esters are high in captive rhesus (Macaca mulatta) and marmoset (Callithrix jacchus) monkeys. J Nutr 133 4202-6 2003

Penniston KL, Tanumihardjo SA. Subtoxic hepatic vitamin A concentrations in captive Rhesus monkeys (Macaca mulatta). J. Nutr. 131: 2904-2909. 2001

SEX IN THE BRAIN: HOW DO MALE MONKEYS EVALUATE MATES?

SPID(s): 0295

(From UW-Madison press release 1-28-04)

A pint-sized, tree-dwelling Brazilian monkey has proven to be strikingly similar to humans when it comes to sexual responses, a national research team has discovered.

Through functional magnetic resonance imaging, or fMRI, scientists from the University of Wisconsin-Madison and collaborating institutions for the first time peered into the brains of fully conscious nonhuman primates to learn what's really on their minds when it comes to sex. The research appears in the February 2004 issue of the Journal of Magnetic Resonance Imaging.

Common marmosets, like humans, live in family groups and have to make careful choices when confronted with the scent of an attractive female, a team of marmoset experts led by Charles T. Snowdon, UW-Madison professor of psychology, discovered.

"We were surprised to observe high levels of neural activity in areas of the brain important for decision-making, as well as in purely sexual arousal areas, in response to olfactory cues," Snowdon says. "Lighting up far more brightly than we expected were areas associated with decision-making and memory, emotional processing and reward, and cognitive control."

The marmoset fMRI findings add strong weight to the mounting evidence that, when faced with a novel, sexually attractive and receptive female, males even in monogamous species aren't necessarily just acting on some primal urge to procreate, without a second thought. Rather, they exhibit highly organized, complex neural processes.

"This is the first time anyone has imaged an awake nonhuman primate in response to emotionally arousing stimuli; it is also the first link between external sexual odors and the internal sexual arousal system," Snowdon says. "This opens up a whole new field of research possibilities."

The marmoset data corresponded surprisingly close to human fMRI studies, the scientists found. "The benefit of the nonhuman primate model is that we can control and know the developmental and social histories of our study subjects, to carry out studies not possible in humans," Snowdon says.

Joining Snowdon in working with the marmosets were Toni Ziegler, Nancy Schultz-Darken and [redacted] of the Wisconsin National Primate Research Center at UW-Madison. The Primate Center provided four male marmosets for the study. The researchers trained and transported them from the University of Wisconsin to the University of Minnesota, where the imaging took place.

The researchers imaged the male marmosets' neural activity while they were presented with anogenital gland secretion samples from periovulatory females, those at or close to ovulation. Other samples, taken from ovariectomized females, gave the researchers a way to compare how the males responded to female marmoset scents containing no sexual cues, according to Ziegler. When the same males smelled the "sexier scents" from the ovulating females, the scientists could discern which neural areas showed further activation, thus identifying areas where information processing occurs.

"We were surprised to learn how great a role the neural areas related to cognitive processing play in determining how males respond to sexually receptive females," Ziegler says.

To preempt stress to the animals, Ziegler and Schultz-Darken brought the marmosets' cage-mates along on the road trip. "The marmosets were trained in advance, over brief periods, to get used to a mock imaging process," Ziegler says. "By the time they underwent the real thing, they did not

exhibit any signs of stress."

"We acted as advocates for the marmosets," adds Schultz-Darken, who is also a colony manager at the Primate Center. "It was very important to properly habituate them to the imaging equipment. We had a wonderful experience with the facility and the people at the University of Minnesota."

Lead author Craig Ferris is a professor of psychiatry at the University of Massachusetts Medical School (UMMS) and director of the Center for Comparative Neuroimaging, collaboration between UMMS and Worcester Polytechnic Institute. The study was funded by the National Institute of Mental Health.

The collaboration also included [ ] and [ ] of the Department of Electrical Engineering at the Worcester Polytechnic Institute. Other scientists included [ ] UMMS associate professor of psychiatry [ ] Harvard Medical School; and [ ] and [ ] at the University of Minnesota, departments of Radiology, Electrical Engineering and Biomedical Engineering.

names

Publications:

Ferris CF, Snowdon CT, King JA, Sullivan JM Jr, Ziegler TE, Olson DP, Schultz-Darken NJ, Tannenbaum PL, Ludwig R, Wu Z, Einspanier A, Vaughan JT, Duong TQ. Activation of neural pathways associated with sexual arousal in non-human primates. J Magn Reson Imaging. Feb; 19(2): 168-75. 2004

STEM CELLS ILLUMINATE EARLY STAGES OF HUMAN DEVELOPMENT

SPID(s): 0285

(From UW-Madison press release 12-22-03)

When introduced to the world in 1998, human embryonic stem cells were considered heralds of a new age of transplant medicine. The prospect of an unlimited supply of cells and tissue of all kinds to treat disease captured public imagination and enthusiasm.

But lost in the glitz of the cells' potential to treat an array of devastating and sometimes fatal diseases was another quality that, when all is said and done, could match even the prospect of remaking transplant technology.

"Much of the excitement surrounding embryonic stem cell research focuses on their potential for transplantation to repair diseased organs," according to Thaddeus G. Golos, a University of Wisconsin-Madison professor of obstetrics and gynecology. "The cells are also a valuable model for beginning to understand the puzzles of early human development."

Indeed, a team led by Golos and colleagues at the Wisconsin National Primate Research Center has now taken some of the first critical steps to putting stem cells to use to understand early development and maternal and fetal health. Writing in the December online editions of the journal Endocrinology, the team led by Golos reports the development of a stem cell model that mimics the formation of the placenta during the earliest stages of human development.

The lab feat is important because prior to the advent of human embryonic stem cells, science's primary window to early development was through studies of mice and other animal models. Human embryonic stem cells and the work of Golos' team has now brought the very first stages of human development, as an embryo implants itself in the uterus, within reach of science. The work could one day help clinicians better understand and treat diseases of pregnancy such as preeclampsia, a disorder that occurs only during pregnancy and the postpartum period and that, by conservative estimates, kills at least 76,000 women and infants each year.

A key aspect of the work by the Wisconsin team was the creation of embryoid bodies, clumps of cells that arise when undifferentiated stem cells are removed from flat culture plates and grown in a suspended culture of proteins and hormones.

"Embryoid bodies are not embryos, but are spherical structures that form when embryonic stem cell colonies are released from the culture surface and grown in suspension," Golos explains.

In that environment, the team subsequently observed the development of trophoblast cells from the embryoid bodies. These specialized cells are the building blocks that lead to the formation of the placenta, which orchestrates a maternal environment that protects and nurtures a fetus during pregnancy.

Golos said that when the embryoid bodies were transferred into an artificial matrix that mimics the network of proteins that surrounds all of the cells in our bodies, his group observed a dramatic increase in trophoblasts' secretion of hormones associated with pregnancy.

"Moreover, the cell outgrowths that we observed from the embryoid bodies resembled aspects of the process by which placenta formation occurs as the embryo implants into the womb," Golos explains. "The opportunity to model these processes with embryonic stem cells is important because the earliest stages of placental function and how its development is controlled cannot be studied in human embryos or early human pregnancy."

By using embryonic stem cells to create a window to these very early stages of human development, scientists now can gain access to the cellular and chemical secrets of how such critical

features as extraembryonic membranes, especially the placenta, grow and develop during pregnancy.

"These steps are essential for the establishment and maintenance of pregnancy," says Golos. "The establishment of mammalian pregnancy requires that the early embryo make a timely decision to begin to form the placenta, the first functional fetal organ."

The big picture, according to Golos, is that a better basic understanding of the events that occur during human pregnancy will ultimately lead to advances in maternal and fetal health. Down the road, such knowledge may lead to fewer birth defects, a lower incidence of miscarriage, and improved health for women and infants.

Co-authors of the new Endocrinology paper include Behzad Gerami-Naini, Oksana V. Dovzhenko, Maureen Durning and Frederick H. Wegner of the Wisconsin National Primate Research Center, and James A. Thomson of the Wisconsin National Primate Research Center and the UW-Madison Medical School's Department of Anatomy.

The C private funds and the National Institutes of Health supported the work of the Wisconsin team.

Publications:

Gerami-Naini B, Dovzhenko OV, Durning M, Wegner FH, Thomson JA, Golos TG. Trophoblast differentiation in embryoid bodies derived from human embryonic stem cells. Endocrinology. Dec 18 [e-pub], Dec 24 [print] 2003

STUDIES OFFER NEW INSIGHT INTO HIV VACCINE DEVELOPMENT

SPID(s): 0147

(From UW-Madison pres release 2-16-04)

Mutations that allow AIDS viruses to escape detection by the immune system may also hinder the viruses' ability to grow after transmission to new hosts, scientists at the University of Wisconsin-Madison announced this week in the journal Nature Medicine.

The discovery may help researchers design vaccines that exploit the notorious mutability of HIV by training the immune system to attack the virus where it's most vulnerable. The work appears alongside a study of HIV-infected people performed by scientists at Harvard Medical School and Oxford University. The Wisconsin study's lead author, Thomas Friedrich, is a doctoral student working under the direction of David Watkins, professor of pathology at UW-Madison and senior scientist at the Wisconsin National Primate Research Center.

Watkins' team produced an "escaped" AIDS virus that mimicked events that occur in HIV infection when the virus mutates to become unrecognizable to killer cells known as cytotoxic T-lymphocytes, or CTL. The researchers found that the mutant virus did not grow as well as the original strain. The mutations, while allowing the virus to escape immune recognition, had also weakened the virus. To model the transmission of escaped viruses between people, the team inoculated monkeys with the mutant virus strain. They discovered that most of the escape mutations were lost as the virus grew in the monkeys, often restoring original sequences that killer cells could recognize.

Some scientists have theorized that HIV could adapt to the human immune system as the AIDS epidemic develops, becoming less and less recognizable. Watkins said that his group's findings should help allay these fears.

The UW-Madison group has been studying immunity to AIDS viruses since the early 1990s. Most recently, the researchers have been studying the ways in which viruses mutate to "escape" recognition by the body's killer cells. Killer cells are white blood cells that perform immune "surveillance" throughout the body, detecting infected cells and eliminating them before the virus can spread.

