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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

5P51RR000166-42
NATIONAL PRIMATE RESEARCH CENTER

Final

UNIVERSITY OF WASHINGTON

ANNUAL PROGRESS REPORT

Reporting From: 05/01/2003
Reporting To: 04/30/2004

51.800% AIDS Related

Signature

5/4/04
Date

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Patent or Copyright was awarded this grant year.

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MAY 18 2004

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RESEARCH SUBPROJECTS

RESEARCH RESOURCES

PERSONNEL ROSTER

Core Doctoral Scientists

Name, Degree	Department	Non-Host Institution: State, Country
AGY, MICHAEL B, PHD	NPRC	
ANDERSON, DAVID M, DVM	NPRC	
[illegible]	NPRC	
[illegible]	NPRC	
BEKELE, GIRMA, DVM	NPRC	
[illegible]	NPRC	
BENTSON, KATHY, PHD	NPRC	
[illegible]	NPRC	
BOWDEN, DOUGLAS M, MD	PSYCHIATRY&BEHAV SCI	
[illegible]	NPRC	
[illegible]	NPRC	
BURBACHER, THOMAS M, PHD	ENVIRONMENTAL HEALTH	
[illegible]	PATHOBIOLOGY	
CLARK, EDWARD A, PHD	MICROBIOLOGY	
CONRAD, SUZANNE, MD	NPRC	
CROCKETT, CAROLYN M, PHD	NPRC	
[illegible]	NPRC	
[illegible]	NPRC	
DACEY, DENNIS M, PHD	BIOLOGICAL STRUCTURE	
[illegible]	NPRC	
[illegible]	NPRC	
[illegible]	NPRC	
[illegible]	NPRC	
[illegible]	NPRC	
EMAU, PETER, BVS, PHD	NPRC	
EVANS, DAVID T., PHD	NPRC, PATHOBIOLOGY	
FERGUSON, BETSY, PHD	NPRC	
[illegible]	NPRC	
FETZ, EBERHARD E, PHD	PHYSIOL & BIOPHYS	
FIRPO, PATRICIA, PHD	NPRC	
FUCHS, ALBERT F, PHD	PHYSIOL & BIOPHYS	
[illegible]	NPRC	
GLOMSET, JOHN A, MD	MEDICINE; BIOCHEM, HHMI	
[illegible]	NPRC	
GRANT, RICHARD, PHD	NPRC	
HAYES, ERIC, PHD	NPRC	
[illegible]	NPRC	
HU, SHIU-LOK, PHD	PHARMACEUTICS	
JAGADEESH, BARATHI, PHD	PHYSIOL & BIOPHYS	
[illegible]	NPRC	
KAJA, MURALI-KRISHNA, PHD	IMMUNOLOGY	
KATZE, MICHAEL G, PHD	MICROBIOLOGY	
KELLEY, STEPHEN, DVM	NPRC	

Core Doctoral Scientists

Name, Degree	Department	Non-Host Institution: State, Country
[illegible]	NPRC	
[illegible]	NPRC	
KYES, KELLY B, PHD	NPRC	
KYES, RANDALL C, PHD	NPRC, PSYCHOLOGY	
[illegible]	NPRC	
[illegible]	NPRC	
LETSCHER, ROBERT, DVM	NPRC	
LIGGITT, H DENNY, DVM, PHD	COMPARATIVE MEDICINE	
LONGLEY, ALLISON, PHD	NPRC	
[illegible]	NPRC	
[illegible]	NPRC	
[illegible]	NPRC	
MILES, FRANK P, PHD	NPRC	
[illegible]	NPRC	
MORROW, W JOHN, PHD	NPRC	
MORTON, WILLIAM R, VMD	NPRC	
[illegible]	NPRC	
[illegible]	BIOLOGICAL STRUCTURE	
[illegible]	NPRC	
PRITCHARD, JACKIE, PHD	NPRC	
ROBERTSON, PAUL, DDS	NPRC	
SACKETT, GENE P, PHD	PSYCHOLOGY	
[illegible]	NPRC	
SCHILLACI, MICHAEL, PHD	NPRC	
[illegible]	NPRC	
SHADLEN, MICHAEL N, MD, PHD	PHYSIOL & BIOPHYS, HHMI	
SHEIKH, NADEEM, PHD	PHARMACEUTICS	
[illegible]	NPRC	
[illegible]	NPRC	
[illegible]	NPRC	
TSAI, CHE-CHUNG, DVM, PHD	NPRC	
VOGEL, KEITH, DVM	NPRC	
[illegible]	NPRC	
WANG, YBING, MD	NPRC	
WORLEIN, JULIE M, PHD	NPRC	
YOUNG, MELINDA	NPRC	

Affiliated

Name, Degree	Department	Non-Host Institution: State, Country
[illegible]	COMPARATIVE MEDICINE	U OF SOUTH ALABAMA: AL, USA
[illegible]		INSTITUTE FOR SYSTEMS BIOLOGY: WA, USA
[illegible]	BIOLOGY	CHIANG MAI UNIVERSITY, CHINA
[illegible]	VACCINE RESEARCH CTR.	EMORY UNIVERSITY: GA, USA

Affiliated

Name, Degree	Department	Non-Host Institution: State, Country
		INSTITUTE OF SYSTEMS BIOLOGY: WA, USA
	VIROLOGY & IMMUNOLOGY	SOUTHWEST FDTN BIOMEDICAL RSCH: NM, USA
		LONDON SCHOOL OF PHARMACY, UK
	PATHOLOGY	
	NEUROPATHOLOGY	
	YERKES NPRC	EMORY UNIVERSITY: GA, USA
	PHARMACEUTICAL SCIENCES	UNIVERSITY OF KENTUCKY: KY, USA
ANDERSON, MARJORIE E, PHD	PHYSIOL & BIOPHYS	
	HEMATOL/ONCOL	
	NEUROINFORMATICS	UCLA MEDICAL SCHOOL: CA, USA
	BIOLOGY	EMORY UNIVERSITY: GA, USA
	PHYSIOL & BIOPHYS	
	AIDS VACCINE PROGRAM	NIH: MD, USA
	EPIDEMIOLOGY	
		UNIVERSITY OF SOUTHAMPTON, UK
	RADIOLOGY	
		TUNPRC: LA, USA
	NEUROLOGY AND PEDIATRICS	
	IMMUNOLOGY	BAYLOR INSTITUTE FOR IMMUNOLOGICAL RESEARCH: TX, USA
	FAMILY AND CHILD NURSING	
	UROLOGY	U OF WASHINGTON: WA, USA
		CHIRON CORP.: CA, USA
		US EPA: DC, USA
	COMPARATIVE MEDICINE	U OF CALIFORNIA DAVIS: CA, USA
	PSYCHOLOGY	
	MOLECULAR VIROLOGY	SOUTHERN RESEARCH INSTITUTE: AL, USA
	OBSTETRICS AND GYNECOLOGY	
	PEDIATRICS	
	PEDIATRICS	
		NCI: MD, USA
		VAX-GEN, INC.: CA, USA
	EDUCATIONAL PSYCHOLOGY	
		HUMBOLDT U BERLIN, GERMANY

Affiliated

Name, Degree	Department	Non-Host Institution: State, Country
		SINGAPORE EYE RESEARCH INSTITUTE, SINGAPORE
	SPECIAL EDUCATION	
		NCI-FCRDC: MD, USA
		SCRIPPS RESEARCH: CA, USA
	NEUROLOGY AND MEDICAL GENETICS	
	PSYCHOLOGY	VANDERBILT UNIVERSITY: TN, USA
	IMMUNOLOGY	SCRIPPS RESEARCH: CA, USA
		YERKES NPRC: GA, USA
		UNIVERSITY OF IDAHO: ID, USA
		UNIVERSITY OF IDAHO: ID, USA
	FAMILY AND CHILD NURSING	
	PATHOLOGY/NEUROPATHOLOGY	
	PATHOBIOLOGY	NORTHWEST BIOTHERAPEUTICS: WA, USA
	NEUROSCIENCE	U OF CALIFORNIA-LOS ANGELES: CA, USA
		TRIAD TECHNOLOGY CENTER: MD, USA
		LDS INC.: MN, USA
	USA CANCER RESEARCH	UNIVERSITY OF SOUTH ALABAMA: AL, USA
	PHYSIOL & BIOPHYS	
BRIGANDI, RICHARD A., MD		GLAXOSMITHKLINE: PA, USA
	MEDICINE	
	BRAIN AND COGNITIVE SCIENCES	MIT: MA, USA
	MEDICINE	
		COLD SPRING HARBOR LABORATORIES: NY, USA
		OHIO STATE UNIVERSITY: OH, USA
	NEUROBIOLOGY & BEHAVIOR	
BUMGARNER, ROGER E, PHD	MOLECULAR BIOTECHNOLOGY	
	CHEMISTRY	INDIANA UNIVERSITY: IN, USA
	ANESTHESIOLOGY	
	DAIDS	NIAID, NIH: MD, USA
	PSYCHIATRY AND BEHAV. SCIENCES	
	FAMILY AND CHILD NURSING	
		MICROBRIGHTFIELD, INC.: VT, USA
	MEDICINE	HARVARD: MA, USA

Affiliated

Name, Degree	Department	Non-Host Institution: State, Country
		NATURAL HISTORY SOCIETY OF NEPAL, NEPAL
	PEDIATRICS AND NEUROLOGY	
		ICOS PHARMACEUTICALS: WA, USA
	ENVIRONMENTAL HEALTH	
		AARON DIAMOND AIDS RSCH CTR.: NY, USA
		U OF CALIFORNIA-IRVINE: CA, USA
		INSTITUTE OF MEDICAL PRIMATOLOGY, RUSSIA
	MECHANICAL ENGINEERING	
	EXPERIMENTAL SURGERY	SINGAPORE GENERAL HOSPITAL, SINGAPORE
		ARIAD PHARMACEUTICALS: MA, USA
	SCIENCE AND TECHNOLOGY	ARIAD PHARMACEUTICALS, INC: MA, USA
CLOWES, ALEXANDER W, MD	SURGERY	
		RXKINETICS: CO, USA
	SPEECH AND HEARING SCIENCES	
		CORIELL BIOMEDICAL INSTITUTE: NJ, USA
		STANFORD UNIVERSITY: CA, USA
	CELL GENETICS	CORIELL INSTITUTE FOR MEDICAL RESEARCH: NJ, USA
		ORNPRC: OR, USA
	MICROBIOLOGY	
	PSYCHIATRY AND BEHAV. SCIENCES	
	MEDICINE	
	LABORATORY MEDICINE	
	MEDICINE	
	PSYCHOLOGY	
	PSYCHIATRY & BEHAVIORAL SCIENC	
	PEDIATRICS	
	PSYCHIATRY AND BEHAV. SCIENCES	
	NEUROLOGICAL SURGERY	
	NEUROBIOLOGY AND BEHAVIOR	
	TOXICOLOGY	STEINER ENTERPRISES: WA, USA
		AMGEN: WA, USA

Affiliated

Name, Degree	Department	Non-Host Institution: State, Country
	PEDIATRIC AND EPIDEMIOLOGY	
	PSYCHOLOGY	
		SHEFFIELD UNIVERSITY, UK
	GENOMICS	FHCRC: WA, USA
	COMPARATIVE MEDICINE	
	PHYSIOLOGY AND BIOLOGY	UNIVERSITY OF NOTTINGHAM, UK
	MICROBIOLOGY	NENPRC: MA, USA
	PHYSIOLOGY AND BIOPHYSICS	
	MICROBIOLOGY	
	NEUROGENOMICS DIVISION	TRANSLATIONAL GENOMICS RESEARCH INSTITUTE: AZ, USA
	REHABILITATION MEDICINE	
	HHMI	
		CHIRON CORP.: CA, USA
		LONDON SCHOOL HYG./TROP. MED., UK
		VRC/NIH: MD, USA
	PSYCHIATRY&BEHAV SCI	
	VETERINARY PATHOBIOLOGY	OKLAHOMA STATE UNIV.: OK, USA
	VACCINE DEVELOPMENT	IAVI: NY, USA
	NEUROLOGICAL SURGERY	
		VAXGEN, INC.: CA, USA
		SWEDISH MEDICAL CENTER: WA, USA
	NATIONAL CANCER INSTITUTE	NIH: MD, USA
	SURGERY	
		U OF CALIFORNIA DAVIS: CA, USA
	MEDICINE/INFECTIOUS DISEASE	
	DERMATOLOGY	U OF WISCONSIN: WI, USA
	REHABILITATIVE MEDICINE	
	PEDIATRICS	
	NEUROLOGY	
		ROBERT WOOD JOHNSON PHARMACEUTICAL RESEARCH INSTITUTE: NJ, USA
	ENVIRONMENTAL HEALTH	
	PATHOLOGY	
	ZOOLOGY	JAHANGIRNAGAR UNIVERSITY, THAILAND

Affiliated

Name, Degree	Department	Non-Host Institution: State, Country
		GENE THERAPY SYSTEMS INC: CA, USA
		NIH: MD, USA
	MICROBIOLOGY	
	SPEECH AND HEARING SCIENCES	
	PEDIATRICS & INF DIS	
	PHYSIOLOGY AND BIOPHYSICS	
names	ANTHROPOLOGY	U OF NOTRE DAME: IN, USA
	UNKNOWN	HOKKAIDO U, JAPAN
	MICROBIOLOGY	
	PSYCHOLOGY	UNIVERSITY OF COPENHAGEN, DENMARK
	BLOOMBERG SCHL PUBLIC HEALTH	JOHN HOPKINS UNIVERSITY: MD, USA
		KECK INSTITUTE FOR GRADUATE STUDIES: CA, USA
	VISION SCIENCE RESEARCH CENTER	U ALABAMA: AL, USA
	MATHEMATICS	UNIVERSITY OF FLORIDA: FL, USA
	MICROBIOLOGY	MNT SINAI SCHOOL OF MED: NY, USA
	NEUROLOGY	
GAUR, LAKSHMI, PHD	MEDICINE AND GENETICS	
		PUGET SOUND BLOOD CENTER: WA, USA
	SOCIAL WORK	
	PEDIATRICS	
	PEDIATRICS	
names	NEUROSCIENCE	UNIV. OF PENNSYLVANIA: PA, USA
	NEUROLOGY	U OF TEXAS: TX, USA
		U OF CALIFORNIA-DAVIS: CA, USA
	PEDIATRIC NEUROLOGY	
	ENVIRONMENTAL HEALTH	
	PSYCHIATRY AND BEHAV. SCIENCES	
GREENBERG, PHILIP D, MD	SIDNEY BRENNER LAB	UC BERKELEY: CA, USA
	MEDICAL ONCOLOGY	
names	BIOMED INFORMATICS RSCH NETWK	U OF ILLINOIS: IL, USA
		U OF CALIFORNIA-SAN DIEGO: CA, USA
	PEDIATRICS/MEDICINE	DEF. SCI. TECH. LAB, UK

Affiliated

Name, Degree	Department	Non-Host Institution: State, Country
	PSYCHOLOGY	
	PHYSIOLOGY & BIOPHYSICS	
	DAIDS	NIAID, NIH: MD, USA
	PSYCHOLOGY AND PEDIATRICS	
	CENTER FOR CANCER RESEARCH	NCI: MD, USA
	PSYCHOLOGY	
	PATHOBIOLOGY	SBRI: WA, USA
	FAMILY AND CHILD NURSING	
		IDEC PHARM.: CA, USA
	MEDICAL GENETICS	
	DIABETES INSTITUTE OF IMMUNOLO	U OF MINNESOTA: MN, USA
		IDEC: CA, USA
	RADIOLOGY	
	NATIONAL EYE INSTITUTE	NATIONAL INSTITUTE OF HEALTH: MD, USA
	COMPARATIVE MEDICINE	U OF NEW MEXICO: NM, USA
	BIOL STRUCT	
	REHABILITATION MEDICINE	
	OB-GYN	U PITTSBURGH: PA, USA
	PEDIATRICS	
	NEUROLOGY	OREGON HEALTH SCIENCES: OR, USA
HO, RODNEY J Y, PHD	PHARMACEUTICS	
	NATIONAL LIBRARY OF MEDICINE	NIH: MD, USA
	CENTER FOR AIDS AND STD	HARBORVIEW MEDICAL CENTER: WA, USA
		INSTITUTE FOR SYSTEMS BIOLOGY: WA, USA
	BIOCHEMISTRY	
		UFAW, UK
	HEALTH SERVICES	
	COMPARATIVE MEDICINE	U OF CALIFORNIA DAVIS: CA, USA
	BIOSTATISTICS	
	PHYSIOLOGY & BIOPHYSICS	
		UNIVERSITY COLLEGE, LONDON, UK
		IPPB, INDONESIA
	VIROLOGY	IPPB, INDONESIA
	PHYSIOLOGY	INST. BASIC MED SCIENCES, JAPAN
	PEDIATRICS	
	DEPT OF NEUROSCIENCES	UC SAN DIEGO: CA, USA

Affiliated

Name, Degree	Department	Non-Host Institution: State, Country
names	ANESTHESIOLOGY	
	PHYSIOLOGY BIOLOGY	
JUUL, SANDRA, MD, PHD	NE-NPRC	HARVARD UNIVERSITY: MA, USA
	PEDIATRICS	
names		TAYNA CENTER FOR CONSERVATION BIOLOGY, DEMOCRATIC REPUBLIC OF CONGO
		COLUMBIA UNIVERSITY: NY, USA
	CENTRE FOR CELL-MATRIX RESEARC	U OF MANCHESTER, UK
KANEKO, CHRIS R S, PHD	PHYSIOL & BIOPHYS	
	IMMUNOLOGY	HARVARD: MA, USA
	PHYSIOLOGY	GIFU UNIVERSITY, JAPAN
	OPTHAMOLOGY	
	CTR FOR MORPHOMETRIC ANALYSIS	MASS GEN HOSP, HARVARD U.: MA, USA
	MICROBIOLOGY AND IMMUNOLOGY	UNIVERSITY OF MELBOURNE, AUSTRALIA
names	MICROBIOLOGY	UNIVERSITY OF MIAMI: FL, USA
		NIAVARAN, IRAN
	MEDICINE	
		SWFBR: TX, USA
		GLAXOSMITHKLINE: PA, USA
	PHARMACEUTICS	
		CTR FOR NEURAL SCI NYU: NY, USA
	LAB ANIMAL RESOURCES	MERCK RESEARCH LABORATORIES: NJ, USA
		ZYMOGENETICS: WA, USA
		UNITED BIOMED.: NY, USA
		INSTITUTE OF MEDICAL PRIMATOLGOY, RUSSIA
		SCIMEDX CORPORATION: NJ, USA
	MICROBIOLOGY	
	NEUROINFORMATICS DIVISION	NIMH: MD, USA
	VOGT INSTITUT FÜR HIRNFORSCHUN	HEINRICH HEINE UNIVERSITY, GERMANY
	REHABILITATIVE MEDICINE	
	IMMUNOLOGY	ROSWELL PARK CANCER INST.: NY, USA
	SPEECH & HEARING SCIENCES	
		KALEIDOS PHARMA INC.: WA, USA

Affiliated

Name, Degree	Department	Non-Host Institution: State, Country
L	RADIOLOGY, BIOENGINEERING	
		TULANE NPRC: LA, USA
	ZOOLOGY	
		INSTITUTE OF MEDICAL PRIMATOLOGY (RAMS), RUSSIA
	LABORATORY MEDICINE	
	PSYCHIATRY	U COLORADO: CO, USA
	OPTOMETRY	STATE UNIVERSITY OF NEW YORK-NYC: NY, USA
	PSYCHOLOGY	
	NPRC	
	PEDIATRICS	
		MIT: MA, USA
	MEDICINE	
	DEPT. OF MEDICINE	HARVARD SCHOOL OF MEDICINE: MA, USA
	NEUROLOGY	
	UNKNOWN	UCSF: CA, USA
Nanny	PHARMACEUTICS	
	RADIOLOGY	
	MICROBIOLOGY	OSEL, INC.: CA, USA
	SCHOOL OF LIFE SCIENCES	ANHUI UNIVERSITY, CHINA
	NEUROSCIENCE AND MEDICINE	JOHN HOPKINS SCHOOL OF MEDICINE: MD, USA
		NCI: MD, USA
	PATHOBIOLOGY	
	NUCLEAR MEDICINE	
		SHIN NIPPON SANGYO LTD., JAPAN
	OPTHAMOLOGY	UNIVERSITY OF TEXAS-GALVESTON: TX, USA
	PSYCHOLOGY	
	COMP. MED.	UC DAVIS: CA, USA
	MEDICINE	
		CALIFORNIA INSTITUTE OF TECHNOLOGY: CA, USA
	NEUROINFORMATICS	UCLA: CA, USA
	ELECTRONIC PRODUCTS GROUP	ELSEVIER SCIENCE: MO, USA
	PSYCHOLOGY	
		ALCON LABORATORIES: TX, USA
	GENETICS	
	RADIOLOGY	
		YALE CENTER FOR MEDICAL INFORMATICS: CT, USA

Affiliated

Name, Degree	Department	Non-Host Institution: State, Country
	NEUROBIOLOGY AND ANATOMY	UNIVERSITY OF TX MEDICAL CTR: TX, USA
	REHABILITATIVE MEDICINE	
	PATHOLOGY	
	NEUROSCIENCES	U OF CALIFORNIA-SAN DIEGO: CA, USA
	TROP. MED.	TULANE, UHSC: LA, USA
	PHYSIOLOGY & BIOPHYSICS	
		PUGET SOUND BLOOD CENTER: WA, USA
	PEDIATRICS	
	PRODUCT/DRUG DEVELOPMENT	STARPHARMA PTY LTD, AUSTRALIA
		INT. THERAPEUTICS: WA, USA
		FHCRC: WA, USA
	PEDIATRICS	
	PSYCHOLOGY	
	CALIFORNIA NPRC	U OF CALIFORNIA-DAVIS: CA, USA
MILLER, SAMUEL I., MD	SVEU, NIAID	NIH: MD, USA
MINOSHIMA, SATOSHI, MD, PHD	MEDICINE	
	RADIOLOGY	
	PEDIATRICS	
		FUJISAWA PHARMACY, JAPAN
		DUKE UNIVERSITY: NC, USA
	NEUROLOGICAL SURGERY	
		CORIXA: WA, USA
	INSTITUTE OF VIROLOGY	PHILLIPS UNIVERSITY OF MARBURG, GERMANY
	MICROBIOLOGY	
	PATHOLOGY	
	PHARMACEUTICS	UNIVERSITY OF KENTUCKY: KY, USA
		IMPER. COLLEGE, UK
		NATIONAL BRAIN RESEARCH CENTER, INDIA
	ANATOMY AND NEUROBIOLOGY	UNIVERSITY OF TENNESSEE: TN, USA
	SCHOOL OF PHARMACY	
	UNKNOWN	VIRGINIA MASON HOSP: WA, USA
	ANTHROPOLOGY	
	NEUROBIOLOGY	STANFORD U SCHOOL OF MEDICINE: CA, USA
	NEUROBIOLOGY	DUKE UNIVERSITY: NC, USA
	MEDICINE, PHYSIOLOGY	UNIVERSITY OF COPENHAGEN, DENMARK
	PHYSIOLOGY & BIOPHYSICS	

Affiliated

Name, Degree	Department	Non-Host Institution: State, Country
	INST OF VIROLOGY & IMMUNOLOGY	U OF CALIFORNIA-SAN FRANCISCO: CA, USA
	OTOLARYNGOLOGY	
NOVAK, MELINDA, PHD		U OF MASSACHUSSETTS: MA, USA
	PEDIATRICS	
	OTOLARYNGOLOGY	
	VACCINE DELIVERY	CHIRON CORPORATION: CA, USA
	IMMUNOLOGY	
	NEUROL SURG	
	GENOME SCIENCE	
	SPEECH AND HEARING SCIENCES	
	PEDIATRICS	
	MICROBIOLOGY	
	BIOLOGICAL STRUCTURE	
	PATHOLOGY AND PERIODONTICS	
	OPHTHALMOLOGY	
	RESPIRATORY & ENTERIC VIRUSES	CENTERS FOR DISEASE CONTROL: GA, USA
	PSYCHOLOGY	
		IPPB, INDONESIA
	WANPRC	INDONESIAN PRIMATE RESEARCH CTR, INDONESIA
	PEDIATRICS	
		NEXIST, INC.: CA, USA
	PHYSIOLOGY AND BIOLOGY	UNIVERSITY OF NOTTINGHAM, UK
	IMMUNOLOGY	CNRS, FRANCE
PATTON, DOROTHY L, PHD	OB-GYN	
PERLMUTTER, STEVEN I I, PHD	PHYSIOL & BIOPHYS	
	ANTIGEN DISCOVERY	CORIXA CORPORATION: WA, USA
	OTOLARYNGOLOGY	
	PATHOLOGY	OR. HEALTH SCI. UNIVERSITY: OR, USA
	MATHEMATICS	UNIVERSITY OF FLORIDA: FL, USA
	PEDIATRICS AND MICROBIOLOGY	CHILDREN'S HOSPITAL: LA, USA
	VISUAL SCIENCE LABORATORIES	U CHICAGO: IL, USA
		CHIRON CORPORATION: CA, USA
	VETERINARY SCIENCE	AP AGRICULTURAL UNIVERSITY RAJENDRANAGAR HDERABAD, INDIA
	PHYSIOL & BIOPHYS	

Affiliated

Name, Degree	Department	Non-Host Institution State, Country
	MICROBIOLOGY	BEN GURION UNIVERSITY, ISRAEL
	NEUROLOGY	
	PHARMACEUTICS	CHIRON, ITALY
	MEDICINE	
		DANA FARBER: MA, USA
		NIH: MD, USA
		INBIOS: WA, USA
		BATTELLE TOXICOLOGY NORTHWEST: WA, USA
		PUGET SOUND BLOOD CENTER: WA, USA
names		RUTGERS: NJ, USA
		US EPA: DC, USA
	RADIOLOGY	
	EPIDEMIOLOGY	
		FRED HUTCHINSON CANCER RES CTR: WA, USA
ROBINSON, FARREL R, PHD	BIOLOGICAL STRUCTURE	
		EMORY UNIVERSITY: GA, USA
	PEDIATRIC INFECTIOUS DISEASE	TULANE UNIVERSITY: LA, USA
	NPRC PROGRAM	NCRR, NIH: MD, USA
	GENETICS	SWFBR: TX, USA
	NEUROBIOL&BEHAV	
	PATHOLOGY	YALE UNIVERSITY: CT, USA
names	PATHOBIOLOGY	
		PROCELL CORPORATION: MD, USA
	BIOLOGICAL STRUCTURE	
	PHYSIOLOGY AND BIOPHYSIOLOGY	
	PEDIATRICS	
		MOLECULAR TOXICOLOGY INC: NC, USA
		UNIVERSITY OF PITTSBURGH: PA, USA
	DEPT. OF MEDICINE	HARVARD MEDICAL SCHOOL: MA, USA
	PRIMATE RESEARCH CENTER	BOGOR AGRICULTURAL UNIVERSITY, INDONESIA
	PATHOLOGY	HARVARD: MA, USA
	PRIMATE RESEARCH CENTER	U OF BOGOR, INDONESIA
	GENOMICS	FHCRC: WA, USA
	MICROBIOLOGY	

Affiliated

Name, Degree	Department	Non-Host Institution: State, Country
	PSYCHIATRY	U OF CALIFORNIA-IRVINE: CA, USA
	GENETICS RESEARCH	MERCK: NJ, USA
	PSYCHOLOGY	VANDERBILT UNIVERSITY: TN, USA
	VETERINARY SCIENCES	U OF TEXAS: TX, USA
		ORPRC: OR, USA
	MEDICINE	
	PHARMACEUTICS	
	PEDIATRICS	
	PHYSIOL & BIOPHYS	
	COGNITIVE PSYCHOLOGY	U OF CALIFORNIA-SAN DIEGO: CA, USA
		NEUROSCIENCES INSTITUTE: CA, USA
		LA JOLLA INST ALLERGY/IMMUNOLOGY: CA, USA
	INFECTIOUS DISEASES	ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, UK
	PATHOLOGY/NEUROPATHOLOGY	
	PHARMACEUTICS	
	OB/GYN	
	MEDICINE	HARBORVIEW MEDICAL CENTER: WA, USA
		NCTR: CA, USA
	PSYCHIATRIC INSTITUTE	U OF ILLINOIS: IL, USA
	MICROBIOLOGY	
	ANTHROPOLOGY	U OF CALIFORNIA DAVIS: CA, USA
	PHYSIOLOGY BIOPHYSICS	
		UNIVERSITY OF MELBOURNE, AUSTRALIA
	VISUAL SCIENCE LABORATORIES	U CHICAGO: IL, USA
	NEUROLOGY	U OF CALIFORNIA SAN FRANCISCO: CA, USA
		MEDICAL COLLEGE OF GEORGIA: GA, USA
	PHARMACEUTICS	
	NEUROSCIENCE	BAYLOR COLLEGE OF MEDICINE: TX, USA
	BIOENGINEERING	
	PSYCHIATRY AND BEHAV. SCIENCES	
	CENTER FOR NEUROSCIENCE	U OF CALIFORNIA DAVIS: CA, USA

names

Affiliated

Name, Degree	Department	Non-Host Institution: State, Country
	FAMILY AND CHILD NURSING	
		SCRIPPS INST.: CA, USA
STAMATATOS, LEONIDAS, PHD	PATHOBIOLOGY	SBRI: WA, USA
	GENETICS	
	EPIDIMIOLOGY	
names	INTERNAL MEDICINE	U OF IOWA: IA, USA
	MEDICINE	UNIVERSITY OF PENNSYLVANIA: PA, USA
	PHYSIOL & BIOPHYS	
		VETERANS ADMINISTRATION MEDICAL CENTER: ID, USA
	OTOLARYNGOLOGY	
STOREK, JAN, MD, PHD	MEDICINE/ONCOLOGY	FRED HUTCHINSON CANCER RES CTR: WA, USA
		BIOJECT: OR, USA
	PEDIATRICS	
	PSYCHIATRY AND BEHAV. SCIENCES	
	NEUROBIOLOGY AND PSYCHIATRY	U OF PITTSBURGH: PA, USA
	SD SUPERCOMPUTING CTR	U OF CALIFORNIA SAN DIEGO: CA, USA
names	PSYCHIATRY AND BEHAV. SCIENCE	
	PSYCHIATRY AND BEHAV. SCIENCES	
	PARMACEUTICS	
	MEDICINE	
	RADIOLOGY	
		SINGAPORE EYE RESEARCH INSTITUTE, SINGAPORE
	NEUROLOGY	
PHD,	CELLULAR PATHOLOGY	ARMED FORCES INSTITUTE OF PATHOLOGY: DC, USA
		UNIVERSITY OF LEEDS, UK
	PSYCHOLOGY	
	OTOLARYNGOLOGY	
	NPRC	
		DEF. SCI. TECH. LAB, UK
	NEUROLOGY	UCLA SCHOOL OF MEDICINE: CA, USA
		PSIMEDICA, UK
TOTTEN, PATRICIA, PHD	INFECTIOUS DISEASES	HARBORVIEW MED CTR: WA, USA
Lname		LINCOLN PARK ZOO: IL, USA

Affiliated

Name, Degree	Department	Non-Host Institution: State, Country
	INFLUENZA BRANCH	CENTERS FOR DISEASE CONTROL: GA, USA
	PHARMACEUTICS	
	PSYCHIATRY	SACRED HEART MEDICAL CENTER: WA, USA
		INST ANIMAL SCIENCE/HEALTH, NETHERLANDS
	NEUROBIOLOGY	WASHINGTON UNIVERSITY: MO, USA
	CTR FOR COGNITIVE NEUROSCIENCE	DARTMOUTH COLLEGE: NH, USA
names	PSYCHIATRY AND BEHAV. SCIENCES	
	PEDIATRICS	JOHNS HOPKINS UNIVERSITY: MD, USA
	NEUROLOGY AND PSYCHOLOGY	KU LEUVEN MEDICAL SCHOOL, BELGIUM
		GLAXOSMITHKLINE, BELGIUM, BELGIUM
		UNIV OF OKLAHOMA: OK, USA
		BRANDEIS UNIVERSITY: MA, USA
	FAMILY AND CHILD NURSING	
	VETERINARY RESOURCES	NIH: MD, USA
		BASTYR UNIVERSITY: WA, USA
	SPEECH AND HEARING SCIENCES	
	FAMILY AND CHILD NURSING	
	NEUROLOGICAL SURGERY	
	MICROBIOLOGY, IMMUNOLOGY	EMORY UNIV: GA, USA
	CANCER IMMUNOLOGY AND AIDS	DANA FARBER CANCER INSTITUTE: MA, USA
	ANTHROPOLOGY	UNIV OF NEW MEXICO: NM, USA
	ANATOMY	U ROCHESTER: NY, USA
	ANATOMY AND NEUROBIOLOGY	UNIVERSITY OF TENNESEE: TN, USA
	IMMUNOLOGY	
	OPTHAMOLOGY	
	PATHOBIOLOGY AND IMMUNOLOGY	ORNPRC: OR, USA
	RADIOLOGY INFORMATICS LAB.	U OF CALIFORNIA-SAN DIEGO: CA, USA
	MEDICINE BIOLOGY	UCSD: CA, USA
	PEDIATRICS	
	MICROBIOLOGY	LONDON SCHOOL, UK
	PARMACY	NATIONAL UNIVERSITY, TAIWAN
	BUSINESS DEVELOPMENT	BIOWISDOM, UK

Affiliated

Name, Degree	Department	Non-Host Institution: State, Country
L	NEUROSCIENCE	JOHN HOPKINS SCHOOL OF MEDICINE: MD, USA
names	OPTHAMOLOGY HHMI	
1	LABORATORY MEDICINE	
		SBRI: WA, USA

Graduate Student/Postdoctoral Scientists

Name, Degree	Department	Non-Host Institution: State, Country
L	NEUROBIOL&BEHAV	
	PATHOBIOLOGY	
	PHYSIOL & BIOPHYS	
	MICROBIOLOGY	
	MICROBIOLOGY	
	PHYSIOLOGY AND BIOPHYSICS	
	PHARMACOLOGY	
	NEUROBIOLOGY & BEHAVIOR	
	ANTHROPOLOGY	
	PHYSIOLOGY AND BIOLOGY	
	PHYSIOLOGY AND BIOLOGY	
	PSYCHOLOGY	
	OPTHAMOLOGY	
names	PHYSIOLOGY AND BIOLOGY	
	PATHOBIOLOGY	
	PSYCHOLOGY	
	NEUROBIOLOGY, BIOMEDICAL ENGIN	
	NPRC	
	PHYSIOL & BIOPHYS	
	MICROBIOLOGY	
	PHYSIOL & BIOPHYS	
	MED SCIENCES	
	BIOSTRUCTURE	
	PATHOBIOLOGY	
	P-BIO	
	NEUROBIOLOGY	
	PHYSIOL & BIOPHYS	
	BIOENGINEERING	
	PHYSIOLOGY/BIOLOGY	
	NEUROSCIENCE	
	PHYSOLOGY AND BIOLOGY	
	PHYSIO BIO	
1	MICROBIOLOGY	

SUBPROJECT DESCRIPTIONS

NPRC MANAGEMENT SUBPROJECTS

RESEARCH REVIEW COMMITTEE (0258)

NPRC UNIT: ADMINISTRATIVE

%NPRC $: 0.700%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
MORTON, WILLIAM R	VMD	C	NPRC	
	DVM	C	NPRC	
	MD	C	PSYCHIATRY&BEHAV SCI	
	PHD	C	BIOLOGICAL STRUCTURE	
	PHD	A	PATHOBIOLOGY	SBRI, WA USA
	DDS	A	PATHOLOGY AND PERIODONTICS	

AXIS I CODES: 28(ADMINISTRATION) **AXIS II CODES**38

ABSTRACT

This Committee is composed of the NPRC Director; two Core Staff scientists; two University of Washington (UW) faculty members who are not employees of the Primate Center, and the Associate Director for Primate and Research Resources. The committee reviews all animal-related research proposals for the NPRC, evaluating them for scientific merit and applicability regarding research to be carried out at a primate research center. If any proposal has not been peer-reviewed by a major granting agency and the members feel it necessary, the Committee may seek external review by one or two ad hoc reviewer(s) who have expertise in the field. New proposals are distributed to RRC members and are discussed/ reviewed via monthly scheduled meetings and/or e-mail communication, including interchanges with the investigator and NPRC colony veterinary personnel, as necessary. The Committee Coordinator (Assistant to the Director) coordinates RRC activities, communicates with new investigators, committee members and NPRC staff as required, and maintains records of the decisions of all Committee members and all approved NPRC research projects. The RRC reviewed and evaluated proposed venture/pilot and colony health-related projects, choosing relevant projects to be included in the NPRC grant application, and continues to review and consider all venture/pilot proposals submitted to the NPRC for the duration of this 5-year grant, when applicable. Current members are listed as co-investigators above.