"Over 40 million people are now infected with HIV worldwide, and a vaccine is urgently needed," Watkins said. "We hope that our findings can be used to help design vaccines that show killer cells how to fight the virus most effectively."

Publications:

Friedrich TC, Dodds EJ, Yant LJ, Vojnov L, Rudersdorf R, Cullen C, Evans DT, Desrosiers RC, Mothe BR, Sidney J, Sette A, Kunstman K, Wolinsky S, Piatak M, Lifson J, Hughes AL, Wilson N, O'Connor DH, Watkins DI. Reversion of CTL escape-variant immunodeficiency viruses in vivo. Nat Med. Feb 15 [Epub ahead of print] 2004

ADMINISTRATIVE INFORMATION

ALLOCATION OF RESOURCE ACCESS

Access to the resources supported by this grant is provided to investigators and other users approved by the director on a charge-back basis. Potential users of the resources and services of the WNPRC typically establish contact via a member of the Senior Management team, the head of a service unit or with the Director. In most cases, the request is quickly approved and subsequently handled through the service units. For cases that would put a very heavy demand on our resources, there is discussion by the Executive Committee. When we are unable to accommodate a meritorious request because of insufficient resources, the potential user is referred to another NPRC or to NCRR.

Numerous entities and committees guide and approve research protocols, which include the appropriate use of the Center's animals and other resources. Internally, these include the Senior Management team (the Director and the Associate/Assistant Directors) and the Executive Committee (the Senior Management team plus tenured core staff investigators). Externally entities are:

--IACUC (Institutional Animal Care and Use Committee, UW-Madison Graduate School)
--RARC (Research Animal Resource Center)
--AAALAC-I (Association for Assessment and Accreditation of Laboratory Animal Care - International)
--University of Wisconsin Biological Safety Committee
--University of Wisconsin Occupational Health and Safety Committee
--USDA, through its published "Guidelines for the Humane Use of Laboratory Animals," which sets forth standards for the humane care and treatment of laboratory animals as mandated under the Animal Welfare Act.
--NIH agencies that award grants for scientific proposals.
--Scientists, by sharing new ideas for humane lab animal use and alternatives or reductions to animal use, and by approving their peers' publications, to ensure continuing funding for promising and humane research activities.

DISSEMINATION

The Wisconsin National Primate Research Center is widely known by scientists and the public. This is due to our extensive presence on the Internet, in the news media and at outreach events throughout the year. Our scientists publish their findings in numerous peer-reviewed journal articles, books, book chapters and meeting abstracts every year. Scientists also share their discoveries and ideas with colleagues and potential collaborators through numerous national and international scientific conferences, seminars, workshops and retreats throughout the year.

AWARDS, HONORS, SPECIAL RECOGNITIONS

MAJOR FY03-04 AWARDS TO WNPRC SCIENTISTS

James Thomson, V.M.D., Ph.D., received two major national awards in 2003-2004.

Dr. Thomson was named the recipient of the 2003 Frank Annunzio Award from the Christopher Columbus Fellowship Foundation, an independent federal government agency. Annunzio Awards are presented annually to living Americans for improving the world through ingenuity and innovation, and are intended to provide incentive for continuing research or a specific project.

Thomson was also named a John D. MacArthur Professor. The appointment carries with it a five-year award for research and scholarly work. The chair was established by a grant from the John D. and Catherine T. MacArthur Foundation. MacArthur purchased Bankers Life and Casualty in 1935 and built it into a highly successful company. He died in 1978, establishing a foundation that has awarded substantial grants to individuals and liberal arts colleges, as well as research institutions.

A UW professor of anatomy, Thomson is Stem Cell Unit chief at the National Primate Research Center at the University of Wisconsin-Madison, and scientific director of WiCell Institute. He earned his advanced degrees in veterinary medicine and molecular biology at the University of Pennsylvania, Philadelphia. He is board certified in veterinary pathology.

Thomson was the first to isolate and culture nonhuman primate embryonic stem cells (PNAS 1995), and human ES cells (Science 1998). He aims to use these cells to improve knowledge of basic reproductive biology, and to explore new treatments for degenerative diseases such as diabetes, heart disease, leukemia and Parkinson's. He has published more than 60 scientific papers on reproductive biology and embryonic stem cells. He has also testified in support of ES cell research to both the Wisconsin and U.S. Congresses.

David I. Watkins, Ph.D., was appointed to the AIDS Vaccine Research Working Group (AVRWG)

Dr. Watkins was invited to be a member of the AIDS Vaccine Research Working Group (AVRWG). The AVRWG assists the NIH in developing a comprehensive research program aimed at expediting the discovery and development of an HIV/AIDS vaccine. Group members provide advice regarding the vaccine research programs at the NIH with respect to scientific opportunities, gaps in knowledge, and future directions of research. As a subcommittee of the NIAID Council, the AVRWG makes recommendations to NIAID, the Office of AIDS Research (OAR) and the NIH on key scientific questions in vaccine development. These include new vaccine designs, efforts to understand the mechanisms of protection in animal models and potential new targets for vaccines.

Sherry Tanumihardjo, Ph.D., received the Alex Malaspina Future Leader Award from the International Life Sciences Institute, Washington D.C.

Dr. Tanumihardjo, assistant professor of nutritional sciences and WNPRC affiliate, was recently awarded the 2004-2006 International Life Sciences Institute Alex Malaspina Future Leader Award. The research award is only the second award of its kind ever to be given. ILSI is a worldwide foundation that is making a difference in public health by advancing the understanding of scientific issues related to nutrition, food safety, toxicology and the environment.

Ashley T. Haase, M.D. was elected a member of the Institute of Medicine of the National Academies Washington, D.C.

Dr. Haase, Regents' Professor and head, Department of Microbiology, University of Minnesota Medical School, was elected to the Institute of Medicine based on professional achievement, conduct of studies, and other Institute inquiries into matters of national policy for health. Election to active membership is a prestigious honor and represents a commitment to serve in Institute affairs. A staff of professionals, drawn from many disciplines and experienced in health and biomedical science policy considerations, supports and augments the work of members. The Institute is recognized as a national resource for independent, scientifically informed analysis and recommendations on issues related to human health.

INFRASTRUCTURE

See appended Infrastructure Word document

Others

None this Fiscal Year.

COMMITTEE MEMBERS

WNPRC EXECUTIVE COMMITTEE MEMBERS

*KEMNITZ, JOSEPH W
AGING
WNPRC DIRECTOR & PHYSIOLOGY

[Admin Personnel]
COLONY MANAGEMENT
COLONY/FACILITIES

COE, CHRISTOPHER L
BEHAVIOR
WNPRC & PSYCHOLOGY

KNABLE, STEVEN M
RESEARCH ADMINISTRATION
OPERATIONAL SERVICES/WNPRC

THOMSON, JAMES A
STEM CELL
WNPRC STEM CELL RES & ANATOMY

WEINDRUCH, RICHARD
GERIATRICS
WNPRC & MEDICINE & VA-GRECC

ABBOTT, DAVID H
REPRODUCTION AND DEVELOPMENT
WNPRC ASSAY SERVICES & OB/GYN

BOLTON, IRIS
VETERINARY MEDICINE
WNPRC ANIMAL SERVICES

GOLOS, THADDEUS G
PLACENTAL BIOLOGY
WNPRC & OB/GYN

TERASAWA, EI
NEUROBIOLOGY
WNPRC ASSAY SERVICES & PEDS

WATKINS, DAVID I
AIDS/HIV
WNPRC & PATHLAB MED

WNPRC EXTERNAL SCIENTIFIC ADVISORY BOARD MEMBERS

ALTMANN, JEANNE
PRINCETON:NJ, USA

[name]
[name]
[name]
[name]
[name]
[name]
[name]
[name]
[name]

ORGANIZATIONAL CHART

University of Wisconsin-Madison Graduate School

Principal Investigator Dean: Martin Cadwallader
Associate Dean, Research: Timothy Mulcahy
Fiscal Dean: Jim Knickmeyer
Personnel Dean: Marcia Douglas

Wisconsin National Primate Research Center

Directors Office
Director: Dr. Joseph Kemnitz
Executive Assistant: [name]
Public Information Officer/Outreach Coordinator: Jordana Lenon
Quality Assurance Coordinator: [name]

Operational Services
Associate Director: Steven Knable
Facilities Management: [name]
Human Resources: [name]
Payroll/Benefits: [name]
Data Management: [name]
Grants Management: [name]
General Shop & Security: [name]
Stores/Delivery: [name]
Accounting Services/Travel: [name]
Purchasing Services: [name]

Research Services
Associate Director: Dr. Amy Usborne
Assay Services: Dr. David Abbott, Dr. Toni Ziegler
Virology Services: [name]
Immunology Services: Dr. Eva Rakasz
Pathology Services: Dr. Amy Usborne
Library Services: Cynthia Robinson

Animal Services
Associate Director: Dr. Iris Bolton
Colony Management: Dr. Nancy Schultz-Darken and [name]
Colony Records: [name]
Clinical Medicine: Dr. Michelle Harke and Dr. Charles Schobert
Centralized Protocol Implementation: Dr. Kevin Brunner

Other Resources
Aging Resource: Dr. Ricki Colman
Genetics Resource: Dr. David Watkins
Stem Cell Resource: Dr. James Thomson

WNPRC APR 2003-2004 INFRASTRUCTURE

1. Physical Plant (S. Knable)

Major Equipment Purchased 5/1/03 through 4/30/04

The center was able to purchase over $800,000 in scientific equipment with institutional support combined with base grant funds. A number of items where purchased to replacing aging equipment throughout the Center. Of particular note, $490,000 of equipment was purchase to augment the AIDS and Stem Cell units.