SCIENTIFIC ADVISORY COMMITTEE (0257)

NPRC UNIT: ADMINISTRATIVE

%NPRC $: 1.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
NOVAK, MELINDA	PHD	A		U OF MASSACHUSSETTS, MA USA
	DVM	A	COMPARATIVE MEDICINE	U OF SOUTH ALABAMA, AL USA
	PHD	A	AIDS VACCINE PROGRAM	NIH, MD USA
	PHD	A	IMMUNOLOGY	BAYLOR INSTITUTE FOR IMMUNOLOGICAL RESEARCH, TX USA
	MD, PHD	A		INSTITUTE FOR SYSTEMS BIOLOGY WA USA
	PHD	A	NEUROBIOLOGY	STANFORD U SCHOOL OF MEDICINE, CA USA
	MD, PHD	A	DEPT. OF MEDICINE	HARVARD MEDICAL SCHOOL, MA USA
	PHD	A	NEUROSCIENCE	BAYLOR COLLEGE OF MEDICINE, TX USA
	PHD	A	NEUROBIOLOGY AND PSYCHIATRY	U OF PITTSBURGH, PA USA

AXIS I CODES: 28(ADMINISTRATION) **AXIS II CODES**38

ABSTRACT

This Committee is made up of nationally recognized scientists in various disciplines to cover the scientific research scope of the Center. It usually meets once per year, or as required, to provide critical review and recommendations for scientific research. The Committee provides direct input to the University of Washington Health Sciences Administration and the University of Washington President on the progress and relevance of the scientific programs of the Center. The Committee also conducts exit interviews with the Director and Staff and submits a written report to the Core Grant PI. Current members are listed as co-investigators here.

SAFETY ADVISORY COMMITTEE (0259)

NPRC UNIT: ADMINISTRATIVE

%NPRC $: 1.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
YOUNG, MELINDA		C	NPRC	
L names	DVM	C	NPRC	
	DVM	C	NPRC	
		C	WANPRC	

AXIS I CODES: 28(ADMINISTRATION) **AXIS II CODES**92(HEALTH AND SAFETY)

ABSTRACT

This committee meets on a monthly basis to discuss policy related to occupational health and safety in the care and use of research animals. Chair of this committee is Melinda Young, head of the Center's Occupational Health and Safety Program.

HEALTH AND SAFETY COMMITTEE (0261)

NPRC UNIT: ADMINISTRATIVE

%NPRC $: 1.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
YOUNG, MELINDA		C	NPRC	
		C	NPRC	
		C	NPRC	
	PHD	C	PHYSIOL & BIOPHYS	
		C	NPRC	
	PHD	C	NPRC	
		C	NPRC	
	PHD	C	PHARMACEUTICS	
		C	NPRC	
		C	NPRC	

AXIS I CODES: 28(ADMINISTRATION) **AXIS II CODES**92(HEALTH AND SAFETY)

ABSTRACT

The aim of this committee is to assist in providing a safe working environment for employees and to address general occupational health and safety concerns. The committee reviews the Center's written Health and Safety Plan, addresses emergency planning issues as required by the University of Washington administration and advises on health and safety training programs. Melinda Young appoints the committee members from a variety of the Center's Divisions

SPECIAL CLINICAL CASES (0209)

NPRC UNIT: COLONY HEALTH

%NPRC $: 1.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ANDERSON, DAVID M	DVM	C	NPRC	
[name]	DVM	C	NPRC	

AXIS I CODES: 1A **AXIS II CODES:** 44, 50, 63, 65, 66

ABSTRACT

This project identifies special clinical cases of a spontaneous nature in primates located in the research, colony, and quarantine colonies in the WaNPRC. The animals usually present with an abnorality or disease that necessitates in depth clinical examination and obersvation. In cases when the animals are on current research assignments, the principal investigator is notified, and the case is discussed. Assignment to Special Clinical Cases ensures optimal clinical care and careful data collection for further dissemination to the Research and Veterinary community.

RESEARCH SPECIMEN COLLECTION (0241)

NPRC UNIT: COLONY HEALTH

%NPRC $: 1.700% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ANDERSON, DAVID M	DVM	C	NPRC	
Lewis J	DVM	C	NPRC	

AXIS I CODES: 1D **AXIS II CODES** 31, 39, 54, 55, 56, 59, 62, 63, 64, 65, 66, 76, 77, 83, 91

ABSTRACT

This project is designed to provide a resource for investigators requiring blood or other fluid samples without necessitating the purchase of a whole animal. Samples that would collected include blood, bone marrow, cerebrospinal fluid and others. These procedures are all performed under sedation, and result in only minimal distress or discomfort to the animal. The volumes collected of any sample type represent only a small percentage of the animals' total volume, and is readily replaced by normal physiologic mechanisms.

SPECIFIC PATHOGEN FREE BREEDING COLONY (0268)

NPRC UNIT: COLONY HEALTH

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ANDERSON, DAVID M	DVM	C	NPRC	
	PHD	C	NPRC	
	DVM	A	VIROLOGY	IPPB, INDONESIA
	PHD	C	NPRC, PSYCHOLOGY	
	VMD	C	NPRC	
	DVM	A		IPPB, INDONESIA

AXIS I CODES: 1A **AXIS II CODES:** 66

ABSTRACT

The objective of this project is to produce a large, self-sustaining colony of Macaca nemestrina free of several pathogens, including Simian Retroviruses (SRV), Simian Immunodeficiency Viruses (SIV), Simian T-lymphotrophic Virus (STLV), and Cercopithecine Herpesvirus 1 (B virus). SRV, STLV, and SIV have immunomodulatory effects with the potential to alter the host immune response in infectious disease studies. Therefore, support has been provided to provide macaques free of these pathogens for AIDS-related research studies Herpes B virus has the potential for zoonotic transmission to animal care or research staff and is therefore desirable to eliminate. This year is the first of five years support for development of this colony. The Washington National Primate Research Center has met many of the milestones prescribed for the first year of the SPF colony of Macaca nemestrina.

One component of the program is the development of a large breeding colony at the Tulane National Primate Research Center. Second, existing collaborative relationships with Bogor University, Indonesia, will be utilized to access feral breeding stock from sources available in this country for this species. Onsite breeding colonies of Macaca nemestrina will be established from feral sources with subsequent SPF offspring shipped to Tulane to supplement the domestic SPF colony.

PSYCHOLOGICAL WELL-BEING PROGRAM (0207)

NPRC UNIT: COLONY HEALTH

%NPRC $: 1.700% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
CROCKETT, CAROLYN M	PHD	C	NPRC	
	DVM	C	NPRC	
	PHD	A		TUNPRC, LA USA
	PHD	C	NPRC	
		C	NPRC	
	PHD	A		YERKES NPRC, GA USA
	PHD	A		U OF CALIFORNIA-IRVINE, CA USA
	PHD	A		ORNPRC, OR USA
		A		STEINER ENTERPRISES, WA USA
	BS	C	NPRC	
	PHD	C	PHYSIOL & BIOPHYS	
	PHD	A		UNIVERSITY OF PENNSYLVANIA, P USA
	DVM	A		U OF TEXAS, TX USA
	BA	C	NPRC	
	PHD	A		U OF ILLINOIS, IL USA
	PHD	A	PSYCHOLOGY	
	PHD	A		UFAW, UK
	DVM	A		COLUMBIA UNIVERSITY, NY USA
	DVM	C	NPRC	
	PHD	C	NPRC, PSYCHOLOGY	
	BS	C	NPRC	
		A		ALCON LABORATORIES, TX USA
	PHD	A	ANATOMY AND NEUROBIOLOGY	UNIVERSITY OF TENNESSEE, TN USA
	PHD	A		U OF MASSACHUSSETTS, MA USA
	BS	A		UNIVERSITY OF PITTSBURGH, PA USA
	PHD	C	PSYCHOLOGY	
	MD	A	PSYCHIATRY	U OF CALIFORNIA-IRVINE, CA USA
	DVM		WANPRC	
	BS	C	NPRC	
	BS	C	NPRC	
	DVM, PHD	C	NPRC	
	PHD	A		UNIV OF OKLAHOMA, OK USA
	PHD	A	VETERINARY RESOURCES	NIH, MD USA

AXIS I CODES: 1A **AXIS II CODES:** 31, 36, 92(PSYCHOLOGICAL WELL-BEING)

ABSTRACT

The Psychological Well being (PWB) Program oversees the implementation of the Federally-required Environmental Enhancement Plan for nonhuman primates at the WaNPRC. The purpose of the Environmental Enhancement Plan is to provide a psychologically enriching environment for laboratory primates housed at the WaNPRC to address their psychological needs while also meeting or exceeding regulatory requirements. The PWB Program utilizes a multi faceted approach to provide enrichment opportunities for nonhuman primates compatible with housing requirements and research objectives. PWB Program staff evaluate new enrichment options before widespread adoption. The diagnosis and treatment of behavioral problems of WaNPRC primates is in the domain of the Program. Behavioral assessments and interventions are conducted by the PWB Program Coordinator and Enrichment/Research Technologists. Enrichment and behavioral issues relating to the physical health and medical conditions of the animals are reviewed by veterinary staff. Husbandry staff, under the supervision of the Colony Manager, implement certain aspects of Environmental Enhancement Plan. To achieve the goal of maximizing the mental health of laboratory primates, PWB Staff develop protocols and forms for monitoring and documenting enrichment, social compatibility, behavioral assessment and intervention strategies. Communication among PWB staff, husbandry staff, and veterinary staff is facilitated by frequent meetings of the Environmental Enhancement Committee, which serves as a forum for ideas, implementation, and communication with respect to environmental enrichment and behavioral health issues of the WaNPRC's laboratory primates. PWB staff also present training seminars for WaNPRC personnel to provide extensive information regarding nonhuman primate behavior and the PWB Program. The Washington National Primate Research Center's Psychological Well-being Program is incorporating knowledge gained from its research to modify animal management and environmental enhancement plans, thereby improving nonhuman primate psychological well-being and overall health. Finally, Carolyn Crockett, PWB program head was the Breakout Session Chair for the Nonhuman Primate section of "Assessment of Environmental Enrichment - Science vs. Welfare Concerns" session of the ILAR International Workshop on Development of Science-based Guidelines for Laboratory Animal Care," Nov. 2003, Georgetown University. This meeting served as a medium for information on the proper care of simians in captivity.

PSYCHOLOGICAL WELL-BEING AND ENVIRONMENTAL ENRICHMENT COMMITTEE (0262)

NPRC UNIT: COLONY HEALTH

%NPRC $: 1.700% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
CROCKETT, CAROLYN M	PHD	C	NPRC	
L	DVM	C	NPRC	
	BA	C	NPRC	
names	DVM	A	COMPARATIVE MEDICINE	
		C	NPRC	
	BA	C	NPRC	
	DVM	C	NPRC	
	BS	C	NPRC	
		C	NPRC	
		C	NPRC	

AXIS I CODES: 28(ADMINISTRATION) **AXIS II CODES:** 31, 38

ABSTRACT

This committee is an informal body that meets regularly to discuss environmental enrichment issues. The Committee serves in an advisory capacity to the Attending Veterinarian. Current members are listed as co-investigators above. In addition to these members, any interested members of the WaNPRC husbandry, veterinary, and research staff, Infant Primate Research Laboratory representatives, and student researchers participating in Psychological Well-Being Program projects are invited to attend meetings and submit comments or ideas.

SVEU HOLDING (0211)

NPRC UNIT PRIMATE RESOURCES

%NPRC $: 1.700% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ANDERSON, DAVID M	DVM	C	NPRC	
	PHD	A	AIDS VACCINE PROGRAM	NIH, MD USA
	MD, PHD	A		NCI, MD USA
	PHD	C	NPRC	
	MD	A	MEDICAL ONCOLOGY	
	PHD	A	PATHOBIOLOGY	SBRI, WA USA
	PHD	C	PHARMACEUTICS	
	MD	A	DEPT. OF MEDICINE	HARVARD SCHOOL OF MEDICINE, MA USA
	PHD	A	SVEU, NIAID	NIH, MD USA
	VMD	C	NPRC	
	PHD	A	IMMUNOLOGY	
	PHD	A		GLAXOSMITHKLINE, BELGIUM, BELGIUM
	MD	A	MEDICINE BIOLOGY	UCSD, CA USA

AXIS I CODES: 1A **AXIS II CODES** 31, 64, 66, 83, 91

ABSTRACT

This project holds animals that have been pre-screened as candidates for vaccine projects directed by the Simian Vaccine Evaluation Unit contract.

DIVISION OF INTERNATIONAL PROGRAMS (0204)

NPRC UNIT: PRIMATE RESOURCES

%NPRC $: 1.700% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KYES, RANDALL C	PHD	C	NPRC, PSYCHOLOGY	
	MS	A	BIOLOGY	CHIANG MAI UNIVERSITY, CHINA
	PHD	C	NPRC	
	PHD	A	VIROLOGY & IMMUNOLOGY	SOUTHWEST FDTN BIOMEDICAL RSCH, NM USA
	PHD	A	COMPARATIVE MEDICINE	U OF CALIFORNIA DAVIS, CA USA
		A	MOLECULAR VIROLOGY	SOUTHERN RESEARCH INSTITUTE, AL USA
	PHD	A		SINGAPORE EYE RESEARCH INSTITUTE, SINGAPORE
	PHD	A		NATURAL HISTORY SOCIETY OF NEPAL, NEPAL
	MD	A	EXPERIMENTAL SURGERY	SINGAPORE GENERAL HOSPITAL, SINGAPORE
	PHD	A	VETERINARY PATHOBIOLOGY	OKLAHOMA STATE UNIV., OK USA
	MD, MPH	A		SWEDISH MEDICAL CENTER, WA USA
	MD, MPH	A	NATIONAL CANCER INSTITUTE	NIH, MD USA
	PHD	A	ZOOLOGY	JAHANGIRNAGAR UNIVERSITY, THAILAND
	PHD	C	NPRC	
	PHD	A	ANTHROPOLOGY	U OF NOTRE DAME, IN USA
	PHD	A	BLOOMBERG SCHL PUBLIC HEALTH	JOHN HOPKINS UNIVERSITY, MD USA
	PHD	C	NPRC	
	DVM, PHD	A	COMPARATIVE MEDICINE	U OF NEW MEXICO, NM USA
	BA	G	ANTHROPOLOGY	
	PHD	A	COMPARATIVE MEDICINE	U OF CALIFORNIA DAVIS, CA USA
	BS	G	PSYCHOLOGY	
	MS	A		IPPB, INDONESIA
	DVM	A	VIROLOGY	IPPB, INDONESIA
	PHD	G	PSYCHOLOGY	
	BA	C	NPRC	
		A		TAYNA CENTER FOR CONSERVATION BIOLOGY, DEMOCRATIC REPUBLIC OF CONGO
	DVM	C	NPRC	
	PHD	C	NPRC	

[redacted]	MD	A		INSTITUTE OF MEDICAL PRIMATOLOGY (RAMS), RUSSIA
	BS	A	PSYCHOLOGY	
	PHD	A	SCHOOL OF LIFE SCIENCES	ANHUI UNIVERSITY, CHINA
	VMD	C	NPRC	
	PHD	A	RESPIRATORY & ENTERIC VIRUSES	CENTERS FOR DISEASE CONTROL, GA USA
	DVM	A		IPPB, INDONESIA
names	DVM, PHD	A	PRIMATE RESEARCH CENTER	U OF BOGOR, INDONESIA
	PHD	C	NPRC	
	PHD	A	ANTHROPOLOGY	U OF CALIFORNIA DAVIS, CA USA
	PHD	A		SINGAPORE EYE RESEARCH INSTITUTE, SINGAPORE
	PHD	A		LINCOLN PARK ZOO, IL USA
	MD	A	PEDIATRICS	JOHNS HOPKINS UNIVERSITY, MD USA
[redacted]	MS	A	ANTHROPOLOGY	UNIV OF NEW MEXICO, NM USA

AXIS I CODES: 1A, 1D, 4 **AXIS II CODES**31, 36, 92(CONSERVATION)

ABSTRACT

The Division of International Programs at the Washington National Primate Research Center (WaNPRC) is a formal administrative division that oversees the Center's international programs. Dr. Randall Kyes who has been involved in the Center's international activities for 12 years heads the division. The objectives of the International Programs Division include the following: to support international breeding operations so as to ensure the availability of primate resources; to facilitate joint research opportunities with collaborating institutions; to provide educational and training opportunities in primatology for students and staff from collaborating institutions; and to assist in efforts to help manage and conserve naturally occurring primate populations in habitat countries. The Center currently supports two long-standing, international programs in Indonesia (established in 1991 with the Primate Research Center at Bogor Agricultural University) and Russia (established in 1992 with the Institute of Medical Primatology of the Russian Academy of Medical Sciences). A third program in Nepal (with the Natural History Society of Nepal) was formally established in July 2001. Recent program additions include: the China Program (established October, 2002 with Anhui University), the Bangladesh Program (established October, 2003 with Jahangimagar University), and the Thailand Program (established January, 2003 with Chiang Mai University). A seventh international program is in development with the Singapore General Hospital and the Singapore Eye Research Institute. There were several new personnel appointments in the Division of International Programs during 2002-03. They include [redacted] name [redacted] Postdoctoral Fellow and Research Associate, [redacted] name [redacted] Research Scientist, Michael Schillaci, PhD, Research Scientist (appointment through March 2003), and [redacted] name [redacted] Program Coordinator. [redacted] name [redacted] has a strong background in bi-directional disease transmission research and will play a significant role in the Division's expanding research focus on conservation biology and emerging infectious disease.