AIDS
PCR, $57,500
NUCLEOFECTOR, $11,500
FOTO/ANALYST INVESTIGATOR, $9,495
LIGHTCYCLER 2.0. $130,000
LN2 FREEZER, $13,000
NANODROP SPEC SYSTEM, $9,350
TOTAL, $230,845

COLONY
STEREOTAXIC APPARATUS, $32,745
COLONY TOTAL, $32,745

PATHOLOGY
OLYMPUS CKX31 INVERTED MICROSCOPE, $3,756
CAMERA USBORNE MICROSCOPE, $5,000
TISSUE CULTURE INCUBATOR HOOD, $30,000
OLYMPUS BX41 MICROSCOPE PATH RESIDENT, $6,500
G4 NOTEBOOK, $2,299
HIGH RESOLUTION DIGITAL CAMERA, $29,000
DIODE LASER FOR CONFOCAL, $63,153
FLUORESCENCE MODULE FOR CONFOCAL, $45,000
TOTAL $184,708

STEMCELL
FPLC + ACCESSORIES, $81,000
GUAVA PCA SYSTEM, $69,500
ULTRACENTRIFUGE, $69,000
INCUBATORS, $20,000
FREEZER, $9,000
SPECTOPHOTOMETER, $11,500
TOTAL, $260,000

ASSAY
COULOCHEM SYSTEM. $47,702
CENTRIFUGE, $20,000
WATER BATH, $4,567
FLAMMABLE STORAGE REFRIGERATOR, $3,057

TOTAL, $75,326

VIROLOGY
WATER PURIFICATION SYSTEM, $6,167
CO2 INCUBATOR (TWO), $8,000
REFRIGERATED CENTRIFUGE, $6,500
CENTRIVAP DNA SYSTEM, $5,682
TOTAL,$26,349

LIBRARY
CARPET, $25,000
SHELVING, $2,100
FURNITURE, $12,000
TOTAL$39,100

Grand Total, $849,073

2. Progress in Core Service Units

A. Director's Office (J.W. Kemnitz)

i. Director's Activities (J.W. Kemnitz)

The Director's Office enjoyed full staffing, with three associate directors of Operations, Research Services, and Animal Services, as well as its quality assurance coordinator. All of these individuals were highly productive in their areas of expertise.

Successes included expanded use of the center's new building addition for animal housing, procedures preparation, surgery, animal food preparation, pathology, histology, and necropsy.

Challenges continued to include major space and budget restrictions. However, the Primate Centers' base operating grant was increased this past FY, which allowed the improvement of administrative and service functions and their necessary additional support staff.

Among ongoing activities, the Director's Office processed several grants, including a National Institute on Aging contract to develop and manage the Primate Center Aging Database. Dr. Joe Kemnitz is the principal investigator.

[redacted], joined the University of Wisconsin-Madison as Manager of its new Wisconsin Stem Cell Program in 2003. Many of her activities involve working with WNPRC staff and scientists.

The office hosted several meetings in FY2003-2004. [redacted], administrative specialist, coordinated these meetings throughout the year. [redacted], Dr. Kemnitz and other staff also began planning the American Society of Primatology meeting for June 2004.

Notable visitors to the Center included the following:

[ ], May 2003. [ ] met with Dr. Kemnitz to discuss collaborative research opportunities in India.

[ ], April 2003. [ ] gave an invited University of Wisconsin Lecture on behavioral correlates of serotonin in infant monkeys and the consequences of having different alleles for this neurotransmitter and its transporters. She also spoke on the genetics of anxiety in primates, and discussed her research on stress, fertility and pregnancy with center staff.

[ ] December 2003. [ ] presented a seminar, "Comparative Anatomy of Primate Genitalia Touch Receptors." His work involved the use of WNPRC Pathology Services.

[ ], May 2003. [ ], a candidate for a UW faculty position, presented a seminar, "Gene Therapy in Nonhuman Primate Models of Parkinson's Disease."

[ ], January and February. [ ] presented a roundtable in January and a seminar in February. He is on sabbatical in 2004 and is based in the UW-Madison Anthropology Department. He is using the Primate Center Library and Assay Services (for training his student) while at the UW-Madison. He directs research programs in the Primatology Lab of the field station at Los Tuxtlas, Instituto de Biología, Universidad Nacional Autónoma de México in southern Mexico. These programs encompass projects with wild primates, other mammals, birds and some insect groups of the tropical rain forests of southern Mexico.

Robert Freedman, August 2003. Dr. Freedman presented a seminar on his research on physiological mechanisms of menopausal hot flashes. His research on this topic is presented elsewhere in this report.

[ ], August 2003. [ ] spent the month of August working with the Watkins SIV/HIV research team, and presented a seminar on AIDS vaccine research at the Center.

[ ] October 2003. [ ] is assisting with his government's plans to establish a new Primate Center. Center Director Joe Kemnitz hosted his visit, which included attending the AAALAS meetings in Seattle.

Erwin Montgomery, September 2003. Dr. Montgomery visited the Center early in 2003, then moved from the Cleveland Clinic to the University of Wisconsin-Madison in September. He has established a medical practice at UW Hospital and Clinics, and a lab at the Primate Center to develop a nonhuman primate model for studying deep brain stimulation as a method to treat Parkinson's disease.

[ ] February 2004. [ ] presented a seminar on accelerating protein discovery, characterization, ID and assay in clinical and research proteomics.

[ ], April 2004. [ ] presented a seminar about the UW Biotechnology Center, a close affiliate department with the Primate Center. (Stem cells, genetics, outreach and more).

[ ] and [ ] Kinetics Foundation, October 2003. [ ] were interested in possibly funding Parkinson's and Stem Cell research at the University of Wisconsin-Madison. WNPRC Director Joe Kemnitz and [ ] of the UW Foundation hosted their visit.

Clive Svendsen and James Thomson have new Parkinson's Disease grants from the private funding which appear elsewhere in this report.

[ ] October. [ ] presented a seminar, "The Search for New Obesity Treatments: Clinical Trials of Axokine, Activation of Leptin Pathways, and Assessment of New Targets using High-throughput Functional Genomics."

[ ], October 2003. [ ] presented a seminar, "Monkeys, Memory and Magic" on his Alzheimer's research.

Other notable visitors to the WNPRC included:
[ ], October 2003. [ ] writer and science correspondent for the New York Times, was the Fall 2003 science writer in residence at UW-Madison. She met with Dr. Kemnitz to discuss topics in neuroscience and aging.

[ ] Elizabeth R. Griffin Foundation, July 2003. Chief of Animal Services Dr. Iris Bolton hosted his visit. [ ] presented a seminar on family friend [ ], who contracted and died of a Herpes B virus infection in 1997, and the risks of working with nonhuman primates.

Director's Meetings

Dr. Kemnitz hosted four general staff meetings and two retreats, including a multi-session strategic planning retreat in 2003-2004.

Dr. Kemnitz also attended the following meetings off-site in FY 2003-2004:

Wisconsin Symposium III: From DNA to Molecular Medicine in Madison, WI, May 2003.

Endocrine Society Annual Meeting, Philadelphia, PA, June 2003

American Society of Primatologists 26th Annual meeting in Calgary, Canada, July to August 2003.

NIA-B Study Section (Biology of Aging) in Bethesda, Maryland, October 2003. and March 2004.

Primate Center Directors' meeting and 21st Annual Symposium on Nonhuman Primate Models for AIDS in Seattle, Washington, October 2003.

Gerontological Society of America 56th Annual meeting in San Diego, CA, November 2003.

NIH meetings with National Primate Research Centers' representatives in Washington, DC, December 2003.

Meetings at NIH and with staff from the National Institute on Aging in Washington, DC, January 2004.

Primate Centers Directors' meeting in Washington, DC, April 2004.

Delegation of NPRC representatives to Congress, April 2004.

ii. Public Information and Outreach (J. Lenon)

Center Publications: Managed by Jordana Lenon, B.S., B.A., the Public Information Office continued to produce and disseminate the center's electronic staff newsletter, *Primate Pulse*, and the center's printed and Web versions of its science newsletter, *Centerline*. The office disseminated more than 2,000 copies of its five fact sheets (overview, rhesus, marmoset, aging, women's health) to new employees, the public, the media and others.

Annual Progress Report to NCRR and Congress: Updating and producing this Web-based report continues to be a major component of the Public Information Office. Ms. Lenon hired an assistant in 2004 assist with the APR and other publications, media and outreach needs.

WABRE report featuring the WNPRC: Ms. Lenon worked closely with [name], executive director of the Wisconsin Association for Biomedical Research in Fall 2003 to produce both stem cell and Primate Center feature stories in WABRE's annual report. They worked with scientists and other WABRE members to disseminate WABRE's strong research message in person to Wisconsin legislators and citizens.

New Web Committee: While Ms. Lenon continued as web content editor, [name] joined the Data Management staff in 2003 and became the center's new Webmaster. Ms. Lenon, [name] and others formed a new Center Web Committee. This committee redesigned and overhauled most of the Center's web site this past year, to make it more informative, attractive and easier to use (www.primate.wisc.edu). The committee also developed a new logo for the Primate Center, which has met with wide approval, as it communicates our scientific mission more clearly than the old logo. The committee continues to meet regularly to improve the web site.

Media: Thanks to near-weekly media inquiries and interviews, center scientists and their achievements graced numerous mainstream media articles in 2003-2004. Eight UW-Madison and Primate Center press releases generated much of the media activity. These releases highlighted the work of WNPRC researchers James Thomson, Ted Golos, David Abbott, Nancy Wilson, Toni Ziegler, Chuck Snowdon, Nancy Schultz-Darken retiring Librarian [name], and Center staff and scientists participation in Science Expeditions, the UW-Madison's first ever campus-wide science open house. Center research also featured prominently in original stories that appeared in Newsweek, BBC World Service, National Press Club (Washington, D.C.), The Scientist, Milwaukee Journal-Sentinel, Baltimore Sun, Racine Journal-Times, Boston Globe, Atlanta Journal Constitution, Der Zeitung, and more. Ms. Lenon responded to numerous media requests for center-produced research videotapes.

Outreach: Ms. Lenon handled a large increase in outreach activities, largely due to stem cell publicity. To educate the public about center research, and as an active member of the UW Speaker's Bureau, Ms. Lenon gave several talks on stem cells for a variety of venues both on and off campus. She coordinated other speakers to assist as much as possible. Ms. Lenon planned the Primate Center's participation in the UW-Madison's second annual science open house, "Science Expeditions," in April 2004. The Public Information Office continued to assist the WNPRC Library with its extensive outreach and education mission.

NPRCs brochure to Congress, supporters, taxpayers: Ms. Lenon and the consortium of Primate Center PIOs distributed to target audiences thousands of copies of the new, joint brochure, "Linking Research to Healthy Living," to help gain support for critical primate research.