SIMIAN VACCINE EVALUATION UNIT (SVEU) (0190)

NPRC UNIT: PRIMATE RESOURCES

%NPRC $: 1.200% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
MORTON, WILLIAM R	VMD	C	NPRC	
	DVM	C	NPRC	
	PHD	A	AIDS VACCINE PROGRAM	NIH, MD USA
	MD, PHD	A		NCI, MD USA
	PHD	C	NPRC	
	MD	A	MEDICAL ONCOLOGY	
	PHD	A	PATHOBIOLOGY	SBRI, WA USA
	PHD	C	PHARMACEUTICS	
	MD	A	DEPT. OF MEDICINE	HARVARD SCHOOL OF MEDICINE, MA USA
	PHD	A	SVEU, NIAID	NIH, MD USA
	PHD	A	IMMUNOLOGY	
	PHD	A		GLAXOSMITHKLINE, BELGIUM, BELGIUM
	MD	A	MEDICINE BIOLOGY	UCSD, CA USA

AXIS I CODES: 1D **AXIS II CODES:** 31, 91

ABSTRACT

The Simian Vaccine Evaluation Unit provides an important and integral part of vaccine programs around the United States. This unit uses nonhuman primate models of AIDS to test the efficacy of newly developed vaccines that may lead to prevention of infection and disease. Simian models for AIDS are the most relevant to human AIDS because the causative viruses, human and simian immunodeficiency viruses (HIV and SIV), are very similar in their biological characteristics and cause very similar diseases in their respective hosts. For the purposes of testing vaccines against HIV, the simian model has also been adapted to use chimeric viruses (SHIV) that contain the vaccine portions of HIV and the non-vaccine portions of SIV. The SVEU has utilized the new chimeric SHIV model and the traditional SIV model to evaluate candidate vaccines by measuring the immune responses induced by the vaccines, by measuring levels of virus in the blood and by monitoring clinical health of animals after challenge with SIV or SHIV. Projects to evaluate key viral proteins, Nef and Tat, as well as vaccines containing core proteins and envelope glycoproteins, have been part of the SVEU this year. Inactivated whole SIV has also been used as a vaccine preparation this year with results still pending. It is anticipated that vaccine evaluations in nonhuman primate models for AIDS will lead to better understanding of vaccines to be used in humans.

BIOSTRUCTURE TECHNOLOGY LABORATORY (BSTL) (0194)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
BOWDEN, DOUGLAS M	MD	C	PSYCHIATRY&BEHAV SCI	
	PHD	A	NEUROINFORMATICS	UCLA MEDICAL SCHOOL, CA USA
	PHD	A	NEUROSCIENCE	U OF CALIFORNIA-LOS ANGELES, CA USA
	PHD	A		OHIO STATE UNIVERSITY, OH USA
	PHD	C	ENVIRONMENTAL HEALTH	
		A		MICROBRIGHTFIELD, INC., VT USA
	PHD	A		CORIELL BIOMEDICAL INSTITUTE, NJ USA
	PHD	C	BIOLOGICAL STRUCTURE	
	PHD	A	NEUROGENOMICS DIVISION	TRANSLATIONAL GENOMICS RESEARCH INSTITUTE, AZ USA
	PHD	C	PHYSIOL & BIOPHYS	
	PHD	C	PHYSIOL & BIOPHYS	
	PHD	A	PSYCHOLOGY	UNIVERSITY OF COPENHAGEN, DENMARK
	MD	C	MEDICINE; BIOCHEM, HHMI	
	MD	A	NEUROLOGY	U OF CALIFORNIA-DAVIS, CA USA
	PHD	A	BIOMED INFORMATICS RSCH NETWK	U OF CALIFORNIA-SAN DIEGO, CA USA
	PHD	A	BIOL STRUCT	
	MD	A	NATIONAL LIBRARY OF MEDICINE	NIH, MD USA
	PHD	G	PHYSIOLOGY AND BIOLOGY	
	PHD	A	DEPT OF NEUROSCIENCES	UC SAN DIEGO, CA USA
	PHD	A	PHYSIOL & BIOPHYS	
	PHD	A	CTR FOR MORPHOMETRIC ANALYSIS	MASS GEN HOSP, HARVARD U., M/ USA
	PHD	G	NPRC	
	MD, PHD	A	NEUROINFORMATICS DIVISION	NIMH, MD USA
	PHD	A	VOGT INSTITUT FÜR HIRNFORSCHUN	HEINRICH HEINE UNIVERSITY, GERMANY
	PHD	G	PHYSIOL & BIOPHYS	
	PHD	A	ELECTRONIC PRODUCTS GROUP	ELSEVIER SCIENCE, MO USA

	MD	A		YALE CENTER FOR MEDICAL INFORMATICS, CT USA
	PHD	A	NEUROSCIENCES	U OF CALIFORNIA-SAN DIEGO, CA USA
		A		NEXIST, INC., CA USA
	PHD	A	PHYSIOL & BIOPHYS	
		C	BIOLOGICAL STRUCTURE	
	PHD	A	BIOLOGICAL STRUCTURE	
	MD	A	BIOLOGICAL STRUCTURE	
	MS	G	PHYSIOL & BIOPHYS	
	PHD	A	COGNITIVE PSYCHOLOGY	U OF CALIFORNIA-SAN DIEGO, CA USA
	PHD	A		NEUROSCIENCES INSTITUTE, CA USA
	MD, PHD	A	PSYCHIATRIC INSTITUTE	U OF ILLINOIS, IL USA
	PHD	A	SD SUPERCOMPUTING CTR	U OF CALIFORNIA SAN DIEGO, CA USA
	PHD	A	NEUROLOGY	UCLA SCHOOL OF MEDICINE, CA USA
	PHD	A	NEUROBIOLOGY	WASHINGTON UNIVERSITY, MO USA
	PHD	A	CTR FOR COGNITIVE NEUROSCIENCE	DARTMOUTH COLLEGE, NH USA
	PHD	A	ANATOMY AND NEUROBIOLOGY	UNIVERSITY OF TENNESEE, TN USA
	PHD	A	RADIOLOGY INFORMATICS LAB.	U OF CALIFORNIA-SAN DIEGO, CA USA
	PHD	A	BUSINESS DEVELOPMENT	BIOWISDOM, UK

AXIS I CODES: 1D, 9, 21 **AXIS II CODES:** 63C, 63I, 68, 70

ABSTRACT

The Biostructure Technology Laboratory is a core facility of the Neurosciences Division of the WaNPRC. It includes two components: a Neurohistology Laboratory, which provides slide preparation services to scientists in primate research, and a Microscopy/Image Processing Laboratory, which provides access to a state-of-the-art light microscope and a digital imaging system for quantitative microscopy and image analysis. The computerized microscope stage, digital video camera and frame-grabber allow investigators to map the location of neurotransmitters, receptors, nerve pathways and gene expression with a high degree of accuracy and efficiency. A workstation is used to map images to a template atlas of the macaque brain. Data mapped to the Template Atlas developed at the WaNPRC are published on the BrainInfo website (http://braininfo.rprc.washington.edu).

In 2003, the Neurohistology Laboratory provided services for 23 of Core Staff scientists, Research Affiliates, Collaborators, Postdoctoral Fellows and Graduate Students. The BrainInfo website (http://braininfo.rprc.washington.edu) provided software for indexing neuroscience databases to 21 individuals and institutions and displayed more than 1,130,000 pages to some 26,500 unique users from 99 countries (68% US); reasons given for visiting BrainInfo continued to be: research interest (35%), teaching or studying neuroanatomy (35%), clinical interest (10%), "just curious" (20%).

THE NORTHWEST GENE EXPRESSION CONFERENCE (0338)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.450%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
BUMGARNER, ROGER E	PHD	A	MOLECULAR BIOTECHNOLOGY	
[redacted]	PHD	A		INSTITUTE OF SYSTEMS BIOLOGY, WA USA
[redacted]	PHD	A		KECK INSTITUTE FOR GRADUATE STUDIES, CA USA
	PHD	A	SIDNEY BRENNER LAB	UC BERKELEY, CA USA
	PHD	A	NEUROLOGY	OREGON HEALTH SCIENCES, OR USA
	PHD	A	MICROBIOLOGY	
[redacted]	PHD	A	GENETICS RESEARCH	MERCK, NJ USA

AXIS I CODES: 28(GENETIC MATERIAL) **AXIS II CODES**55, 58, 59, 74G

ABSTRACT

The NorthWest Gene Expression Conference, NwGEC (previously known as Northwest Microarray Conference) is one of the largest international conferences in gene-profiling organized by academia rather than industry. The conference has become one of the major events in functional genomics, and scientists from all over the world attend and present. Over the past 3 years, attendance at the conference has ranged from 150-250 people and at a typical conference researchers from more than 15 countries are represented. The meeting is highly informative to the researchers in the field because internationally recognized experts present their up-to-date progresses in the application and development of gene profiling technology.

In 2003, the conference was held at the Seattle Sheraton and was attended by approximately 175 people. In addition, the conference is co-sponsored by a number of companies which produce products in the gene expression market space. A total of 12 vendors set-up booths as part of the 2003 NwGEC tradeshow.

The agenda of past year's conference consisted of 5 sessions:

Wed., August 27th Array Studies of Viral and Bacterial Pathogenesis

Thurs, August 28th Systems Biology
New Technologies/Methods for High Throughput Expression Analysis

Fri, August 29th General Applications of Arrays
Bioinformatics for High Throughput Expression Analysis

The special session on Thursday - "Systems Biology" was co-organized by [redacted] of the Institute for Systems Biology. Invited Speakers in this session included:

- [redacted] – Director of the Keck Institute for Graduate Studies, former Director of DOE Genome Sciences Program
- [redacted] Director of Genetics Research, Merck
- [redacted], Chair Department of Neurology, Oregon Health Sciences
- [redacted] from the Sidney Brenner lab at UC Berkeley
- [redacted] Institute of Systems Biology, Seattle WA.
- [redacted] Department of Microbiology, University of

Washington

Topics covered in this special session ranged from modeling biological networks to integration of genetics and gene expression data, to current understanding of alternative splicing and non-sense mediated mRNA decay. Many of the premier scientists nationwide working in systems biology research were present or represented in this special session.

INFANT PRIMATE RESEARCH LABORATORY CORE (0264)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
BURBACHER, THOMAS M	PHD	C	ENVIRONMENTAL HEALTH	
	MD	A	NEUROPATHOLOGY	
	PHD	A	EPIDEMIOLOGY	
	PHD	A	RADIOLOGY	
	MD	A	NEUROLOGY AND PEDIATRICS	
	PHD	A	FAMILY AND CHILD NURSING	
	PHD	A		US EPA, DC USA
	PHD	A	PSYCHOLOGY	
	MD, MHA	A	OBSTETRICS AND GYNECOLOGY	
	PHD	A	PEDIATRICS	
	MD	A	PEDIATRICS	
	PHD	A	EDUCATIONAL PSYCHOLOGY	
	PHD	A	SPECIAL EDUCATION	
	MD	A	NEUROLOGY AND MEDICAL GENETICS	
	PHD	A	FAMILY AND CHILD NURSING	
	MD, PHD	A	PATHOLOGY/NEUROPATHOLOGY	
	MD	A	MEDICINE	
		A	ANESTHESIOLOGY	
	PHD	A	PSYCHIATRY AND BEHAV. SCIENCES	
	PHD	A	FAMILY AND CHILD NURSING	
	MD	A	PEDIATRICS AND NEUROLOGY	
	PHD	A		ICOS PHARMACEUTICALS, WA USA
	PHD	A	ENVIRONMENTAL HEALTH	
		A	SCIENCE AND TECHNOLOGY	ARIAD PHARMACEUTICALS, INC, MA USA
	PHD	A	SPEECH AND HEARING SCIENCES	
	PHD	A	PSYCHIATRY AND BEHAV. SCIENCES	
	PHD	A	PSYCHOLOGY	
	PHD	C	NPRC	
	MD, PHD	A	PEDIATRICS	

names

L	MD	A	PSYCHIATRY AND BEHAV. SCIENCES	
		A	NEUROLOGICAL SURGERY	
	MD, MPH	A	PEDIATRIC AND EPIDEMIOLOGY	
	PHD	A	PSYCHOLOGY	
	PHD	A	REHABILITATION MEDICINE	
	PHD	A	PSYCHIATRY&BEHAV SCI	
	MD, PHD	A	NEUROLOGICAL SURGERY	
names	PHD	A	PEDIATRICS	
	MD	A	NEUROLOGY	
	PHD	A	ENVIRONMENTAL HEALTH	
	PHD	A	SPEECH AND HEARING SCIENCES	
	MD	A	PEDIATRICS & INF DIS	
	MD, PHD	A	NEUROLOGY	
	PHD	A	MEDICINE AND GENETICS	
	PHD	A	SOCIAL WORK	
	MD	A	PEDIATRICS	
	MD	A	PEDIATRICS	
	MD, PHD	A	PEDIATRIC NEUROLOGY	
	PHD	A	PSYCHIATRY AND BEHAV. SCIENCES	
	PHD	A	PSYCHOLOGY	
			CHDD	
	PHD	A	PSYCHOLOGY	
	PHD	A	PATHOBIOLOGY	SBRI, WA USA
	PHD	A	FAMILY AND CHILD NURSING	
	PHD	A	MEDICAL GENETICS	
	MD, PHD	A	RADIOLOGY	
	PHD	A	BIOL STRUCT	
	PHD, PT	A	REHABILITATION MEDICINE	
	PHD	A	PEDIATRICS	
	PHD	A	PHARMACEUTICS	
	PHD	A	HEALTH SERVICES	
	MD	A	PEDIATRICS	
	MD	A	ANESTHESIOLOGY	
	MD, PHD	A	PEDIATRICS	
	PHD	A	OPTHAMOLOGY	
⌟	PHD	A		CTR FOR NEURAL SCI NYU, NY US

PHD	A	SPEECH & HEARING SCIENCES	
MD, PHD	A	RADIOLOGY, BIOENGINEERING	
PHD	A	ZOOLOGY	
MD, PHD	A	LABORATORY MEDICINE	
MD	A	PEDIATRICS	
MD	A	NEUROLOGY	
PHD	A	PHARMACEUTICS	
PHD	A	PSYCHOLOGY	
BS	A	PSYCHOLOGY	
MD	A	RADIOLOGY	
MD	A	PATHOLOGY	
MD	A	PEDIATRICS	
MD	A	PEDIATRICS	
PHD	A	PSYCHOLOGY	
MD, PHD	A	RADIOLOGY	
PHD	A	PEDIATRICS	
PHD	A	NEUROLOGICAL SURGERY	
VMD	C	NPRC	
PHD	A	OTOLARYNGOLOGY	
	A	PEDIATRICS	
PHD	A	OTOLARYNGOLOGY	
PHD	A	SPEECH AND HEARING SCIENCES	
PHD	A	PEDIATRICS	
PHD	A	OPHTHALMOLOGY	
MD, PHD	A	PEDIATRICS	
PHD	A	OTOLARYNGOLOGY	
MD, PHD	A	NEUROLOGY	
MD, PHD	A	MEDICINE	
PHD	A		RUTGERS, NJ USA
PHD	A		US EPA, DC USA
PHD	A	RADIOLOGY	
PHD	A	PHYSIOLOGY AND BIOPHYSIOLOGY	
MD, PHD	A	PEDIATRICS	
PHD	C	PSYCHOLOGY	
PHD	A	MEDICINE	
MD	A	PEDIATRICS	
MD	A	PATHOLOGY/NEUROPATHOLOGY	
MD	A	OB/GYN	
PHD	A		NCTR, CA USA

names

	PHD	A	PSYCHIATRY AND BEHAV. SCIENCES
	PHD	A	FAMILY AND CHILD NURSING
	PHD	A	OTOLARYNGOLOGY
	MD	A	PEDIATRICS
	PHD	A	PSYCHIATRY AND BEHAV. SCIENCES
	PHD	A	PSYCHIATRY AND BEHAV. SCIENCES
	MD	A	RADIOLOGY
	MD, PHD	A	NEUROLOGY
	PHD	A	PSYCHOLOGY
	PHD	A	OTOLARYNGOLOGY
names	PHD	A	PHARMACEUTICS
	PHD	A	PSYCHIATRY AND BEHAV. SCIENCES
	PHD	A	FAMILY AND CHILD NURSING
	PHD	A	SPEECH AND HEARING SCIENCES
	PHD	A	FAMILY AND CHILD NURSING
	MD, PHD	A	NEUROLOGICAL SURGERY
	MD	A	IMMUNOLOGY
	MD	A	PEDIATRICS
	PHD	C	NPRC

AXIS I CODES: 1A, 21, 23, 25A, 25B **AXIS II CODES**36, 41, 44, 45, 60, 63C, 63E, 63G, 71, 77

ABSTRACT

The Infant Primate Research Laboratory (IPRL) is supported as a core facility of both the Center on Human Development and Disability (CHDD) and the Washington National Primate Research Center. For over 30 years, the overall objective of this Core has been to provide a range of services, equipment and supplies to CHDD Research Affiliates using nonhuman primates in research related to developmental disabilities. Over the years, the IPRL services have been especially valuable in research on the developmental consequences of premature birth and maternal/fetal exposure to environmental chemicals, drugs and viruses. The following broad range of services is provided to individual investigators:

(1) Consultation services regarding appropriate research designs, methods and data analysis techniques are provided to assist investigators who are unfamiliar with the unique characteristics of nonhuman primate research;

(2) Routine and specialized housing and care for animals are provided twenty four hours a day, seven days a week for studies conducted by affiliates to optimize animal survival and minimize morbidity;

(3) Specialized equipment, protocols and databases are provided to affiliates for assessing the development of physical growth as well as sensory, motor, social and cognitive development in nonhuman primates;

(4) Experienced laboratory personnel provide assistance, training and on-site supervision to the staff of Research Affiliates conducting research in the IPRL.

PREDICTING AND REDUCING SEVERE BEHAVIOR DISORDERS IN LABORATORY MONKEYS (0303)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
CROCKETT, CAROLYN M	PHD	C	NPRC	
L	BA	C	NPRC	
	PHD	C	NPRC	
names	PHD	A	PSYCHOLOGY	
	DVM	C	NPRC	
	PHD	C	PSYCHOLOGY	

AXIS I CODES: 1A, 15 **AXIS II CODES**36, 72, 85

ABSTRACT

The aim of this research is to increase the mental health and psychological well-being of laboratory primates through prediction, prevention, and cure of severe behavior disorders that negatively impact research and research subjects. We are identifying in laboratory macaques and baboons the behavioral, hormonal, environmental, and demographic factors associated with increased risk for developing serious behavior problems, especially self-injurious behavior (SIB) or high levels of stereotyped motor behavior. Investigation into the predictive factors, eliciting circumstances, and physiological correlates of SIB will be coupled with testing the effectiveness of behavioral modification and drug therapies in reducing SIB and other severe behavior disorders. We are developing a reliable method whereby primates in a colony can be screened for potential development of behavior problems. We are following a sample of macaques and baboons assigned to projects requiring long-term individual housing beginning in juvenility, a known risk factor for abnormal behavior. These monkeys will be studied to identify behavioral, hormonal, and research-related factors that predict which animals will and will not develop serious behavior problems. We are investigating whether monkeys with a history of SIB or extreme stereotypy are found to have sleep disturbance and a correlated disorder of POMC, a super hormone involved in the production of ACTH and beta endorphin. We are evaluating the usefulness of behavioral assessment measures and selected physiological measures to predict successful adaptation to tethering and neurosciences projects. Animal health and well-being will be improved, and data loss minimized, by better matching of subjects to projects for which they are suited and by initiating effective therapies and interventions before behavior problems emerge. The Washington National Primate Research Center's Psychological Well-being Program is incorporating knowledge gained from these studies to modify animal management and environmental enhancement plans, thereby improving nonhuman primate psychological well-being and overall health.

TISSUE DISTRIBUTION PROGRAM (0248)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
LIGGITT, H DENNY	DVM, PHD	C	COMPARATIVE MEDICINE	
	PHD	C	NPRC	
		A	PATHOLOGY	
	MD	A	HEMATOL/ONCOL	
	PHD	A	UROLOGY	U OF WASHINGTON, WA USA
		A		TRIAD TECHNOLOGY CENTER, MD USA
		A		LDS INC., MN USA
	MD	C	PSYCHIATRY&BEHAV SCI	
	PHD	C	MICROBIOLOGY	
	PHD	A	CELL GENETICS	CORIELL INSTITUTE FOR MEDICAL RESEARCH, NJ USA
	PHD	C	BIOLOGICAL STRUCTURE	
		A	DERMATOLOGY	U OF WISCONSIN, WI USA
	MD	A		NIH, MD USA
	PHD	A	VISION SCIENCE RESEARCH CENTER	U ALABAMA, AL USA
	PHD	A		PUGET SOUND BLOOD CENTER, W/ USA
	MD	C	MEDICINE; BIOCHEM, HHMI	
	MD	A	MEDICAL ONCOLOGY	
		A	DIABETES INSTITUTE OF IMMUNOLO	U OF MINNESOTA, MN USA
	PHD	C	NPRC	
	PHD	A	PHARMACEUTICS	
	MD	A	MEDICINE	
	PHD	A		SCIMEDX CORPORATION, NJ USA
		A		KALEIDOS PHARMA INC., WA USA
		A		PUGET SOUND BLOOD CENTER, W/ USA
	PHD	A	ANTHROPOLOGY	
	PHD	A	OPHTHALMOLOGY	
	PHD	A	PHYSIOL & BIOPHYS	
		A		BATTELLE TOXICOLOGY NORTHWEST, WA USA
		A		PUGET SOUND BLOOD CENTER, W/ USA
	PHD	A	BIOLOGICAL STRUCTURE	
	PHD	A	PATHOBIOLOGY	

names

L		A		PROCELL CORPORATION, MD USA
		A		MOLECULAR TOXICOLOGY INC, NC USA
		A		MEDICAL COLLEGE OF GEORGIA, GA USA
names		A	MEDICINE	UNIVERSITY OF PENNSYLVANIA, P USA
	MD, PHD	A	MEDICINE/ONCOLOGY	FRED HUTCHINSON CANCER RES CTR, WA USA
1	DVM, PHD	C	NPRC	

AXIS I CODES: 1D, 13, 14, 15, 16, 16A, 16C, 16D, 16E, 16F, 17, 18, 19, 20, 21, 22, 23, 24, 25, 25A, 25B, 26, 27

AXIS II CODES: 49, 50, 52, 58, 63G, 68, 77, 83, 86, 89

ABSTRACT

The Tissue Distribution was founded in order to achieve the widest possible benefit of our colony to advances in biomedical research. The program has supplied samples of non human primate tissues, organs, and cellular material to researchers, both nationally and internationally. Tissues are available from M. fascicularis, M. nemestrina, P. cynocephalus, and occasionally, M. mulatta. The program is coordinated by an onsite individual. Requests for tissues are sent to the coordinator who determines if the request is legitimate and feasible, and if the tissue can be obtained.

Affiliated scientists listed on this subproject were recipients of the Tissue Distribution Program during this reporting year.

TOPICAL MICROBICIDES FOR PREVENTION OF STDS/HIV INFECTION (0273)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.200% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
PATTON, DOROTHY L	PHD	A	OB-GYN	
[redacted]	PHD	A	OB-GYN	U PITTSBURGH, PA USA

AXIS I CODES: 1A, 2, 7A, 23, 28(RECTUM) **AXIS II CODES** 31, 64, 66, 83, 93, 94

ABSTRACT

Following validation of the nonhuman primate rectal model we have assessed the effects of multiple applications of rectally applied topical microbicide products on rectal flora and mucosal tissues. At each of 3 visits, a pre-application rectal wash, pH and a swab for rectal microbiology were collected. A rectal wash was collected before and 15 minutes after product application. On the fourth day, final wash, pH and microbiology samples were collected as 24 hour follow up.

Product safety is determined by close examination and characterization of rectal lavage samples, microbiological assessments, relying heavily on protection of H2O2 producing microorganisms, pH and histology.

RESEARCH SUBPROJECTS

CHRONIC ATYPICAL NEUROLEPTIC TREATMENT IN NORMALLY DEVELOPING MACACA NEMESTRINA (0278)

NPRC UNIT: COLONY HEALTH

%NPRC $: 1.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
SACKETT, GENE P	PHD	C	PSYCHOLOGY	
L names	PHD	A	PSYCHIATRY	U COLORADO, CO USA
	PHD	A	ANTHROPOLOGY	
_1	MD	A	PSYCHIATRY	SACRED HEART MEDICAL CENTER WA USA

AXIS I CODES: 1A, 3, 13, 15, 17, 19, 21, 24, 25B **AXIS II CODES** 36, 41, 50B, 60, 64, 72, 74B, 85
26

ABSTRACT

Atypical neuroleptic drugs are being used frequently in children and adolescents with severe psychopathology. The effects of these agents on normal growth and development are unknown. This 5-year project treats normally developing non-human primates (macaque nemestrina) with risperidone, quetiapine, or placebo from 13-20 months of age, followed by a 4 month post-drug period. 12 males will receive a low dose of risperidone or quetiapine for 4 months, then switched to a high dose for 4 months. 24 males will be assigned to the placebo condition. Animals are being tested before, during, and after drug or placebo treatment for (1) social, emotional, exploratory, learning and memory, motor skill, and perceptual behavior; and (2) physical assessments of health, somatic growth, bone mineralization, and hormonal function. The study design permits both between-group and within-individual comparisons to examine drug group differences as well as dose effects. Since m. nemestrina monkeys demonstrate psychological and somatic development comparable to humans, this project will identify aspects of human development that are likely to be affected by chronic treatment with these agents. 12-16 monkeys will be studied each year, with 16 currently being tested.

REPRODUCTIVE BIOLOGY PROGRAM (0288)

NPRC UNIT: PRIMATE RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
HAYES, ERIC	PHD	C	NPRC	
[illegible]		C	NPRC	

AXIS I CODES: 23 **AXIS II CODES:** 77

ABSTRACT

A constant barrier to the development of safe and effective human medicines is the limited application of information derived from non-primate mammalian test species to human beings. Several species of non-human primates represent valuable pre-clinical test species as a result of physiological and, more importantly, pathophysiological similarities to human beings. Despite these obvious benefits largely unknown differences in the genetic make-up of out-bred non-human primate test subjects of the same species often prevent an unambiguous understanding of the disease process under investigation and, its susceptibility to therapeutic intervention. Although studying out-bred populations more clearly reflects the human situation in large clinical efficacy trials, unknown genetic differences ensure that studies on small numbers of macaques are difficult to interpret. As a result, large numbers of test animals are needed to gain pathophysiological and therapeutic information. Therefore production of genetically identical individuals (twins) of clinically relevant non-human primate species would be expected to significantly enhance translational research in fields of biomedicine where a limitation in genetic variation is critical to an understanding of the disease process and its therapeutic sensitivity (e.g. gene therapy, tissue transplantation, vaccine development and developmental and behavioral disease/modeling). In addition, reduced numbers of identical animals will be required for a given project due to known genetic similarities in identical animal pairs, thus reducing the numbers of wild-caught out-bred macaques required each year for biomedical research.

IN VIVO EVALUATION OF PRIMATE LENTIVIRUSES II (0330)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.700% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ANDERSON, DAVID M	DVM	C	NPRC	
	PHD	C	PHARMACEUTICS	
	VMD	C	NPRC	

AXIS I CODES: 1A, 7B **AXIS II CODES**31, 64, 66, 83

ABSTRACT

To clarify the determinants of vaccine protection in an SIVmne/M. nemestrina model several clones of SIVmne have been produced. SIVmneClone 8 is an infectious and pathogenic molecular clone derived from the previously cocultivated single cell clone SIVmneE11S. SIVmne170 is an isolate from the late stage of in vivo infection of Clone 8. Two chimeras of these two viruses were constructed: 8/170, containing the 3' half of the viral genome of SIVmne170wks (vpr, tat, rev, env, nef), is low in replicative capacity and cytopathicity in vitro; 170/8, containing the 3' half of the viral genome of SIVmneClone 8, is highly replicative and cytopathic in vitro. This project was initiated to determine the in vivo infectivity and pathogenicity and the in vivo infection titers of challenge stocks of the two parent viruses and of the two chimeric viruses.

To determine the infectivity of the chimeric viruses one Macaca nemestrina was inoculated intravenously with each of the chimeras. Both animals became infected with high peak viremias (107-108), which declined to set-points between 105 and 106 copies/ml plasma. CD4+ T lymphocyte populations have declined to less than 200 cells/ul in both animals, but both remain clinically healthy 37 weeks after virus inoculation. Further studies are planned to determine the in vivo infection titers of both chimeric viruses.

To determine the in vivo titer of the two parent viruses, SIVmneClone 8 and SIVmne170, four M. nemestrina were inoculated intravenously with each virus, two with 10 TCID50 and two with 1 TCID50. All animals became infected. Peak viral loads ranged from 104 to 108 in the Clone 8-infected animals. Two eventually controlled their virus, one was euthanized at week 16 with severe weight loss, anemia, and diarrhea, and the fourth remains clinically healthy with increasing an increasing viral load. Three of the SIVmne170 animals developed peak viral loads 108 copies/ml plasma, but the viral load in the fourth animal was only 103. Two animals have been euthanized and two remain clinically healthy at 20 weeks post-inoculation. Additional animals will be inoculated with lower virus doses to determine the endpoint in vivo titer of both viruses.

EFFICACY OF AN SIV VACCINE PREPARED WITH DIFFERENT ADJUVANTS (0331)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.700% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ANDERSON, DAVID M	DVM	C	NPRC	
[redacted]	PHD	A		GLAXOSMITHKLINE, BELGIUM, BELGIUM

AXIS I CODES: 1A **AXIS II CODES:** 31, 64, 66, 83, 91

ABSTRACT

The animals were immunized with a vaccine composed of HIV proteins, gp120 and nef/tat, and SIV nef protein, administered along with a proprietory adjuvant. After 3 immunizations, the animals were challenged intravenously with SHIV89.6p in 1999. This experiment was transferred to the WaNPRC by the SVEU in 2001. SVEU support continues through the current year. Samples are collected from the surviving animals as requested by the home laboratory, and as needed for health monitoring.

EVALUATION OF SECONDARY CTL RESPONSE FOLLOWING CHALLENGE WITH SIV (0332)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.700% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ANDERSON, DAVID M	DVM	C	NPRC	
[redacted]	MD	A	DEPT. OF MEDICINE	HARVARD SCHOOL OF MEDICINE, MA USA

AXIS I CODES: 1A **AXIS II CODES:** 31, 64, 66, 83, 91

ABSTRACT

The animals were immunized with SIV gag vaccine in 1998, and challenged with SIVsmE660 in 1999. This experiment was transferred to the WaNPRC in 2001 by the SVEU. SVEU support continues through the current year. Samples are collected from these animals as directed by the home laboratory in Boston, MA, and as needed for health monitoring.

CORTICOTHALAMIC INPUT TO THE MOTOR THALAMUS (0334)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ANDERSON, MARJORIE E	PHD	A	PHYSIOL & BIOPHYS	
L rames	MD	G	P-BIO	
	MS	G	PHYSIOL & BIOPHYS	

AXIS I CODES: 1A, 20, 21 **AXIS II CODES:** 46, 92(MOVEMENT DISORDERS)

ABSTRACT

Little is known about the signals carried by corticothalamic neurons, especially those that project to the motor thalamus and provide the most numerous glutamatergic boutons to both cerebellar- and basal ganglia-receiving areas of the thalamus. These corticothalamic axons derive from cortical layers V and VI.

We have reported that motor cortical neurons driven antidromically at long latencies and high stimulus intensity by thalamic stimulation had almost no activity during any condition that we were able to test. With a change in stimulating electrodes that produce a briefer stimulus artifact, we now have identified corticothalamic cells that are driven antidromically at short latency by thalamic stimulation. These cells have tonic and directionally tuned movement-related activity similar to that usually described in studies of motor cortex. Thus, we have identified two classes of corticothalamic neurons, large ones with ongoing, task-related activity and one with almost no activity during the same task.

In humans with Parkinson's disease (PD) and in animal models of PD, thalamic neurons in basal ganglia-receiving regions have been reported to have oscillatory, and sometimes busting, patterns of discharge. We have examined the discharge patterns of neurons throughout the thalamus in one animal before and after administration of MPTP to make a PD model. Low threshold calcium bursts were almost never seen in the awake, normal animal, but were present in a restricted region of the thalamus after unilateral DA depletion when the animal was awake, but not working with his contralateral arm. He would work with the arm ipsilateral to recording, and in this case, very few bursts were seen. This has led us to hypothesize that the bursts are related to the animal's state of attention, and an animal is being trained in a tasked designed to vary the attention requirements of the task.

DEEP BRAIN STIMULATION IN PARKINSON MODELS (0335)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ANDERSON, MARJORIE E	PHD	A	PHYSIOL & BIOPHYS	
	BSE	C	NPRC	
	PHD	A	REHABILITATIVE MEDICINE	
	BS	A	REHABILITATIVE MEDICINE	
name	PHD	A	NUCLEAR MEDICINE	
		A		SHIN NIPPON SANGYO LTD., JAPA
	BS	A	REHABILITATIVE MEDICINE	
	MD, PHD	A	RADIOLOGY	
	MD	G	P-BIO	
		G	NEUROBIOLOGY	

AXIS I CODES: 1A, 20, 21 **AXIS II CODES:** 46, 92(MOVEMENT DISORDERS)

ABSTRACT

Continuous high frequency deep brain stimulation (DBS) in the internal globus pallidus (GPi) or the subthalamic nucleus (STN) has become standard treatment for L-DOPA resistant symptoms of advanced Parkinson's disease (PD). The mechanisms by which stimulation and lesions in GPi or STN both reduce symptoms remains to be determined.