Meetings: Ms. Lenon is organizing a roundtable of Primate Center PIO's and others in the field for the June 2004 American Society of Primatologists annual meeting in Madison. Ms. Lenon also co-organized, with Dr. Kemnitz and [redacted] a successful Fall Seminar Series, as well as special seminars throughout the year.

Grants: Ms. Lenon successfully applied for two grants in 2003-2004; one to bring Dr. Stuart Zola, YNPRC Director, as a speaker on Alzheimer's research to the Primate Center, Waisman Center and campus community; the other an academic staff development grant to attend scientific talks, updates and a science journalists roundtable at Experimental Biology Conference 2004 in Washington, D.C.

Solutions: The Primate Center Director approved the hiring of a permanent assistant, [redacted], who began in January 2004 and has already proven extremely productive in helping Ms. Lenon maintain the first-rate communications standards the Wisconsin National Primate Research Center currently upholds.

Challenges: The Public Information Office, along with some Operational Services units, moved off campus, to UW Research Park in 2003. This is a temporary move necessitated by inadequate space on campus. Constructing or acquiring additional space on campus continues to be a priority.

iii. Quality Assurance [redacted]

[redacted] has worked over the last year to develop her role as Quality Assurance Coordinator. She acts as a liaison between Center Investigators and the Graduate School Institutional Animal Care and Use Committee, and assists Investigators in writing their research protocols. She monitors research and various aspects of animal care at the Center for compliance with USDA regulations and AAALAC-I guidelines.

In addition to her monitoring responsibilities, [redacted] coordinates the paperwork for shipping animals and renewing drug licenses with the DEA and Wisconsin State Government. Since starting little over a year ago, she has also coordinated efforts to create a new database to monitor TB testing of all employees working with our primates. In addition, she has worked with IT staff to create a website to store WNPRC standard operating procedure (SOPs) and track employee reading of them. She monitors these websites to track compliance with TB testing policy and SOP training.

[redacted] is also responsible for providing training as needed, either one-on-one or via seminars. She presented one seminar in Fall 2003 for all researchers on how to use the WNPRC colony records database to stay in compliance with USDA regulations. She presented another seminar in February 2004 to train research staff on good documentation practices.

← Admin personnel →

B. Operational Services (S. Knable)

Operational Services consists of seven units, which provide overall business and support services to the operations of WNPRC. These units are, Business Office, Human Resources, Purchasing, Data Management, Accounting, General Shop, and Facilities and Resource Development.

i. Business Office (S. Knable)

The Business Office provides all of the fiscal administration, grants management, and physical plant infrastructure services at the institutional level at the University of Wisconsin – Madison. The Business office serves as the principal interface with the Graduate School, WNPRC reporting administrative unit.

The Business Office maintains day-to-day fiscal administration of the Base Grant with the University of Wisconsin's Research and Sponsored Programs (RSP).

During the last fiscal year, the Business office has added the services of a grants manager. Overall pre and post grants activity has increased at WNPRC where the need for a full time professional grants manger position became a critical need to support researchers.

ii. Human Resources [redacted]

Human Resources provides all of WNPRC personnel needs with respect to recruitment, performance evaluation, and personnel administration for approximately 200 WNPRC staff. [redacted] manages human Resources with two support staff. In addition, payroll and benefits are administered for the centers classified, academic, and student staff in the Human Resources unit.

iii. Purchasing [redacted]

WNPRC processes over $3 million in requisitions for equipment, supplies and services annually. Due to this large volume of purchasing, the University of Wisconsin has granted delegated purchasing authority to the WNPRC. The purchasing department consists of three purchasing assistants reporting to S. Knable, Associate Director of Business Operations. [redacted] serves as lead purchasing assistant and is the representative for the delegated purchasing authority at WNPRC.

In March 2004, a new Web based purchasing system was completed. This Web based system has streamlined the purchasing process for principal investigators and staff. The new system has greatly reduced paper processing and increased overall efficiency of WNPRC purchasing.

iv. Data Management [redacted]

This unit provides computing and networking services for research and service unit support, and daily operations support. It also provides digital imaging and graphics support to investigators. The unit consists of the manager, two programmers [redacted] and a media specialist [redacted]

Central computing resources are provided on 8 computers running the UNIX operating system: a SunBlade 1000, a Sun Ultra 10, 5 Apple Xserve servers and a Sun Ultra 1. The SunBlade 1000 serves as the main database, email, and web server. The Sun Ultra 10 is used for general multi-user access. The Sun Ultra 1 is the "public" access web server. The Xserve systems provide network file, print, and Internet services to a network of approximately 200 Macintosh desktop computers and about 10 Windows based personal computers spread over four buildings.

Networking facilities are based on a switched ethernet that connects our buildings to the campus wide ethernet of the University of Wisconsin, Madison via fiber-optic links. The four Primate Center network locations are configured into a single virtual local area network (VLAN). This VLAN allows all Primate Center computers to communicate as if they were located in the same facility and to be protected behind the same internet firewall system. The campus network is currently undergoing a major upgrade (21st Century Network) that will eventually bring Gigabit speeds to the desktop. In 2003 the Primate Center's connections to the campus were upgraded to the "21st Century Platform".

In 2003 the unit was responsible for design, programming, and implementation of an on-line animal observations system. The intranet web based design allows for on-line data entry of abnormal observations by the animal care staff equipped with wireless personal digital assistants (PDA). The unit also designed, programmed, and implemented a problem oriented veterinarian medical records system. This system allows on-line processing of health related animal records for both clinical and research procedures.

The unit also upgraded and modernized the Center's purchasing system by providing a web based interface for submitting purchase orders and is in the process of upgrading and streamlining the Center's financial systems.

Digital imaging and graphics support (provided by [redacted] includes the creation, editing, output and archival storage of images and graphics used in Center grant applications; journal publications; slide presentations; computer presentations; poster presentations; press articles and Web sites.

v. Accounting [redacted]

The Accounting unit is under the day-to-day supervision of [redacted] Supported by two financial specialists. The Accounting unit is responsible for establishing the entire Center's charge back accounts and monthly reconciliation of billings. In addition, all travel vouchers and reimbursements are processed through this unit.

The Accounting unit along with Data Management is working to upgrade the Center's financial management reporting system. Currently the system is UNIX based and utilizes an old version of FileMake Pro software. The new financial system will be designed to better interface with the new University's financial system. In addition, the Center's financial system will incorporate the new version of FileMake Pro software and the overall system will be excel based. These upgrades are schedule for implementation in the fall of 2004.

vi. General Shop [redacted]

The General Shop continued to provide specialized services to center staff to fill needs involving unique research equipment. This includes the design and development of prototype apparatuses along with modifications and repairs of existing equipment.

In 2003-2004, we continued to improve and maintain our animal housing. We also supported many environmental enrichment projects. Shop staff also addressed and analyzed special facility needs to create a safe, secure and superior operation.

Publication: [redacted]
In Press Publication

vii. Facilities and Resource Development [redacted]

The Facilities and Resources Development unit is responsible for addressing the Center's short and long term space, building and facilities requirements. This unit is under the supervision of [redacted] who has extensive experience in construction and facilities management. Having recently completed the center's new wing, [redacted] is work on short and long term solutions to the center's space needs. The

long-term approach envisions an aggressive capitol-building plan. Over the next several years, utilizing CO6 grant opportunities as well as State and private foundations, the long term plan seeks to add an addition [ ] square feet of laboratory and office space to the WNPRC. In the short term [ ] square feet of administrative offices have been leased at Research Park, an off campus facility. With the growth in the center's AIDS, Stem Cell, and Parkinson research programs, additional short-term laboratory space is currently under evaluation. The WNPRC is seeking approximately [ ] square feet to address short term laboratory needs.

C. Research Services (A. Usborne)

Amy Usborne, ~~D.~~V.M., ~~Diplomate~~ A.C.V.P., Associate Director for Research Services, oversees activities in the ~~five~~ service units of Assay, Virology Services, Immunology, Pathology, and Library and Information.

i. Assay Services (D. Abbott and T. Ziegler)

Assay Services
Web page: http://ink.primate.wisc.edu/~assay/assay.php

Our diversified and multidisciplinary endocrine service provided critical information for 23 publications, this year, illustrating the continuing importance of Assay Services' research support for cutting-edge projects across a variety of biomedical and basic science fields. This year's research highlights include:
[1] calorie restriction improves pancreatic beta-cell sensing of and insulin response to glucose in rhesus monkeys (Gresl et al, 2003), as a model for increased longevity,
[2] fetal androgen excess impairs ovarian follicle endocrine responses to recombinant human follicle stimulating hormone in adulthood in female rhesus monkeys (Dumesic et al, 2003), as a model for polycystic ovary syndrome in women,
[3] ratio of socially subordinate to dominant cortisol levels (blood or urinary determinations) indicate how social rank may differ in its physiological manifestations among primate societies (Abbott et al, 2003), as a model for stress-related pathology,
[4] aging-related decrease in growth hormone (GH) release is due to a reduction in the pulse amplitude and baseline levels, but not pulse frequency, of GH-releasing hormone, and to an increase in pulse amplitude and baseline levels, but not pulse frequency, of somatostatin (Nakamura et al., 2003), as a model for reproductive aging,
[5] hormonal analyses of embryoid bodies derived from human embryonic stem cells, and cultured under special conditions, provide key confirmatory characteristics of differentiated human trophoblast cells (Gerami-Naini et al, 2003), as a model for studies of placental pathology, including pre-eclampsia,
[6] ovulation chemical cues in female common marmosets stimulate androgen production in male marmosets (Ziegler et al, 2004), as a model for sexual dysfunction,
[7] cortisol levels in wild female muriquis are higher than in males in the same group prior to the conception season, consistent with the predicition that energy reserves may be associated with breeding readiness in females, but not males, in this species (Strier et al, 2003), as a model for metabolic regulation of reproductive function, and

In Press

Assay Services contributed to 24% of published papers and 35% of published abstracts reported in WNPRC 2003-04 publications. Our technique capability increased to 32 steroid hormone or steroid hormone conjugate assays, 37 peptide hormone and neurotransmitter assays and six metabolic biomarker assays, as well as increased multiple steroid determinations by high performance liquid chromatography (HPLC) for urine and fecal samples in a total of 30 primate species, including humans. This year, we have also considerably upgraded our technique capabilities by adding liquid chromatography/ mass spectrometry (LC/MS) to our repertoire. We have been engaged in service and methods development of an Agilent LC/MS system since its arrival and setup at the end of August 2003. We are currently adapting the system to measure 10 steroids in a single sample determination: dehydroepiandrosterone, progesterone, androstenedione, testosterone, estrone, estradiol, cortisol, cortisone, corticosterone, and dihydrotestosterone. The LC/MS will allow us to quantify low concentrations of these steroid hormones in any primate species and any biological sample, i.e., blood, cerebrospinal fluid, ovarian follicular fluid, urine, feces and saliva. The LC/MS approach should remove some of the sensitivity limit constraints in detecting low levels of steroid hormones imposed by currently available immunoassays, as well as being able to reduce the volume of sample required for determination. The latter issue is particularly germane when sample volume is limited, as in the case of ovarian follicular fluid. The LC/MS system is presently using a capillary 0.5mm column and separates all 10 of current steroid hormones of interest within 10 minutes.