We reported earlier that DBS using usually produced inhibition of target neurons in the thalamus of normal animals. This was contrary to the clinical prediction, based on reduction of PD symptoms with DBS or pallidotomy, but consistent with the expectation that activation of inhibitory GPi axons would be expected to inhibit thalamus.

Our current objectives are to test (1) the effect of longer duration stimulation, (2) the effect of DBS applied in the STN and (3) the effect on symptoms in monkeys made Parkinsonian.

To enable long-term study of the development of the PD model and to test toxicity of rotenone in primates, we have administered rotenone chronically to two monkeys. Others have reported that this produces a better PD model in some rat strains than the standard MPTP induced model. One young monkey was treated with rotenone for 17 months, but showed no classical signs of PD and no motor deficit retrieving food from a modified Kluver board. He also showed no significant reduction in striatal dopamine terminals, assessed using PET imagining of DTBZ, a marker of the DAT2 monoamine vescicular transporter. An older animal, which showed reduced DTBZ levels (75% of younger) before treatment has been treated with rotenone for 8 months and also has shown no PD symptoms or motor deficits.

Because rotenone does not produce a PK monkey within a workable time period, we will return to MPTP treatment to complete our studies of the effect of DBS in a PK model.

EFFICACY OF AN EXPERIMENTAL DRUG IN A PRIMATE SKIN ALLOGRAFT MODEL (0287)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
BRIGANDI, RICHARD A.	MD	A		GLAXOSMITHKLINE, PA USA
[illegible] names	DVM	C	NPRC	
[illegible]	PHD	A		GLAXOSMITHKLINE, PA USA

AXIS I CODES: 1A, 2, 18 **AXIS II CODES**50B, 64, 88

ABSTRACT

Chronic administration of immunosuppressive compounds has been the mainstay of therapy for prevention of tissue rejection following organ transplantation. Current therapies such as cyclosporin and tacrolimus are very effective, however they are also associated with medically significant side effects. The goal of this study is to discover novel agents that are effective selective immunosuppressants in a primate model of skin transplantation. Efficacy in this model is defined as prevention of skin graft rejection during the drug administration period. Once-daily drug treatment was begun 48 hours prior to skin transplantation and continued for 30 days post-transplantation as follows: 6 animals received experimental drug intravenously; 6 animals received cyclosporine, a currently accepted therapy, intramuscularly, as a positive control; 8 animals received no treatment as a negative control; and 4 animals received both experimental drug, IV, and cyclosporine, IM. A 1cm diameter skin allograft was transplanted to the upper back of all animals and assessed on a 4-point scale for condition and viability daily. Blood samples were drawn to monitor hematological and serum chemistry values every 5 days and to monitor immune function and drug concentration every 10 days. Drugs were maintained at a previously determined therapeutic level throughout the study. No significant side effects, including anemia, tremor and/or seizures, and hepatic or renal toxicity, were noted. Grafts on all animals failed during the 30-day drug administration period. However, animals that received either experimental drug or cyclosporine maintained viable grafts 2 days longer than untreated animals, and animals that received both experimental drug and cyclosporine maintained their grafts one week longer than those receiving either drug alone. Because of these encouraging results with a two-drug regimen, secondary allografts between 3 of the same pairs of animals were transplanted. The period of graft viability was shortened as would be expected, but treated animals maintained their grafts 2 days longer than the untreated animals.

METHANOL EFFECTS ON REPRODUCTION AND POSTNATAL DEVELOPMENT (0309)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
BURBACHER, THOMAS M	PHD	C	ENVIRONMENTAL HEALTH	
	PHD	A	ENVIRONMENTAL HEALTH	
	PHD	A	PHARMACEUTICS	

AXIS I CODES: 1A, 2, 21, 25B **AXIS II CODES:** 36, 41, 54A, 60, 71

ABSTRACT

Methanol is a known neurotoxicant that is being considered as an alternative motor fuel in the United States. The present study was designed to evaluate the reproductive and developmental consequences of prenatal methanol exposure in a closely related primate species (Macaca fascicularis). Offspring of methanol-exposed dams have been followed from birth on a battery of neurobehavioral measures designed to evaluate physical and cognitive growth as well as the development of social behavior. In 2003, we finished the visual contrast sensitivity testing of these animals. The results indicated that methanol was not associated with a loss in contrast vision during adulthood. After completing the functional assessments outlined in the grant, the decision was made to euthanize this cohort to evaluate the effects of in-utero methanol exposure on major organs and the central nervous system. A small grant was obtained from the Environmental Protection Agency to weigh and preserve the tissue for later analysis. The results from this study have provided the only data on the long-term effects of prenatal methanol exposure in primates and will assist in determining whether early exposure to methanol poses a public health risk to human infants and children.

DEVELOPMENTAL EFFECTS OF METHYLMERCURY (0310)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
BURBACHER, THOMAS M	PHD	C	ENVIRONMENTAL HEALTH	
	PHD	A	ENVIRONMENTAL HEALTH	
	PHD	A	PHARMACEUTICS	

AXIS I CODES: 1A, 2, 21, 25A, 25B, 25D **AXIS II CODES**30, 36, 41, 54A, 60, 71

ABSTRACT

Methylmercury is a prevalent environmental pollutant that is associated with adverse health effects, particularly when exposure occurs during fetal development or early childhood. To evaluate the neurobehavioral effects of prenatal mercury exposure, a study was initiated two decades ago using a closely related primate species (Macaca fascicularis). Adult female monkeys were exposed to environmentally relevant levels of methylmercury during pregnancy. Offspring from exposed dams have been closely followed from birth and treatment-related effects have been documented in early cognition, social behavior, and adolescent growth. The animals in this study, now approximately 21 years of age, are being evaluated on a series of tests to evaluate visual-spatial coordination, sensory functioning and memory. Measurements of weight and physical stature are routinely collected on all subjects and menstrual cyclicity is monitored in females. The results from this study will help define the consequences of early methylmercury exposure on physical and neurobehavioral processes across the lifespan. There is increasing evidence from human studies that early exposure to mercury may have a disruptive effect on the normal process of aging. The findings from this investigation will provide the only data on the long-term effects of prenatal methylmercury exposure in primates and will be used to evaluate the possibility that early neurotoxicant exposure may contribute to an acceleration in aging and possibly the onset of neurodegenerative disease.

THIMEROSAL IN VACCINE SAFETY STUDY (0311)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
BURBACHER, THOMAS M	PHD	C	ENVIRONMENTAL HEALTH	
	PHD	A	ENVIRONMENTAL HEALTH	
	PHD	A	PHARMACEUTICS	

AXIS I CODES: 1A, 2, 21 **AXIS II CODES**54A, 74

ABSTRACT

Recent public health concerns have arisen around the use of thimerosal; a preservative containing ethylmercury that is used in some infant vaccines. The purpose of this study was to compare the systemic disposition and brain distribution of total and inorganic mercury in newborn monkeys following thimerosal exposure with newborns exposed to methylmercury. Infant monkeys were exposed to thimerosal (via i.m. injection) or methylmercury (via oral gavage) at birth and at 1, 2, and 3 weeks of age. Blood mercury levels were determined 2, 4 and 7 days after each exposure. Brain mercury levels were assessed 2, 4, 7 or 28 days after the last (3 3-week) exposure. The results indicate that the half-life of mercury in blood following thimerosal exposure is significantly shorter than the half-life of mercury following MeHg exposure. There was minimal accumulation of total blood Hg during weekly thimerosal exposure while continual accumulation of blood Hg occurred during weekly oral doses of MeHg. Accumulation and elimination kinetics of blood mercury following methylmercury exposure conformed a one-compartment model, whereas the kinetics following thimerosal exposure was multiphasic describable by a two-compartment model. The respective initial and terminal half-life of mercury in blood following thimerosal exposure was 2.1 and 8.6 days, which are significantly shorter than the elimination half-life of mercury following MeHg exposure at 25 days. Brain concentrations of total mercury were also significantly lower by ~3-fold for the thimerosal -exposed neonates when compared to the MeHg group immediately following the last (3-week) exposure, while control brain mercury levels were undetectable. The average brain-to-blood concentration ratio over the 28-day washout period was comparable between the thimerosal and methylmercury group (5.1 sd=1.9 vs. 3.6 sd= 1.4). These data demonstrate that significant differences, mainly in systemic distribution and clearance, exist between the clearance of mercury from ethyl-thimerosal and methylmercury in young nonhuman primates.

MECHANISMS OF ARTERIAL GRAFT HEALING (0295)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
CLOWES, ALEXANDER W	MD	A	SURGERY	
[names	MD	A	SURGERY	
	MD	A	BIOCHEMISTRY	
]	PHD	A	PATHOLOGY	

AXIS I CODES: 1A, 1D, 3, 13 **AXIS II CODES:** 48, 86

ABSTRACT

During the last year, we have continued our studies of intimal thickening and regression in baboon PTFE grafts and injured arteries. We have completed a very large gene array experiment of graft intima subjected to high blood flow, the condition under which intima is induced to atrophy. The purpose of this experiment is to define molecular mechanisms that might regulate the atrophy process. A number of genes have been identified. We have chosen to focus on bone morphogenetic protein-4 (BMP-4). [name] doctoral student in the lab, has been able to show that BMP-4 is expressed by the graft endothelium in response to high blood flow; it inhibits vascular smooth muscle cell (SMC) proliferation in vitro, and under some circumstances it induces SMC death. During the next grant cycle, we will attempt through "gain of function" and "loss of function" experiments to discover whether it is the atrophy-inducing gene we have been searching for.

We have completed a series of studies on platelet-derived growth factor (PDGF) and its cognate receptors. In summary, although blockade of PDGFR-Beta with a specific antibody inhibits intimal hyperplasia in baboons, it failed to do so in a human trial of patients undergoing coronary stent angioplasty. This result struck us as odd, because of the wealth of data supporting a vital role for the PDGF receptors in vascular embryogenesis, development, and response to injury. We have therefore repeated our experiments in baboons (performed by [names]) and have shown that blockade with antibodies to both PDGFR-alpha and PDGFR-beta not only suppress intimal thickening but actually induce intimal atrophy. We plan to test a PDGFR kinase inhibitor as a general approach to blocking both receptors with a small molecule antagonist, one that has already been shown to be safe in humans.

DEVELOPMENT OF FEMTOSECOND SCANNING-LASER MICROSCOPY TO MEASURE LIGHT-EVOKED DEN (0290)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
DACEY, DENNIS M	PHD	C	BIOLOGICAL STRUCTURE	
[illegible]		A	NEUROBIOLOGY AND BEHAVIOR	
[illegible]	PHD	A	PHYSIOLOGY AND BIOPHYSICS	
[illegible]	DDS	C	NPRC	

AXIS I CODES: 1D, 25B **AXIS II CODES:** 63B, 63I, 74B

ABSTRACT

The goal of this project is determine how the receptive field surround is established at the level of the ganglion cell and how the surround contributes to color-coding by identifying the cone inputs to the surround. The presynaptic hypothesis predicts that the creation of the cone bipolar center-surround organization is the critical locus for cone opponency. We showed for the first time in a mammalian retina that cone bipolar cells have robust center-surround organization comparable to their ganglion cell counterparts (Dacey et al, 2000). With postdoc [name] we then undertook a series of experiments to attempt to selectively block ganglion cell surrounds. We found, in parasol cells, that either cobalt or the gap-junction blocker, carbenoxolone, selectively reduced surround antagonism ([name] et al, 2003). We are now using these drugs to assess the receptive field surround contribution to color-opponency in a number of ganglion cell classes. In a second series of experiments with post-docs [name] and [name] we developed a new stimulus protocol to measure the strength and sign of L, M and S-cone inputs to the receptive field surrounds of midget and parasol ganglion cell types. The specific goal was to assess how cone signal weighting may be altered during transmission from outer to inner retinal circuitry. We showed that there were no gain changes from the horizontal-bipolar cell level to the ganglion cell surround and concluded that cone type-specific changes in synaptic gain are not a likely mechanism for generating color-opponent signals.

PHYSIOLOGY OF MACAQUE HORIZONTAL CELLS AND THEIR ROLE IN SPATIAL AND COLOR VISIO (0291)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
DACEY, DENNIS M	PHD	C	BIOLOGICAL STRUCTURE	
L	PHD	A	OPTOMETRY	STATE UNIVERSITY OF NEW YORK-NYC, NY USA
	PHD	G	BIOSTRUCTURE	
names	PHD	A	BIOLOGICAL STRUCTURE	
		C	BIOLOGICAL STRUCTURE	
	PHD	A	VISUAL SCIENCE LABORATORIES	U CHICAGO, IL USA
4	PHD	A	VISUAL SCIENCE LABORATORIES	U CHICAGO, IL USA

AXIS I CODES: 1D, 25B **AXIS II CODES:** 74

ABSTRACT

The goal of this project is to determine the role that the cell types of the outer retina play in light adaptation, color-coding and receptive field structure. Over the last year the project has focused on the role of the H1 horizontal cell—a key interneuron—by characterizing sensitivity regulation, receptive field structure and cone input. First, we have made significant progress in understanding how the spatial receptive field of the H1 horizontal cell contributes to the surrounds of inner retinal neurons. The primate H1 horizontal cells are coupled to each other electrically by gap junctions and access the cone-bipolar-ganglion cell pathway by feedback at the cone-H1 synapse. We have determined how direct synaptic input and coupled input interact to form a receptive field and have measured the relative contributions of these components using pharmacology and neural simulations. In the fovea, coupling is reduced and the receptive field size of H1 cells shrinks to create a surround derived from only a handful of cones. These results suggest strongly that this pathway is a critical component of the foveal 'midget' red-green color-opponent pathway. Finally, as part of an ongoing study of sensitivity regulation in the outer retina we have characterized how H1 and H2 horizontal cells contribute to retinal light adaptation by measuring the way in which signals from L, M and S cones are desensitized over the photopic range of light adaptation. From these results we have concluded that the first retinal synapse between H1 cells and photoreceptors is a major site for sensitivity regulation in outer retina.

CIRCUITRY OF THE MIDGET AND PARASOL RECEPTIVE FIELD (0292)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
DACEY, DENNIS M	PHD	C	BIOLOGICAL STRUCTURE	
	PHD	G	BIOSTRUCTURE	
	PHD	A	BIOLOGICAL STRUCTURE	
names		C	BIOLOGICAL STRUCTURE	
	PHD	A	ANATOMY	U ROCHESTER, NY USA

AXIS I CODES: 1A **AXIS II CODES:** 74

ABSTRACT

The goal of this project is determine how the receptive field surround is established at the level of the ganglion cell and how the surround contributes to color-coding by identifying the cone inputs to the surround. The presynaptic hypothesis predicts that the creation of the cone bipolar center-surround organization is the critical locus for cone opponency. We showed for the first time in a mammalian retina that cone bipolar cells have robust center-surround organization comparable to their ganglion cell counterparts (Dacey et al, 2000). With postdoc [name] we then undertook a series of experiments to attempt to selectively block ganglion cell surrounds. We found, in parasol cells, that either cobalt or the gap-junction blocker, carbenoxolone, selectively reduced surround antagonism ([name] et al, 2003). We are now using these drugs to assess the receptive field surround contribution to color-opponency in a number of ganglion cell classes. In a second series of experiments with post-docs [names] we developed a new stimulus protocol to measure the strength and sign of L, M and S-cone inputs to the receptive field surrounds of midget and parasol ganglion cell types. The specific goal was to assess how cone signal weighting may be altered during transmission from outer to inner retinal circuitry. We showed that there were no gain changes from the horizontal-bipolar cell level to the ganglion cell surround and concluded that cone type-specific changes in synaptic gain are not a likely mechanism for generating color-opponent signals.

ANATOMY AND PHYSIOLOGY OF NOVEL GANGLION CELL TYPES IN MACAQUE RETINA (0293)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
DACEY, DENNIS M	PHD	C	BIOLOGICAL STRUCTURE	
	PHD	A	VISION SCIENCE RESEARCH CENTER	U ALABAMA, AL USA
	PHD	A	OPTOMETRY	STATE UNIVERSITY OF NEW YORK-NYC, NY USA
		C	BIOLOGICAL STRUCTURE	
	PHD	A	VISUAL SCIENCE LABORATORIES	U CHICAGO, IL USA
	PHD	A	BIOLOGICAL STRUCTURE	
	PHD	A	VISUAL SCIENCE LABORATORIES	U CHICAGO, IL USA

AXIS I CODES: 1A **AXIS II CODES:** 74

ABSTRACT

The goal of this project is to determine the morphology and physiology and central connections of ganglion cell types using a new retrograde tracing method that we have called 'retrograde photodynamics'. Over the last two years we used rhodamine-dextrans to retrogradely label macaque ganglion cells from tracer injections in the major retinal targets: the superior colliculus, pretectum, and LGN. As expected after retrograde transport, the tracer was sequestered into organelle-like structures within ganglion cell bodies and proximal dendrites. This particulate labeling alone did not allow unambiguous targeting of specific cell types in vitro. We discovered however that when labeled cells were observed microscopically under epifluorescent illumination, the fluorescing organelles appeared to burst—creating a fireworks-like display in the cytoplasm—and the liberated fluorophore rapidly diffused throughout the dendritic tree. At the same time, a large increase in fluorescence intensity within the cytoplasm gave rise to a bright and complete intracellular dye stain. Photostained cells remained anatomically and physiologically viable; we could therefore target morphologically distinct types in vitro for intracellular recording and analysis of receptive field properties. Further, by employing the biotinylated form of rhodamine dextran, it was possible to use horseradish peroxidase (HRP) histochemistry after tissue fixation to permanently recover the detailed morphology of large numbers of cells for anatomical analysis. This method enabled us to rapidly characterize several new ganglion cell populations that project in the primary visual pathway to the LGN (Dacey et al., 2003). Some of these cell groups show novel color-opponent properties and will be a continuing focus of new research projects. One of these groups, the giant monostratified cells, are uniquely photosensitive and form the basis for another project in the lab.

PHYSIOLOGY, ANATOMY AND CENTRAL CONNECTIONS OF THE PHOTORECEPTIVE GANGLION CELL (0294)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
DACEY, DENNIS M	PHD	C	BIOLOGICAL STRUCTURE	
[illegible]	PHD	A	VISION SCIENCE RESEARCH CENTER	U ALABAMA, AL USA
		A	NEUROSCIENCE AND MEDICINE	JOHN HOPKINS SCHOOL OF MEDICINE, MD USA
	PHD	A	NEUROBIOLOGY AND ANATOMY	UNIVERSITY OF TX MEDICAL CTR, TX USA
names		C	BIOLOGICAL STRUCTURE	
	PHD	A	VISUAL SCIENCE LABORATORIES	U CHICAGO, IL USA
	PHD	A	BIOLOGICAL STRUCTURE	
	PHD	A	VISUAL SCIENCE LABORATORIES	U CHICAGO, IL USA
[illegible]	PHD	A	NEUROSCIENCE OPTHAMOLOGY HHMI	JOHN HOPKINS SCHOOL OF MEDICINE, MD USA

AXIS I CODES: 1A **AXIS II CODES:** 74

ABSTRACT

The goal is to characterize a unique ganglion cell population that contains a novel photopigment and is intrinsically photosensitive; these ganglion cells play a key role in entraining human circadian rhythms, driving the pupillary light reflex and may also participate in color perception. This project marks the first steps in the analysis of novel visual pathway and photopigment, not previously recognized in the primate visual system. We have started a collaborative project with [name] employing a human antibody to the putative photopigment melanopsin, and have now determined the detailed morphology and spatial distribution of these ganglion cells in both macaque and human retina. Using retrograde photodynamics we have begun to define the central targets of these cells, showing that these cells project widely to both the superior colliculus and lateral geniculate nucleus as well as the pretectal olivary nucleus. We have targeted these cells in vitro for detailed physiological analysis and have characterized cone inputs, rod inputs and the spectral tuning and dynamics of the intrinsic light response. Intracellular recordings show that both the intrinsic and cone-mediated signals converge to confer unique luminance coding and chromatic properties to this ganglion cell ([names] ., 2003; Dacey et al., 2003).

SINGLE-CYCLE SIV AS A NON-REPLICATING VACCINE STRAIN (0308)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.700% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
EVANS, DAVID T.	PHD	C	NPRC, PATHOBIOLOGY	

AXIS I CODES: 1, 7 **AXIS II CODES:** 31

ABSTRACT

Current AIDS vaccine approaches based on live-attenuated viruses or non-persisting recombinant vectors have drawbacks in terms of safety and efficacy that will likely prevent their widespread use in humans for the foreseeable future. One strategy that has not yet been explored in the use of lentiviruses that are limited to a single cycle of infection. A lentivirus that is limited to a single cycle of integration and protein expression should stimulate a broad spectrum of virus-specific antibody and cellular immune responses, but should not be capable of causing AIDS in immunized individuals. To test this hypothesis, we have developed a novel system for producing single-cycle SIV that minimizes that chances of generating replication-competent virus through recombination or nucleotide reversion. In the first specific aim, we will compare the strength and stability of virus-specific immune responses elicited by intravenous inoculation of macaques with T cell-tropic versus macrophage-tropic single-cycle SIV. In the second specific aim, we will determine whether the selective elimination of N-linked glycosylation sites in gp120 can enhance neutralizing antibody responses elicited by single-cycle SIV. In the third specific aim, we will determine whether repeated vaginal exposure to single-cycle SIV can induce mucosal antibody and cellular immune responses. Macaques immunized with single-cycle viruses will be challenged with wild-type SIV by mucosal routes to assess protection.

CONTROL OF VOLUNTARY LIMB MOVEMENT BY CEREBELLAR NEURONS (0312)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
FETZ, EBERHARD E	PHD	C	PHYSIOL & BIOPHYS	
[illegible]	PHD	G	PHYSIOL & BIOPHYS	

AXIS I CODES: 1A **AXIS II CODES**92(MOTOR CONTROL)

ABSTRACT

In awake primates, coherent periodic activities in the 20-35Hz range (beta oscillations) can appear in primary motor cortex (M1) and muscles, both of which are reciprocally connected with the cerebellar nuclei (CN). To examine the role of cerebellum in these phenomena, we sought and found oscillatory activity in CN in pigtail monkeys performing wrist flexion/extension and forelimb reach-and-grasp movements. Single-pulse microstimuli delivered in CN evoked 2-3 cycles of beta oscillations in stimulus-triggered averages of motor cortex local field potentials (LFP) and of rectified EMG. Periodic responses were more prominent during holding than dynamic movements and were more commonly evoked by stimulation in interpositus than dentate. CN stimuli evoked oscillations across widespread areas of motor cortex and in multiple muscles. These results indicate that interpositus is an important component of the neural circuitry supporting oscillatory activity throughout the motor system.

We propose that the appearance and coherence of beta oscillations at different motor system sites is determined by activity propagating recurrently around a closed neural loop comprising these sites. This mechanism would further suggest that these oscillations could be self-reinforcing due to Hebbian enhancement of transmission across synapses connecting different components of the loop. We looked for evidence of synaptic plasticity between CN, M1 and muscles following paired microstimulation of CN and M1 in a behaving monkey. In a conditioning-test paradigm we delivered test stimuli in CN before and after trains of CN-M1 paired conditioning stimuli. M1 beta oscillations evoked by the test CN stimuli usually underwent a stable and long-term increase in strength following CN-M1 paired conditioning stimuli delivered at beta frequencies. These data are consistent with our proposal that activity propagating recurrently around a closed neural loop supports motor system beta oscillations and show that the oscillations can be potentiated following appropriately timed microstimulation in different motor system nuclei. These observations support a possible role for recurrent loops and beta oscillations in cerebellar motor learning.

CONTROL OF MULTIDIRECTIONAL WRIST MOVEMENTS BY SPINAL CORD INTERNEURONS (0313)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
FETZ, EBERHARD E	PHD	C	PHYSIOL & BIOPHYS	
L names	PHD	A	PHYSIOL & BIOPHYS	
1	PHD	G	PHYSOLOGY AND BIOLOGY	

AXIS I CODES: 1A **AXIS II CODES** 92(MOTOR CONTROL)

ABSTRACT

The neural mechanisms that control voluntary limb movements operate to coordinate the activity of many muscles in patterns appropriate for different movements. To investigate the role of spinal interneurons in generating a repertoire of wrist movements involving different muscle synergies, we trained monkeys to perform two-dimensional visually guided wrist movements [flexion-extension and radial-ulnar deviation] and forearm pronation-supination, as well as a power grip [involving co-contraction of forearm flexor and extensor muscles]. These different movement parameters were simultaneously represented by the position, orientation and size of a rectangular cursor, which the monkey controlled in tracking a comparably coded rectangular target. Once trained the monkeys could perform arbitrary combinations of these basic movements. We recorded activity of cervical spinal cord interneurons and multiple forearm muscles during performance of a complete set of basic movements. Interneurons showed a wider range of tuning characteristics than cortical neurons and were more broadly tuned than forearm muscles. Preferred directions were distributed throughout the flexion-extension/radial-ulnar plane, but many interneurons were also, or primarily, modulated during pronation-supination torques and/or grip. Almost all interneurons were active in the absence of wrist EMG (baseline), and most were not inhibited below baseline for directions opposite their preferred direction (indeed, many showed increased firing for non-preferred torques). These data indicate that spinal pathways exhibit some specificity for behaviors that recruit agonist-antagonist or co-contraction patterns of EMG, rather than specific muscles. Functional linkages to forearm muscles were identified with spike-triggered averages of EMG, providing the first direct comparison between tuning of premotor [PreM] cells and their target muscles. The tuning of excitatory PreM INs that produced post-spike facilitation of target muscles overlapped the tuning of their target muscles, while INs with inhibitory linkages fired in directions opposite and congruent with the preferred direction of their inhibited targets. Thus, these response properties of spinal INs suggest that the excitability of motoneurons is regulated by adjusting the balance of simultaneously converging excitatory and inhibitory synaptic inputs.

ROLE OF SPINAL CORD INTERNEURONS IN PREPARATION FOR VOLUNTARY LIMB MOVEMENT (0314)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
FETZ, EBERHARD E	PHD	C	PHYSIOL & BIOPHYS	
	PHD	A	PHYSIOL & BIOPHYS	
	PHD	A	PHYSIOL & BIOPHYS	
	PHD	A	PHYSIOL & BIOPHYS	

AXIS I CODES: 1A **AXIS II CODES**92(MOTOR CONTROL)

ABSTRACT

Spinal neurons play a crucial role in generating voluntary limb movements, but little is known about their activity during normal movements, since they have been studied primarily in anesthetized animals. We evaluated the extent to which spinal interneurons (INs) are engaged in preparation for voluntary movement by documenting their responses in monkeys performing an instructed delay task. Macaques controlled position of a cursor by making flexion-extension movements about the wrist against an elastic load. Transient visual (V) or proprioceptive (P) cues instructed the monkey of the direction and amplitude of the next required movement, to be made after a "GO" signal that occurred 1-3 seconds later. Activity of many INs in the cervical segments showed significant modulation of rate during the delay period (SDM). Some INs showed different SDM for V and P trials, while others had the same SDM, independently of cue modality. These results suggest that segmental INs are involved in movement preparation just like many cerebral cortex neurons previously documented by others.

In other experiments the modulation of cutaneous input to first-order relay INs was documented as a function of periods of an instructed delay task. Monosynaptic responses evoked by stimulating the superficial radial nerve were reduced during active movement relative to rest, while neural activity increased. The excitability of afferent fibers was reduced during this period, indicating the presence of primary afferent depolarization. These observations indicate that presynaptic inhibition reduced the inputs to the spinal cord during active movement. No comparable reduction was observed during the delay period or during passive movements. One function of this inhibition is to prevent re-afferent activity from interfering with the accurate control of movements by descending commands. Moreover, during active movement we also found a reduction of the cutaneous cortical evoked potentials, which helps to explain why active movements are associated with increased perceptual thresholds.

IMPLANTABLE BRAIN-COMPUTER INTERFACE FOR PRIMATES (0315)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
FETZ, EBERHARD E	PHD	C	PHYSIOL & BIOPHYS	
L manuel	PHD	G	PHYSIOLOGY AND BIOLOGY	

AXIS I CODES: 1A, 21 **AXIS II CODES**92(MOTOR CONTROL)

ABSTRACT

In mammals the motor cortex plays a crucial role in controlling limb movements. After losing connections between motor cortex and muscles (as in spinal cord injury or lesions of the corticospinal tract) primates lose their ability to voluntarily activate limb muscles, although cortex and muscles may remain functional. To test whether this gap can be bridged with an artificial connection, we are developing an implantable "brain-computer interface" for primates, consisting of [1] microelectrode arrays to record activity of motor cortex cells, [2] a miniature programmable computer chip to detect cell activity and generate pulses for stimulation, and [3] a circuit board for delivering appropriate stimulus pulses to physiological sites generating movements. We would investigate three sites for evoking forelimb movements: motor cortex, spinal cord and peripheral arm muscles. Although the recorded cell activity would initially evoke inappropriate movements, the flexibility in control of cortical cell activity that has been demonstrated previously in biofeedback experiments should allow the monkey to adapt to the artificially introduced connection and incorporate it into volitional behavior. This adaptation will be documented by testing changes in cell and muscle activity while the monkey performs a step-tracking task. Development of a successful implantable BCI circuit would have significant clinical applications for treating certain forms of paralysis and would also provide a new research tool for investigating long-term brain-computer interactions.

ROLE OF THE BRAINSTEM IN VOLUNTARY GAZE SHIFTS (0269)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
FUCHS, ALBERT F	PHD	C	PHYSIOL & BIOPHYS	
	PHD	A	PHYSIOL & BIOPHYS	
	PHD	A		SHEFFIELD UNIVERSITY, UK
names	PHD	A	PHYSIOLOGY	INST. BASIC MED SCIENCES, JAPA
	PHD	G	NPRC	
	PHD	G	PHYSIOL & BIOPHYS	
1	PHD	A	OTOLARYNGOLOGY	

AXIS I CODES: 1A **AXIS II CODES**92(NEUROSCIENCE)

ABSTRACT

The rapid saccadic eye movement is generated by a burst of action potentials that are fashioned by a group of neurons in the pontine reticular formation of the brainstem. There are several unresolved issues concerning the functioning of this brainstem burst generator. One is whether the discharge of eye movement motoneurons compensates for non-linearities in the eye muscles when they are stretched or contracted to extremes during very eccentric eye positions. In our current experiments on the head-fixed monkey, we are finding that the burst of spikes in some motoneurons does increase when the same size saccade starts in more eccentric locations. A second issue concerns how neurons in the burst generator and their target motoneurons behave when the head also is free to move. We have found that for neurons in the burst generator, the number of spikes in the burst is better correlated with gaze amplitude (eye movement in the head plus head movement in space), suggesting that the burst generator encodes the overall gaze shift rather than the saccadic eye movement component alone. When we recorded from the motoneurons that control eye movements directly, we were surprised to find their number of spikes also was better correlated with gaze than eye amplitude. These latter data suggest that neurons in the burst generator do not encode gaze amplitude after all but rather reflect the unusual drive required by the motoneurons themselves. Finally, we have been examining the input to the burst generator from the cortical frontal eye fields (FEF). During head-free gaze shifts, several FEF neurons discharge with head movement per se and electrical stimulation delivered to many sites evokes predominantly head movements. These data suggest a heretofore-unrevealed role for the FEF in the generation of the head component of a gaze shift.

NEURAL BASIS OF SACCADIC LEARNING (0270)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
FUCHS, ALBERT F	PHD	C	PHYSIOL & BIOPHYS	
	PHD	A	PHYSIOL & BIOPHYS	
	BS	G	PHYSIOLOGY AND BIOLOGY	
names	PHD	A	PHYSIOLOGY	INST. BASIC MED SCIENCES, JAPA
	PHD	A	PHYSIOL & BIOPHYS	
	PHD	A	OPTHAMOLOGY	UNIVERSITY OF TEXAS-GALVESTON, TX USA
	PHD	A	BIOLOGICAL STRUCTURE	
	PHD	G	BIOENGINEERING	
	MD	G	PHYSIOLOGY/BIOLOGY	

AXIS I CODES: 1A **AXIS II CODES**92(NEUROSCIENCE)

ABSTRACT

This project concerns the neuronal mechanisms that underlie motor learning. We use an experimental paradigm whereby we deceive primates, both human and non-human, into thinking that their saccadic eye movements have become inaccurate. When faced with such persistent errors, primates adapt their dysmetric saccades so they eventually land on target. We have been investigating the site of this motor learning in three sets of experiments. First, in humans, we have adapted a lower level saccade, e.g., an express saccade, which has no time for higher processing, and asked whether the adaptation transfers to a saccade that requires higher level processing, e.g., a saccade guided by a remembered target location. These experiments have shown that adaptation is distributed at different sites in the saccadic system. Second, the cerebellum has been implicated in the motor learning of reflex behaviors. We tested its involvement in the motor learning of a voluntary behavior be recording activity from one of its cells, the Purkinje cell, while a monkey was undergoing saccadic adaptation. When an error existed between eye and target position, there was an increase in the probability of occurrence of complex spikes. The incidence of complex spike occurrence decreased as adaptation progressed and reduced the error. These data suggest that the occurrence of complex spike discharge signals the oculomotor cerebellum that there still is an error that adaptation must correct. Finally, the oculomotor cerebellum receives a prominent input from a pontine nucleus, NRTP. We recorded the activity of its cells during saccadic adaptation and were surprised to find that their firing rates increased substantially after adaptation for saccades of the same size. These data suggest that the site of adaptation of targeting saccades in the monkey is upstream of NRTP, possibly in the superior colliculus, its major source of input.

ADOPTIVE TRANSFER OF AUTOLOGOUS SHIV-SPECIFIC CD+-T CELLS (0283)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.000% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
GREENBERG, PHILIP D	MD	A	MEDICAL ONCOLOGY	
	MD	A	CENTER FOR AIDS AND STD	HARBORVIEW MEDICAL CENTER, WA USA
	BS	C	NPRC	
	VMD	C	NPRC	
	PHD	A	IMMUNOLOGY	

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

ABSTRACT

Despite strong efforts for many years, a safe and efficacious vaccine against HIV is still far from reality. There is strong data showing a role for cytotoxic T cells (CTL) in controlling HIV and SIV infection, while data pointing at a role for CTL in preventing infection are more suggestive. The long-term goal of this project focuses on a critical analysis of the role of CTL in protection of monkeys from infection by SHIV virus by testing the hypothesis "CD8+ T cells alone can prevent SHIV-infection in Macaca nemestrina".

As a pilot experiment, investigating the effector function of CTL during a SHIV infection, we are in the current protocol generating and expanding CTL in vitro from 2 animals that have already been infected with SHIV. The cells will be transferred back to the autologous hosts and we will monitor for toxicity, survival of the T cells, and viral load. Clones have now been expanded and are being characterized for phenotype and function prior to subsequent infusion into the infected autologous host.