In 2003, Assay Services performed a total of 74,253 biochemical measurements in order to determine hormone or biomarker concentrations in 38,593 samples. These numbers were slightly lower than last year. However, the increased complexity of tasks requested, along with greater investigator use of Assay Services personnel in performing all procedures, led to our maintaining a similar number of man hours devoted to the service component (compared to previous years) and an increased $ amount in chargebacks. Assay determinations for PIs accounted for ~74% of our total service time and effort. The remaining time and effort was devoted to research and development. Investigators maintained their increased use of our "full service option", accounting for 30% of all samples assayed. Computerized chargeback billings to investigators (coordinated with our Business Office) increased to $247,489 charged to investigators (93% of total billing: $267,381), with $19,893 charged to WPRC Research Services requests (7% of total billing).

Steroid hormone assays accounted for 45,785 (62%) of all determinations. The most frequent steroid determinations were made for progesterone (26%), cortisol (17%), estradiol (11%) and testosterone (8%), accounting for 62% of steroid determinations. Peptide assays accounted for 28,468 (38%) of the total determinations, including assays for both biological and immunoreactive peptides. The most frequent determinations were for luteinizing hormone/chorionic gonadotropin (LH/CG: 30%), insulin (29%), as well as for GnRH (21%), representing 80% of all peptide/metabolic biomarker measurements. These most frequently requested assays reflect the need for Assay Services to maintain a wide diverse of techniques including radio- and enzyme-immunoassays (RIAs and EIAs), bioassays, HPLC and a variety of sample preparation methods.

Investigator requests in 2003-04 required establishment of new assays or modifications of previously established techniques for new media or species: aging: validation of a highly sensitive 1,25-dihydroxy-vitamin D assay for common marmoset plasma (Abbott and Colman, WNPRC; [ ] U. of Wisconsin), to determine bioactive vitamin D metabolite levels in a novel model for osteoporosis, reproduction: (a) with the discovery of GnRH II, we are establishing an RIA for GnRH II for use with female rhesus serum (Terasawa, WNRC); (b) we are determining which form of estrogen best reflects the viability of the placenta as a steroid synthesizing organ ([ ], SWNPRC; Ziegler, WNPRC). Urinary concentrations of estradiol and estrone were determined in pregnant common marmosets (with or without

caloric restriction), either as native steroid molecules or after deconjugation. Only the native form of estradiol exhibited decreased urinary concentrations during caloric restriction, suggesting that this measure may provide a valuable indicator of compromised placental function; (c) assay techniques developed for humans were validated as reliably quantitative measures of total and unbound ("free") estradiol in the serum of female rhesus and cynomolgus macaques (Wilson, YNPRC and Emory University, GA; [name] Wake Forest University, NC; Abbott, WNPRC), and this will now permit replacement of in-house assays (and their dwindling supplies of assay-specific reagents) with readily available alternatives; (d) usefulness of HPLC quantification of urinary oxytocin measures as a non-invasive indicator of social dysfunction and lactation in humans ([name] U. of Wisconsin; Ziegler, WNPRC) is now progressing through MAULDI-TOFF mass spectral confirmation.

ii. Virology Services [name]

Virology Services (VS) coordinates, facilitates and supports research on AIDS and other infectious diseases utilizing non-human primate models. This is accomplished by: 1.) Developing and implementing complete SIV related research projects for U.W. principal investigators, as well as investigators from other universities and also private industries (if these programs parallel the research goals of the Primate Center). 2.) Providing *in vivo* and *in vitro* assays as well as coordinating usage of other Primate Center services to help complete established AIDS research programs. 3.) Initiating research and development projects as driven by researcher's needs, that will lead to establishment of new innovative services. 4.) Supervising the further development and reorganization of a Specific Pathogen Free breeding colony to support future animal research needs. And 5.) Managing and maintaining a multi-use Biological Safety Level-3 biohazard laboratory available to all eligible principal investigators, providing instruction and training in safe practices for all new personnel.

(VS) coordinates and oversees the animal portion of all Primate Center SIV research conducted within the Infectious Disease Animal Isolation Quarters. As in the past, its goals are to assist principal investigators in development of SIV and other infectious disease research programs, as well as to coordinate and facilitate the completion of these programs through close work with the animal care staff, veterinarians, pathologists, clinical pathologists and other center services. VS is responsible for scheduling and overseeing that all animal aspects of each research project are fulfilled. Additionally, VS develops and seeks approval for required IACUC animal and IBC biological safety protocols, develops weekly experimental schedules and distributes all tissue and blood samples. Also, it is responsible for initial monetary experimental estimates, regular progress reports, final summary reports and regular (and special) billing.

The relocation of the Infectious Disease Animal Isolation Quarters to the Center's newly completed wing has allowed expansion from a capacity of 72 to 256 monkeys. This has dramatically increased the number of animals and research projects being conducted at any one time. Also, a new BSL-2 laboratory for VS has facilitated research and development in the areas of molecular biology and basic cell biology, as well as supported existing basic research needs and general laboratory functions.

This year VS has conducted over 20 individual SIV related projects for several principal investigators affiliated with the Center and other Universities. Many are long term vaccine efficacy studies, while two are attempting to redefine the presently accepted non-human primate model for AIDS utilizing lower viral exposures to better simulate hypothesized exposure levels in the human situation. Also, VS received a $113,000 CFAR grant with Dr. Ashley Haase (University of Minnesota) in collaboration with Dr. Joseph Kemnitz to develop a non-human primate model testing the affect of vaginal inflammation as an amplifier for viral propagation in SIV infection. In addition, VS recently received a second $270,000 grant to

complete an initial pilot study ($130,000) establishing a non-human primate model for "Menopausal Hot Flashes" in collaboration with Dr. Robert Freedman (Wayne State University) and Dr. Joseph Kemnitz.

For the past four years Virology Services has been a fully functional WNPRC service unit with approved rates and established monthly billing procedures for all available services. In addition to directing and overseeing the above mentioned grants, the total amount of revenue directly generated via monthly charge backs in fiscal year 2003-2004 for VS activities is projected to be ~ $165,500. Over the last 12-15 months, VS has directly or indirectly provided data, assay results or supportive services to projects resulting in publication of approximately seven manuscripts in 2003-4.

In 2003, VS continued to organize and lead a multi-disciplinary committee with the goal of establishing and developing a Specific Pathogen Free animal-breeding colony. Over this period VS has performed a combination of serological and large scale nested PCR screening assays for the detection of four specified viruses (Herpes B, SRV, STLV and SIV), repeatedly testing all SPF animals. Two years later and with the cooperative help of many persons from a number of services, that goal has been accomplished. By July of 2004, after completion of the next two scheduled virus screening cycles, the Center's SPF Breeding Colony will consist of 163 adult females (130 AO1 neg., and 33 AO1*) and 61 adult males (46 AO1 neg., and 15 AO1*) - all free of the previously mentioned viruses. This established SPF Breeding Colony now has the capacity to annually produce ~108 SPF infants.

Meanwhile, the number of SPF animals attaining three years of age and thus available for research began modestly with four in 2003, but will continue increasing over 2004 (41 monkeys), 2005 (66 monkeys) and 2006 (83 monkeys). By 2007 the ~108 infants produced in 2004 will have attained the age of three years and be eligible for research programs. One ultimate goal of this program is for the SPF Breeding Colony to completely replace the Center's conventional breeding colony. Also, as time and finances permit, additional viruses will be targeted for detection and elimination from this new SPF Breeding Colony.

New developments.

VS is establishing real time PCR assays to determine quantitative estimates of specific viral RNA loads in plasma of both rhesus and marmosets, and hopes to make this available as a service in the near future. Also, VS is establishing and characterizing isolated cell lines from normal and cancerous rhesus macaque and marmoset tissues. These primary cell lines will be utilized in production of SIV virus stocks, as well as cancer research and other projects specifically requiring purified non-human primate cells.

Finally, VS has finished an internet based web page integrated into the Primate Center's web site, The Virology Services web page describes this unit's mission, summaries services offered, and provides key personnel and contact information as well as frequently asked questions.

iii. Immunology Services (E. Rakasz)

The Immunology Core Laboratory was established with a mission to facilitate cutting edge biomedical research projects applying immunological methods. Routine activities performed by the ICL included a) development of research protocol, b) rhesus macaque vaccination or reagent administration, c) sample collection and processing, d) immune assay performances, e) maintenance and development of a multi-user flow facility, and f) education and hands-on training of flow facility users. During the 2003/2004

fiscal year, the ICL supported 12 on-campus and off-campus laboratories, which were involved in more than 20 federally and non-federally funded biomedical research projects internationally and nationwide:

Dr David I. Watkins-University of Wisconsin-Madison (AIDS research)
Dr James A. Thomson-University of Wisconsin-Madison (Stem cell research)
Dr Thaddeus G. Golos-University of Wisconsin-Madison (Reproductive research)
Dr Christopher Coe-University of Wisconsin-Madison (Behavioral research)
[name] University of Wisconsin-Madison (Basic Immunology research)
[name] Jniversity of Wisconsin-Madison (Chlamydia research)
Dr Richard Weindruch-University of Wisconsin (Aging research)
Dr Ashley Haase-University of Minnesota-St.Paul (AIDS research)
[name] University of California-Davis (AIDS research)
[name] -Northwestern University (AIDS research)
Dr Dennis R. Burton-The Scripps Research Institute (AIDS research)
Dr Kelly MacDonald-University of Toronto, Canada (AIDS research)

In 2003, our charge backs increased by 79%, from ~$46,365 to ~$82,949. We have processed more than 600 blood samples, and shipped out more than 2600 biological samples to other collaborative laboratories. 32 different users operate the two FACSCalibur flowcytometers with minimal help provided by the ICL staff. With the Primate Center's chargeback rates affiliated investigators were able to save $33,820 during the period of 05/01/2003-12/31/2003. A trained operator runs our MoFlo high-speed cell sorter located in a biosafety level-3 laboratory. An average of 4 -6 sort/month is performed. The Primate Center's flow facility users enjoy extended work hours (9:00 AM-10:00 PM) in service support to accommodate their specialized needs. The immune assays accomplished by ICL involved flow cytometric cell phenotype and functional analysis, routine major lymphocyte, antigen specific T- cell subset, SIV specific antibody quantification, SIV mac239 whole proteome IFN-g ELISPOT assay. One of the major objectives of the ICL is to offer reagents for SIVmac239 antigen specific T cell quantification in rhesus macaques with diverse MHC haplotypes, using fluorochrome conjugated peptide-MHC-I tetramer reagents. In the fy 2003/2004 we have been able to produce 48 SIVmac239 specific peptide-MHC I-tetramers. 21 of these reagents proved to be positively reactive, enabling us to broaden our tools to monitor SIVmac239 specific CD8+ T cell responses by 11 new epitopes and an additional three new MHC haplotypes.

Publications supported by the Immunology Core Laboratory activities:

- Gerami-Naini B, Dovzhenko OV, Durning M, Wegner FH, Thomson JA, Golos TG. Trophoblast differentiation in embryoid bodies derived from human embryonic stem cells. Endocrinology. 2003 Dec 18 [Epub ahead of print]
- Kaufman DS, Lewis RL, Hanson ET, Auerbach R, Plendl J, Thomson JA. Functional endothelial cells derived from rhesus monkey embryonic stem cells. Blood. 2003 Oct 16 [Epub ahead of print]
- Vogel TU, Reynolds MR, Fuller DH, Vielhuber K, Shipley T, Fuller JT, Kunstman KJ, Sutter G, Marthas ML, Erfle V, Wolinsky SM, Wang C, Allison DB, Rud EW, Wilson N, Montefiori D, Altman JD, Watkins DI. Multispecific vaccine-induced mucosal cytotoxic T lymphocytes reduce acute-phase viral replication but fail in long-term control of simian immunodeficiency virus SIVmac239. J Virol. 2003. 77(24): 13348-60.
- O'Connor DH, Mothe BR, Weinfurter JT, Fuenger S, Rehrauer WM, Jing P, Rudersdorf RR, Liebl ME, Krebs K, Vasquez J, Dodds E, Loffredo J, Martin S, McDermott AB, Allen TM, Wang C, Doxiadis GG, Montefiori DC, Hughes A, Burton DR, Allison DB, Wolinsky SM, Bontrop R, Picker LJ, Watkins DI. Major histocompatibility complex class I alleles associated with slow simian

immunodeficiency virus disease progression bind epitopes recognized by dominant acute-phase cytotoxic-T-lymphocyte responses. J Virol. 2003. 77(16): 9029-40.

- [In press publication]

- Friedrich, TC, Dodds EJ, Yant LJ, Vojnov L, Rudersdorf R, Cullen C, Evans DT, Desrosiers RC, Mothe BR, Sidney J, Sette A, Kunstman K, Wolinsky S, Piatak M, Lifson JD, Hughes AL, Wilson N, O'Connor DH, and Watkins DI. Reversion of cytotoxic T-lymphocyte escape variant immunodeficiency viruses in vivo. Nat Med . Feb. 15, 2004

- [In press publication]

- Golos TG. Non-human primate placental MHC expression: a model for exploring mechanisms of human maternal-fetal immune tolerance. Human Immunol. 2003. 64(11): 1102-9.

Tetramer Production: May 2003-Present

MHC	*Peptide*	*Fluorophore*	*Test Results*
A*01	TL9	APC	Positive
	TL9	PE	Positive
	QY9	PE	Positive
	CM9	PE	Positive
	CM9	APC	Positive
	EA11	PE	Positive
	SV9	PE	Positive
	GT9	PE	Positive
	VI8	PE	Positive
	SL8	PE	Positive
	FF9	PE	Positive
	LY9(nef)	PE	Positive
	KL9	PE	Not tested
	LM9	PE	Not tested
	RW9	APC	N/A
	YI9	APC	N/A
	IL10	APC	Not tested
	LV10	APC	Not tested
A*02	YY9*	PE	Positive
	YY9	APC	Positive
	GY9	PE	Positive
	KM9	PE	Positive
	RY8	PE	Positive
	KL9	PE	Not tested
	IE2	PE	Not tested
	LM9	PE	N/A
	FF9	PE	Positive
	RY9	PE	Negative

	IW9 (vif)	PE	Negative
	YY10	PE	Not tested
	LY9 (pol)	PE	Not tested
	WY9	PE	Not tested
	SW9 (vif)	PE	Not tested
	RM9	PE	Not tested
	TM10	PE	Not tested
B*17	IW9	PE	Positive
	QY9	PE	Not tested
	VW10	PE	Not tested
	LW9	PE	Not tested
	KL9	PE	Not tested
	LY10	PE	Not tested
	LM9	PE	Not tested
	FF9	PE	Positive
	MF8	PE	Not tested
	TW9	PE	Not tested
	TW9	APC	Not tested
	LY9(nef)	PE	Positive
	SV9	APC	Not tested
A*11	GI8	PE	Positive

iv. Pathology Services (A. Usborne/ C name ?

The Pathology Unit is organized into three sections: anatomic pathology, clinical pathology, and the microscopy and image analysis core. A program assistant is assigned to the Unit at [illegible] and handles office duties and reception for all three sections.

- percentage of effort

Personnel in anatomic pathology include Dr. Amy Usborne, who is board certified in veterinary pathology, an assistant research specialist, and a post-doctorate veterinary trainee in primate pathology. The anatomic pathology section performed 239 necropsies and 45 biopsies on Center owned animals from May 1, 2003 to April 30, 2004. Complete gross necropsies are performed under the direction of Dr. Usborne on all cases, whether the death was related to clinical or investigational causes. Death due to experimentation accounts for approximately 40% of rhesus and 2% of marmoset deaths. The reminder in each species is due to euthanasia for illness or spontaneous death. Histologic examination is performed on approximately 98% of the cases, only being precluded in cases of severe autolysis. Necropsies were also performed on four non-Center owned monkeys for NIH funded investigators on the University of Wisconsin-Madison campus. Biopsy service is also provided for a small colony of monkeys at the Center for Comparative Medicine at Northwestern University in Illinois. Personnel in this section are responsible for the tissue distribution program, which distributed 622 tissues to 31 investigators during this reporting time (see Research Services table elsewhere in this report). Other activities include collaborating with the investigators in the area of aging and metabolic diseases to maintain a tissue bank of samples (fixed and during this reporting period. Veterinary staff made approximately 32 frozen) from monkeys 20 or greater years old and teaching tissue staining, sectioning and photomicrography techniques to graduate students and post-doctorates from various laboratories.

The clinical pathology section continues to provide timely diagnostic testing for all nonhuman primate species at the WNPRC, in support of veterinary and scientific staff. [name] a clinical hematologist, heads the section and is supported by a [name] student worker. Testing is provided on site for hematology, microbiology, parasitology and urinalysis. The laboratory coordinates sample submission to a variety of reference and specialty labs, including routine clinical chemistry. Results were reported and entered into colony records for 5307 requests % of all requests, with the remaining 68% of requests being made by research groups. SIV research groups made one third of all research submissions. The clinical pathology section also coordinated IACUC protocol submission, appropriate animal selection, blood draws, DNA extraction, and shipment of DNA samples to an affiliate researcher at Boys town National Hospital in support of her research on generating macaque models for genetic hearing loss. The glycosylated hemoglobin testing implemented in the previous year was utilized to help an affiliate researcher on the UW- Madison campus obtain data for his studies with mice.

The Microscopy and Image Analysis Core provides training, support and imaging services to Center, under the supervision of [name] microscopy services coordinator. An assistant information-processing consultant assists him. Our equipment includes three research-grade inverted microscopes with digital cameras outfitted for fluorescence and phase contrast observation. Two of these microscopes have environmental chambers for live cell imaging and long-term time-lapse studies. We also have an upright microscope with a digital color camera for imaging stained specimens. Image processing and analysis is performed using IPLab running on Macintosh workstations or on a UNIX workstation with software for image deconvolution and 3-D modeling.

We recently completed installation of a Leica TCS SP2 AOBS confocal and multiphoton microscope. This instrument is equipped with four visible and one pulsed NIR laser, three confocal detectors and two non-descanned detectors for multiphoton imaging. We will be adding environmental controls to the microscope for performing time-lapse studies.

Training in the Pathology Unit is focused on both post-doctorate veterinarians and veterinary students. The post-doctorate trainee (Dr. Sheree Beam) shares necropsy duties with the pathologist, and participates in pathology rounds on campus at both the veterinary and medical schools. She also prepared publications and presentations of cases or current subjects of interest in laboratory animal pathology. The summer veterinary student [name] learned necropsy and histology techniques, and prepared selected cases for oral presentation at the national meeting of primate pathologists (Primate Pathology Workshop 2003, Seattle, WA).

v. Library Services (C.K. Robinson)

The WNPRC Library and Information Service supports the biomedical research programs of the Center and provides a broad range of Internet based information services to both the national and international primatology communities. The following is a summary of major activities of the unit in 2003-2004.

Coordinated Information Services Grant: NCRR/NIH grant P40 RR015311 has provided support for a variety of library services since August of 2000. The grant, titled Coordinated Information Services for Primate Research, supports the coordination of information services among the NPRCs as well as outreach and service to both the national and international primatology communities. Subcontractors on the grant are the Primate Information Center, WaNPRC, Seattle, providing indexing, and the UW Madison Libraries providing technical support for the PrimateLit database.

Current status: 1) The NPRC staff menu has been folded into Primate Info Net (PIN) under the new title Federally Funded Primate Research. The site provides links to NCRR and NPRC web pages as well as the ability to perform web searches for government information related to primate research. A series of pre-configured searches covering areas such as AIDS, gene therapy and Parkinson's disease are provided. 2) The WNPRC Library continues to provide document delivery services to scientists and researchers at the various NPRCs and the Caribbean PRC. Over the past year approximately 12,500 requests have been handled. Because of the continued growth in document delivery the library has expanded and redesigned the space available to this unit. 3) PrimateLit (1940-present) is freely available as an NCRR resource via the Web. Current enhancements under development include the ability to download citations to bibliographic software and migration to a newer more robust version of the SiteSearch Database (version 4.2.2). 4) Primate Info Net (PIN) is undergoing a major redesign that includes a new more up-to-date look, a dynamic front page, a reorganization of the file structure, the use of XHTML and cascading style sheets, database driven link access and maintenance, more intuitive pathways to identify location within the site and additional content. 5) New projects included Primates in the News and access to a variety of primate newsletters converted to digital format and made available through the PrimateLit bibliographic database and Primate Info Net.

Staff, Services and Collections: The WNPRC Library continues to provide top-notch services and resources to Center staff and affiliated scientists. With the Center's library and the UW campus libraries, online availability of a wide variety of electronic journals and databases, and expanded access via Document Delivery and Inter Library Loan, staff and researchers have unprecedented access to scientific information. As a result of the newly available space at Primate Center West (Research Park), the library was able to move the June Northrop Barker archives to better quarters. A SLIS student has been hired at [illegible] FTE to organize and maintain the archives. We are negotiating for the archives to include papers from the American Society of Primatologists, International Primatology Society and author Deborah Blum. percentage of effort

Educational Initiatives: Library staff participated in the Primate Center's involvement with a campus-wide Science Open House using the Learning Lobby resources (marmoset display, Callicam, rhesus mural and handouts) to discuss the Center's work with interested public. In addition the library continues to provide access to the AV Collections for educational use and a variety of resources available through PIN.

University/Center Library Relations: In 2003-2004 the WNPRC Library continued our close collaboration with the UW Libraries. Staff participated in the revival of the Special Purposes Libraries Group, an organization for departmental libraries on campus to share information and ideas. The Director also regularly attended the UW Libraries Science Cluster meetings. This group is responsible for collection development decisions in the sciences across the campus. In addition [illegible] served on library committees for the introduction of Library Express and ILLiad on campus. The Center Library employs graduate students from the UW's School of Library and Information Studies (SLIS) offering students practical experience while they in turn enhance the life of the library.

Staff Changes: Library founder [illegible] retired after a 30-year career at WNPRC. Library staff members were primary participants in the search for, and hiring of, the new director, Cynthia Robinson.

Meetings, Workshops, Professional Development: . [name] chaired the WNPRC's Web Committee to revamp the Center's web presence and create a new logo for the Center. [name] was also a member of this committee.
[name] beginning in January 2004, will be serving a 2-year term as the Media Reviews Editor for *American Journal of Primatology.*
[name] Teacher's Workshop for the annual meeting of the Association of Primate Veterinarians, Tacoma, WA, Oct. 2003.
[name] 'Putting primates in the classroom," American Society of Primatologists K-12 Teacher's Workshop, Calgary, Canada, July/August, 2003.
The library hosted a consortium meeting of staff from the NPRC libraries, the Primate Information Center at the Washington NRPC, and . [name] editor of *Laboratory Primate Newsletter,* April 2003.
Cynthia Robinson, "Libraries in an Electronic Age: The Changing Paradigm of Publishing and its Impact on Libraries." Presented at the Primate Center Fall Seminar Series, Nov. 2003. Invited speaker for the Special Purposes Libraries Group, Feb. 2004. Guest lecturer for the Collection Management course through the School of Library & Information Studies, UW-Madison, Feb. 2004.
[name] Cynthia Robinson are members of the organizational committee for the 2004 American Society of Primatologists meeting to be held at the University of Wisconsin–Madison.

Library Infrastructure and Space Needs: During the past year the library has undergone a major refurbishing. New carpet was installed, walls were painted, office and public use furniture was replaced, and a new circulation desk was installed. At the same time the Barker Archive was moved to better quarters in Research Park. However, space needs continue to be a critical issue. Preliminary planning for a new building continues. The library is an integral part of this process. The plans include the development of a new library facility to meet the ongoing needs of the library's expanding role within the NPRC's and to the broader biomedical research community.

Internet Services: Internet services continue to grow and evolve. Primate Info Net is currently undergoing a major redesign that will enhance its usability. This includes a new more up-to-date look, a dynamic front page, a reorganization of the file structure, the use of XHTML and cascading style sheets, database driven link access and maintenance, more intuitive pathways to identify location within the site and additional content. The 2003-2004 user statistics follow:

- PIN: 9.85 million hits
- Primate-Science: 840 members
- AskPrimate: 1000 questions in 2003, 8800 questions since 1996
- Primate Enrichment Forum: 223 members
- Primate Jobs: averages 35 positions available
- International Directory of Primatology: 170,000 hits per month on average
- World Directory of Primatology: 106,000 hits per month on average

D. Animal Services (I. Bolton)

Iris D. Bolton, D.V.M., was the Associate Director of Animal Services/Attending Veterinarian for the WNPRC. Through March 2004, Animal Services underwent significant re-organization to clarify the veterinary oversight of the resource of the resource period. Animal Services is composed of four unique units: Colony Records, Colony Management, Clinical Medicine and Centralized Protocol Implementation.

The attending veterinarian serves on the local Animal Care and Use Committee, is involved in protocol pre-review, advises research staff on protocol development and provides support, resources and representation to senior management for the units within Animal Services.

During the last year, all Standard Operating Procedures have been reviewed and revised as necessary. There is a plan in place for annual review of all SOPs and they will be revised as necessary. An agreement has been reached with Employee Health extending our association with them for treatment of biohazard exposures. Animal Services Management is taking a more active role in this interface. We have instituted an Office of Biological Safety protocol and a chemical hygiene plan. Although we have no direct facilities oversight, we maintain an active interface with facilities personnel to insure timely action on all facility concerns. Formal training oversight has been set up for all staff. Each person involved in activities with animals is documented verifying training. Persons having the authority to verify training are the professional veterinary staff, colony managers, animal care supervisors, and animal care trainer. In addition, Animal Services continues to offer a monthly, campus wide primate handling/zoonotic disease course through the University of Wisconsin Research Animal Resource Center (RARC).

Colony Records ([name] percentage of effort

The unit of colony records is responsible for the direct input of most information recorded in colony records. This includes all clinical entries, animal location transfers, treatments, procedures, surgeries, blood collections and observations. In the 2003 calendar year, this represented nearly 86,000 entries. The effort necessary to do this job has increased dramatically, [ ] since 1990. With the ever-increasing demand for better documentation of continually more involved manipulations, a senior animal caretaker has augmented the full time efforts of [name] with [ ] support. In addition, [name] has been and continues to be actively involved in the ongoing efforts to create and implement a paper-less medical records system. This operation is most appropriately situated in Animal Services to foster the frequent communication with the personnel actually performing the work being documented.

Colony Management (N. Schultz-Darken, [name]

Colony management consists of two full time colony managers, Nancy Schultz-Darken and [name]. Utilization of the animal resource remains high, with many animals assigned to more than one compatible project. The demand for animals meeting specific criteria for research (breeding age females, major histocompatability defined/genetically defined, minimum weight/size and healthy aged animals) exceeds our resource. In order to alleviate the burden on our existing rhesus macaque colony, we have acquired two additional old-world monkey species in the past year: 1) 60 cynomologous macaques (*Macaca fasicularis*) from breeders in China and Vietnam and (2) 20 African green monkeys (*Cercopithecus aethiops*) from the population on St. Kitts island.

Primate Colony - The colony managers facilitate the high utilization of animals and efficient use of the resource by looking for multiple animal assignments. Investigators submit their specific requests for research animals to the colony managers who then balance those needs with the needs of maintaining the resource and potential acquisitions. A list of potential animals that would fit these needs is provided to the investigators who then submit their assignment to Colony Records. Nancy Schultz-Darken, is also a member of the UW Graduate School Animal Care and Use committee and has familiarity with current regulatory standards and all primate research protocols that have been approved. This allows for a thorough understanding of the research needs for all projects. [name] handles acquisitions of new animals and sales to investigators outside of the Primate Center.

Note: For current population counts, please see the colony statistics section of this Annual Progress Report.

SPF - The WNPRC has identified a core of rhesus macaques sero-negative for Cercopithecine Herpesvirus 1 and viral negative for the retroviruses SRV, STLV-1, and SIV. These pathogens represent a risk from both an occupational health and research standpoint. These SPF animals are separated from the general colony and used for breeding.

Environmental Enrichment - The primary emphasis of the environmental enrichment program continues to recognize the importance of social housing and efforts have been to maintain less than 5% of our animals singly housed without an exemption for clinical, behavioral or scientific reasons. Animals that must be singly housed have priority access to enrichment devices to assure maximum psychological well being within the constraints of research. After a thorough review of our environmental enrichment program, we have instituted the following revisions:

- Formation of an enrichment committee consisting of Laboratory Animal Technicians, Research Technicians and a veterinarian.
- Revision of enrichment SOPs to expand and enhance the enrichment program.
- The facility enrichment document is under review and will undergo necessary revisions.

Nursery care - In the past year, a nursery for intensive care of rejected or orphaned rhesus infants has been established within the Animal Services Division. Infants are given the most basic needs to survive along with a planned socialization strategy as they grow. Every attempt is made for the infant to be reunited with either his or her own mother or a foster mother before resorting to hand rearing. Infants are given a social partner as soon as possible, introduced to solid food around 2 weeks of age, and moved to standard caging by one month.

Oversight of Animal Care Staff - Colony management oversees the animal care staff, consisting of 2 supervisors, 21 full time and 10 part time and student employees who are responsible for all aspects of daily care and husbandry of the colony. In addition, they coordinate the following services offered to researchers: blood draws, research-related treatments, menstrual data collection, and formation of breeding pairs and collection of semen.

Rodents - A small colony of SCID mice is maintained for researchers. They are housed in a ventilated micro isolator system.

Clinical Medicine (M. Harke, C. Schobert)

Preventive medicine - 5 veterinarians and veterinary technicians carry out the provision of veterinary care. An additional veterinary technician is dedicated to providing surgical support to both the researchers and the clinicians for a total of 6 equivalents. Veterinary Services responds to all concerns raised by animal caretakers and researchers, evaluates and diagnoses cases and prescribes care and treatment to accomplish better understanding of morbidity within the colony and related to research use. The information gained is then used in treatment of future cases and considered in the ongoing preventive medicine program. The preventive medicine program still utilizes semi-annual TB testing, physical exams and dental prophylaxis as its core and has been expended to include annual serological surveys of the conventional colony to track the presence of select infectious agents including Cercopithecine Herpes Virus-1, SRV, STLV and SIV.

Centralized Protocol Implementation (K. Brunner)

Centralized Protocol Implementation is a unit composed of members of both Research Services and Animal Services. Members of the Reproductive Research Services Unit are now under new leadership within Centralized Protocol Implementation, under Kevin Brunner, DVM. [name], [name], and [name] have broadened their technical support to a wider range of research needs. The newly formed support service will be working closely with the Research Services component of CPI group to provide training, coordination and direct technical and surgical support for a variety of projects reflecting the major research emphasis of the center and of affiliated scientists.

The CPI group continues to provide essential support in the area of reproduction, through direct technical service and the coordination of monitoring and data collection that helps maximize the utilization of the limited nonhuman primate resource. Ongoing training of male nonhuman primates for semen collection and refinement of equipment and techniques has been emphasized. Efforts in these areas represent overlapping efforts between colony management and CPI and are facilitated by frequent communication with [name] in Colony Management.

As new projects are brought to the CPI group, ongoing efforts are made to develop the skills requested, apply current skills to new paradigms and provide training to research staff as requested. It is the group's intention to continue expansion of the services provided to assure that all procedures and manipulations carried out on research animals exceed the highest standards, assuring both excellence in research results and the best outcomes for the animals.

Dr. Brunner serves as the alternate for the Attending Veterinarian for regulatory issues.

Publications contributed by members of Animal Services:

[In press publication]

[In-press publication]

Saltzman W; Prudom SL ; Schultz-Darken NJ ; Wittwer DJ ; Abbott DH Social suppression of cortisol in female marmoset monkeys: Role of circulating ACTH levels and glucocorticoid negative feedback. Psychoneuroendocrinology. 2004. 29(2). Pgs: 141-161.

Abbott DH ; Barnett DK ; Colman RJ ; Yamamoto ME ; Schultz-Darken NJ Aspects of common marmoset basic biology and life history important for biomedical research. Comparative Medicine. 2003. 53(4). Pgs: 339-350.

Schultz-Darken NJ Sample collection and restraint techniques used for common marmosets *(Callithrix jacchus)*. Comparative Medicine. 2003. 53(4). Pgs: 360-363.

Tardif SD ; Smucny DA ; Abbott DH ; Mansfield K ; Schultz-Darken N ; Yamamoto ME Reproduction in captive common marmosets *(Callithrix jacchus)*. Comparative Medicine. 2003. 53(4). Pgs: 364-368.

Ferris CF, Snowdon CT, King JA, Sullivan JM, Ziegler TE, Olson DP, Schultz-Darken NJ, Tannenbaum PL, Ludwig R, Wu Z, Einspanier A, Vaughan JT, Duong TQ. Activation of neural pathways associated with sexual arousal in non-human primates. Journal of Magnetic Resonance Imaging. 2004. 19. Pgs: 68-175.

[In-press publication]

[In press publication]

E. Other Resources

i. Aging Resource (R. Colman)

As of January 15, 2004, the WNPRC had 108 rhesus monkeys (51 males, 46 females, and 11 experimentally produced female pseudohermaphoridites) over 20 years of age. These include 9 (4 male, and 5 female) older than 30. Support for an identified subset of these animals was provided in part by the National Institute of Aging to maintain theses animals for studies relating to normal aging. During 2003-2004, 15 investigators in studies related to calorie restriction, glucose metabolism, ovarian dysfunction, bone mineral density, and osteoarthritis.

ii. Genetic Resources (D. Watkins)

Finding a vaccine for HIV is one of the most pressing biomedical priorities today. The Genetics Service Unit supports vaccine candidates that elicit strong cytotoxic T lymphocytes (CTL) and helper T lymphocytes (HTL) responses against AIDS viruses.

With more than 30 million HIV-infected individuals, there can be few other more pressing biomedical priorities than to produce an effective vaccine for HIV. Given the important role that cytotoxic T lymphocytes (CTLs) and helper T lymphocytes (HTLs) play in controlling viral replication, it is critical that this vaccine stimulate these cellular responses. The specificity, breadth and magnitude of these responses are largely determined by host genetic factors, most notably the complement of major histocompatibility (MHC) alleles that are unique to every individual. Though simian immunodeficiency virus (SIV) infection of macaques provides the best non-human primate model to evaluate immune responses to the AIDS virus, the utility of this model is limited by our incomplete understanding of the rhesus MHC. Therefore, we are developing technologies to characterize the rhesus MHC, and have already used these tools to identify MHC alleles in over fifteen SIV-infected animals.

Using our current technology, we generate a library of approximately 100 MHC clones per animal and sequence these clones in their entirety. While effective, this method is time-consuming, expensive and technically difficult. We are developing a new methodology, called 'reference strand conformation analysis' (RSCA), that will allow us to identify all of the MHC alleles in an individual animal in less than five reactions.

These tools to characterize, in detail, all of the MHC alleles in rhesus macaques complement the screening methodologies we previously developed for individual alleles. Our MHC typing technique for

the common rhesus MHC allele Mamu-A*01 has been used in countless studies. Indeed, we have now typed over 3200 rhesus macaques with this technique.

We are developing these genetic tools with an eye towards future deployment in other non-human primate species. There is a chronic Indian rhesus macaque shortage for vaccine and pathogenesis studies. Additionally, it is almost impossible to purchase female Indian macaques for these types of studies. We, therefore, are initiating genetic studies that will allow us to test AIDS-virus vaccines in other non-human primate species such as cynomolgous macaques.

Taken together, these genetic tools are improving the quality of our SIV studies and are an indispensable component of our future vaccine initiatives.

iii. Stem Cell Resources (J. Thomson) percentage of effort

The stem cell service component has moved to Animal Services. The new Stem Cell Resources Unit recently hired [redacted] This person is working on developing antisense RNA vectors to determine genetic pathways in embryonic stem cells. Stem Cell Resources personnel continue to provide support to investigators they have previously been trained in embryonic stem cell culture. We have trained an additional two investigators on how to grow rhesus embryonic stem cells. We have provided training on lentiviral and chemical transfection methods. We have provided GFP labeled rhesus embryonic stem cells to two additional research groups at UW. We have also worked with investigators at Ohio State University and Columbia University to attempt to derive baboon embryonic stem cells. To date four attempts have been made. Our unit also plans to provide support for vervet and African Green Monkey stem cell derivations.

Stem Cell Resources has begun cataloging in a database commonly used vectors for transfection. Our goal is to raise awareness among researchers on the vectors we have available, and to provide them with information about the vectors.

F. Committees and Training

i. Institutional Review Committees (Kemnitz)

The WNPRC Executive Committee and the External Scientific Advisory Board are listed under the Committee Members section of this report.

ii. Staff member training requirements

All WNPRC staff undergoes orientation and receives general training in operational procedures when they are hired. As part of this exercise, new staff learns the location of various laboratories and offices and they are introduced to key staff members to whom they can address specific questions or approach for help in solving problems. Unit supervisors are intimately involved in this process.

Targeted training is provided according to the individual's job responsibilities and is conducted within appropriate research groups or service units. This training invariably includes instruction on specific procedures to be used on the job (e.g., how to request an animal assignment or collection of a specimen), but it also includes more general topics (e.g., the appropriate use of animals in research). Campus-wide training/certification is required in certain areas: Radiation Safety, Care and Use of Laboratory Animals, TB surveillance.

A special focus of training pertains to staff that enter macaque housing areas or handle macaques, viz., herpes B virus. These staff members watch videotape and are given written materials for review. There is a quiz on the material and an interview with supervisor(s) on the topic. New staff members attest to completion of this aspect of training by signing a form.

There is continuing instruction for staff, particularly animal care staff. This is provided at their regular staff meetings and consists of review and reminders of standard operating procedures, as well as discussion of changes in procedures.

Additional, specialized training descriptions appear under the individual unit subheadings in this report.

iii. Meetings (J. Kemnitz, [redacted] J. Lenon, others)

Staff Meetings: All Primate Center staff meet at least twice a year, receiving a progress report from the director, followed by questions and discussions.

Ad Hoc Working Groups: Members of the external advisory committee or other staff are asked to form and chair small working groups when required to review any area of Center development and function or when it is appropriate to examine a question or problem in depth. These working parties have replaced standing committees, which can often perpetuate time-wasting bureaucracy or procedures; however, we keep our options open should standing committees be required at any stage. Any staff member can request the formation of a working group, which reports through the external advisory committee to the Director.

Seminars: Dr. Kemnitz, [redacted] and Ms. Lenon coordinated 15 scientific and staff seminars for the Center in 2003-2004. Topics related to Primate Center research and services included caloric restriction, HIV vaccine development, Parkinson's, Alzheimer's, menopausal hot flashes, comparative primate anatomy, primate anxiety and stress. Additional topics included primate conservation, the risks of working with nonhuman primates, library services, and personal financial planning.

Conferences: [redacted] conference coordinator; Dr. Kemnitz, local host; and a committee of Primate Center and Harlow Center staff began planning for the American Society of Primatologists (ASP) 2004 meeting in Madison, Wisconsin, June 8-12, 2004.