KINETICS OF MOTHER TO FETUS HIV-2 TRANSMISSION (0305)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.700% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
HO, RODNEY J Y	PHD	A	PHARMACEUTICS	
names	VMD	C	NPRC	
	PHD	A	PHARMACEUTICS	

AXIS I CODES: 1A, 2, 9, 17, 23 **AXIS II CODES:** 31, 50B, 64, 66, 74F, 83, 86, 91, 94

ABSTRACT

Our long-term goal is to design an effective and safe antigen carrier for human administration. Target selective delivery of antigen and immune enhancers using carriers has been shown to provide optimum HIV and HSV immune stimulation and to increase the margins of safety in small animal models. Recently, the highly pathogenic HIV-2 strain 287 has been shown to produce rapid onset of disease in macaques (M. nemestrina) similar to human AIDS. We are utilizing this macaque model to determine whether the enhanced immune responses provided by antigen presenting carriers will produce clinically measurable outcomes in both virus-infected and uninfected animals. Both of these goals will be accomplished by evaluating the effects of immunizing young macaques that are either healthy or infected with HIV-2287. This virulent strain produces viremia as well as rapid onset and progression of disease. In both uninfected and infected animals, we are determining (1) whether immunization with HIV antigen presented in antigen carriers provides potent antibody and cell-mediated immune responses; determining (2) whether these enhanced or additional immune responses due to immunization translate into clinically measurable outcomes; and (3) characterizing the key parameters that lead to positive clinical outcomes.

CNS DRUG DELIVERY TARGETING THE HIV SANCTUARY (0306)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.700% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
HO, RODNEY J Y	PHD	A	PHARMACEUTICS	
		A	PHARMACEUTICAL SCIENCES	UNIVERSITY OF KENTUCKY, KY USA
	BS	A	NPRC	
	PHD	A	PHARMACEUTICS	
	PHD	C	NPRC	

AXIS I CODES: 1A, 17, 19 **AXIS II CODES:** 31, 36, 50B, 64, 66, 83

ABSTRACT

Due to the likely inability of currently approved drugs to attain sufficient concentrations in the central nervous system (CNS) to completely suppress viral replication over a sustained period of time, concern is growing that the brain may serve as an HIV sanctuary. Adults with advanced HIV disease may suffer a persistent and disabling loss of cognitive and motor function referred to as AIDS dementia complex. HIV induced CNS dysfunction occurs with especially high frequency in HIV infected children, with 88% exhibiting CNS abnormalities. Our long-term goal is to improve CNS delivery of anti-HIV drugs used in combination therapy and to assess the value of such improvements in targeting the reservoirs of replicating HIV in the brain in an infant macaque model of neuro-AIDS. Our initial aim is to test the hypothesis that strategies to improve the CNS delivery of ddi and indinavir when used in combination will in fact reduce HIV viral load in the CNS, reduce CNS damage, and lessen the likelihood that the CNS will serve as a sanctuary for HIV. After inoculating infant macaques with a neurovirulent strain of HIV(HIV287), we have made significant progress towards identifying a viral dose and route that will produce a high incidence of virus replication in the CNS and developmental abnormalities which can be used for therapeutic evaluation.

IMMUNOGENICITY OF ENV AND/OR CORE ANTIGENS OF HIV-1 (0318)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.000% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
HU, SHIU-LOK	PHD	C	PHARMACEUTICS	
	DVM	C	NPRC	
names	PHD	C	NPRC	
	VMD	C	NPRC	
	PHD	C	PHARMACEUTICS	

AXIS I CODES: 1A, 7B **AXIS II CODES** 31, 39, 64, 66

ABSTRACT

The goal of this study is to determine whether animals that were previously immunized with recombinant HIV-1 IIIB vaccines and were protected against SHIV HXBc2 challenge would be protected against a rechallenge with highly pathogenic viruses, SHIVKU-1 or SHIV89.6P. Animals were boosted once and rechallenged two weeks later. Naïve (non-immunized) control animals all show rapid CD4 cell decline within 4 weeks after infection. Of the 5 immunized animals challenged with SHIVKU-1, two animals showed significant reduction (2-3 log10) of plasma viremia within 2-4 month after infection and 3 animals showed CD4 rebound during the same time. Of the 6 immunized animals challenged with SHIV89.6P, only one animal showed significant reduction of plasma viremia after 4 months. No significant difference in CD4 cell level was observed between the control and the immunized groups challenged with SHIV89.6P. These results indicate that partial protection (reduction of viral load and CD4 cell recovery) against a highly pathogenic virus can be achieved by immunization with recombinant vaccines. However, the degree of protection may depend on the nature of the challenge virus, or the relatedness of the vaccine strain and the challenge virus. Aside from ongoing studies on archived specimens to determine possible immune correlates of protection, this project was terminated during the current year. One animal succumbed to AIDS during the study and 19 were euthanatized. Of the latter animals, 9 were found to have AIDS-defining pathology at necropsy. No animal is currently assigned to this project.

DETERMINANTS OF VACCINE PROTECTION IN AN SIV MODEL (0319)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.700% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
HU, SHIU-LOK	PHD	C	PHARMACEUTICS	
	DVM	C	NPRC	
	PHD	C	NPRC	
	PHD	C	PHARMACEUTICS	
	PHD	A	PHARMACEUTICS	
	PHD	A		SBRI, WA USA

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

ABSTRACT

The overall objective of this project is to examine determinants of vaccine protection against primate lentiviruses. Based on observations we made in a moderately pathogenic SIV model, we hypothesize that vaccine protection results from a dynamic interaction between host responses to prevent and control the virus infection on one hand, and the ability of the virus to escape such controls on the other. Viruses that have evolved to evade such responses, to replicate efficiently and to destroy the host defense system, are more likely to overcome vaccine-induced immunity. The ability of a virus to overcome vaccine protection, therefore, may not depend solely on its genotypic relatedness with the vaccine per se, but also on its biological phenotypes, such as viral fitness. On the other hand, vaccines that induce strong antiviral responses via multiple mechanisms against multiple viral targets are more likely to restrict the degree of freedom by which an infecting virus may gain fitness within the host and thereby achieve protection against diverse viral isolates. We propose to test this hypothesis by examining the protective efficacy of multi-component vaccines of various compositions against viruses of different genetic relatedness and phenotypes. The specific aims of this experiment is to determine the efficacy of Gag/Pol/Env vaccines against sequential isolates of the homologous virus that have different phenotypes (typical of early and late isolates). Sixteen animals (Macaca nemestrina) have been immunized with recombinant vaccinia viruses expressing env or gag-pol genes of SIVmne CL8; eight animals with parental vaccinia virus as controls. A second group of 24 macaques will be inoculated in May, 2004, with similar recombinants expressing antigens derived from a late isolate SIVmne Wk 170. So far, no adverse reaction has been observed in any of the immunized animals. SIV specific immune responses are being monitored.

COMPARISON OF RECOMBINANT VACCINIA AND ALDRITHIOL-2 INACTIVATED SIV VACCINES: II (0320)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.700% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
HU, SHIU-LOK	PHD	C	PHARMACEUTICS	
	DVM	C	NPRC	
	PHD	A	AIDS VACCINE PROGRAM	NIH, MD USA
	MD, PHD	A		NCI, MD USA
	PHD	C	NPRC	
	MD	A		NCI, MD USA
	PHD	C	PHARMACEUTICS	
	PHD	A		SBRI, WA USA

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

ABSTRACT

This is Part II of a 2-part study to compare recombinant vaccinia plus recombinant protein ("prime and boost") and aldrithiol-2 inactivated SIV vaccines (Hu 02-01). As described in the Progress Report for Part I (Hu 02-01), preliminary results indicate that priming with recombinant vaccinia viruses expressing the Env and Gag-Pol antigens of SIVmne, followed by boosting with AT-2 inactivated virions resulted in partial protection against a highly pathogenic uncloned SIVmne stock. The degree of protection appeared to be greater than boosting with recombinant protein immunogens. In this study, we aim to examine (1) the role of recombinant vaccinia virus priming; and (2) the role of the envelope protein as an integral part of the inactivated virion in eliciting the protective immunity. Two groups (7 per group) of Macaca nemestrina were immunized with inactivated SIVmne E11S virions, one of which receive virions inactivated only by AT-2 and the other received virions inactivated by heat in addition to AT-2. Heat inactivation resulted in the shedding of envelope antigens from the virions. Four animals received sham adjuvants only. To date, these animals received two inoculations of the immunogens. Both SIV-specific antibody and cell-mediate immune responses have been observed. These animals will be boosted again after a 6-month resting period and will be challenged with the same stock of uncloned SIVmne used for Hu 02-01 study. Immunological, virological and clinical responses will be studied.

COMPARISON OF RECOMBINANT VACCINIA AND ALDRITHIOL-2 INACTIVATED SIV VACCINES: I (0321)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.700% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
HU, SHIU-LOK	PHD	C	PHARMACEUTICS	
	DVM	C	NPRC	
	PHD	A	AIDS VACCINE PROGRAM	NIH, MD USA
	MD, PHD	A		NCI, MD USA
	PHD	C	NPRC	
	MD	A		NCI, MD USA
	VMD	C	NPRC	
	PHD	C	PHARMACEUTICS	
	PHD	A		SBRI, WA USA

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

ABSTRACT

We previously reported that immunization of macaques with a combination immunization regimen resulted in complete protection against infection by an uncloned SIVmne. The vaccines used consist of "priming" with recombinant vaccinia viruses expressing the core and the envelope proteins of SIVmne, and "boosting" with a mixture of recombinant core and envelope proteins. However, the individual contribution of the priming and the boosting immunogens was not evaluated. The purpose of this experiment is to evaluate whether immunization with recombinant vaccinia virus alone, without protein boosting, would suffice. If not, we wish to improve the efficacy of the vaccines by boosting with whole inactivated virus, rather than the mixture of recombinant proteins. Three groups (7 per group) of Macaca nemestrina were primed with two recombinant vaccinia viruses, one expressing gag-pol and one expressing env of SIVmne CL8. One group was boosted with recombinant envelope and core antigens, one with sham adjuvant formulation, and one with AT-2 inactivated SIVmne, which retains the natural conformation of the virus envelope proteins. Three control animals were immunized with parental vaccinia virus and boosted with adjuvant only. Animals were challenged with a highly pathogenic uncloned SIVmne intravenously. Results to-date indicate that (1) immunized animals showed reduced peak viral load, consistent with partial protection; (2) animals boosted with recombinant proteins had increased antibody titers prior to challenge, but no difference in viral load after challenge as compared to animals that did not receive the protein boost, indicating the importance of cell-mediated immunity in reduction of viral load; (3) 3 of 7 animals receiving AT-2 inactivated virion boost showed significant reduction of "set-point" viral load, consistent with greater protective efficacy. We are currently examining immune responses that may correlate with the enhanced protection.

IMMUNOGENICITY OF ENV AND/OR CORE ANTIGENS OF HIV-1 (0322)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.700% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
HU, SHIU-LOK	PHD	C	PHARMACEUTICS	
names	DVM	C	NPRC	
	PHD	C	NPRC	
1	PHD	C	PHARMACEUTICS	

AXIS I CODES: 1A, 7B **AXIS II CODES:** 31, 39, 64, 66

ABSTRACT

Multiple lines of evidence indicate that N-linked glycans in HIV-1 envelope protein play an important role in viral infection and evasion from host immune response. Results from our previous studies indicate that N-linked glycosylation mutants in the V2 loop at amino acid (aa) 188 and aa 198, and in the V3 loop at aa 303 increased viral sensitivity to broadly neutralizing monoclonal antibody IgG1b12 and tetrameric CD4-IgG2 immunoglobulin molecules. This result suggests that carbohydrates at these sites may hinder the access to important neutralizing epitopes on the envelope protein. In this experiment, we aim to examine whether removal of glycans at these specific sites might increase the ability of the envelope glycoproteins to elicit neutralizing antibodies and enhance the protective efficacy against SHIV challenge. Three groups of pig-tailed macaques (6/group) were immunized with the following immunogens: Group 1, vaccinia virus expressing wild-type HIV 89.6 envelope protein gp160; Group 2, vaccinia virus expressing envelope mutant in V2 (aa 198); and Group 3, vaccinia virus expressing envelope mutants in V2 (188, 198) and V3 (303). These animals were also primed with vaccinia virus and boosted with DNA plasmid expressing SIVmac239 gag-pol gene. All experimental animals were also boosted with subunit gp140 corresponding to the immunogen they received in primary immunization (Group 1: wild-type; Group 2: single V2 mutant; Group 3: triple V2/V3 mutant). A control Group 4 was immunized with parental vaccinia virus, boosted with vector DNA and sham adjuvant. As expected, no major adverse effect has been observed. Both antibody and cell-mediated immune responses to HIV Env and SIV Gag proteins have been observed. The protective efficacy of these vaccines will be evaluated against an intrareactal challenge with chimera virus SHIV89.6P in March, 2004.

NEURAL BASIS OF VISUAL LEARNING (0328)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
JAGADEESH, BARATHI	PHD	C	PHYSIOL & BIOPHYS	
	BS	G	NEUROBIOL&BEHAV	
	PHD	A	PHYSIOLOGY AND BIOLOGY	UNIVERSITY OF NOTTINGHAM, UK
		A		SHIN NIPPON SANGYO LTD., JAPA
	PHD	A	PHYSIOLOGY AND BIOLOGY	UNIVERSITY OF NOTTINGHAM, UK

AXIS I CODES: 1A **AXIS II CODES**92(NEUROSCIENCE)

ABSTRACT

We are interested in the neural basis of object recognition. How does the brain translate the visual world into the neural code that we rely on to recognize, discriminate and remember objects? We believe that object recognition is a two way street in which the brain processes the sensory information arriving at the retina in the context of behavioral demands, including attention, learning, and experience. The part of the primate brain thought to be responsible for object recognition is the inferotemporal cortex (IT) the last stage in the ventral, or "what" stream of visual processing. Neurons in IT have selectivity for complex objects, like faces, objects and scenes. The selectivity of these neurons is the basis for our ability to recognize and discriminate a plethora of objects and scenes, an ability that far outstrips the capabilities of any known computational algorithm or machine. We propose that these neurons achieve this high level of performance by processing visual information specifically as needed by task demands – the neuron's selectivity is built up by the needs of the animal, through learning, and is modified on the fly by immediate task demands, including attention and context. Thus, IT neurons are the substrate on which the two-way street of object recognition is structured. We study IT cortex to elucidate this relationship and the role that these neurons play in object recognition.

PHARMACOKINETICS OF ERYTHROPOIETIN IN THE CSF OF MACAQUES NEMESTRINA (0299)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
JUUL, SANDRA	MD, PHD	A	PEDIATRICS	
L Nelson J	PHD	A		ROBERT WOOD JOHNSON PHARMACEUTICAL RESEARCH INSTITUTE, NJ USA

AXIS I CODES: 1A **AXIS II CODES** 50B

ABSTRACT

The purpose of this study is to evaluate the presence of erythropoietin (EPO) in the cerebral spinal fluid of monkeys following a single bolus dose of EPO, or Epo analog by intravenous injection. In addition, brain tissue will be collected upon experimental termination for gene expression profiling analysis.

CD8 T-CELL RESPONSE (0336)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.700% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KAJA, MURALI-KRISHNA	PHD	C	IMMUNOLOGY	
	DVM	C	NPRC	
	MD	A	HEMATOL/ONCOL	

AXIS I CODES: 1A, 1D **AXIS II CODES:** 31

ABSTRACT

The mechanisms of lymphoid homeostasis in primates/ non-human primates are highly complex. Progress in many areas of research, including AIDS research, is critically dependent up on fundamental understanding of these mechanisms. Our goal is, using murine and macaque models, to gain fundamental understanding of homeostatic, innate and adaptive mechanisms that regulate generation, maintenance and protective ability of memory lymphocytes.

SACCADIC EYE MOVEMENT STUDIES (0284)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KANEKO, CHRIS R S	PHD	A	PHYSIOL & BIOPHYS	
[name]	MD, PHD	A	UNKNOWN	HOKKAIDO U, JAPAN

AXIS I CODES: 1A, 21 **AXIS II CODES:** 36, 92(OCULOMOTOR NEUROPHYSIOLOGY)

ABSTRACT

The ultimate goal of our work is to understand how the brain functions. To do this, we study the output (motor) portions, using the oculomotor system as a model. Our recent work has begun to expand our interests into studies of the cortical control of eye movements. In the laboratory of our colleague, Professor [name] at Hokkaido University in Sapporo, we have been studying how the signals there might contribute to the generation of smooth eye movements in primates. We have shown recently that neurons in the caudal portion of an area called the frontal eye fields appear to combine, visual and vestibular signals into commands for movement of the eyes that track objects of interest in three dimensional space. These results not only advance our understanding of how the brain processes information in order to formulate actions based on that information, but they are also basic to the differential neurological diagnosis based on eye-movement signs now commonly used clinically as well as to our understanding of oculomotor processes. They also provide a foundation for studies of more complex aspects of central nervous system function such as interactions between motor systems (e.g., eye and head during orientation) or sensory and motor systems (e.g., the visual and oculomotor systems) and more abstract functions such as attention and memory.

BEHAVIORAL ASSESSMENT IN NONHUMAN PRIMATES (0271)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KYES, RANDALL C	PHD	C	NPRC, PSYCHOLOGY	

AXIS I CODES: 1A **AXIS II CODES:** 36

ABSTRACT

This project is designed primarily as a research and training opportunity for undergraduate students, graduate students, and visiting scientists who wish to learn about primate social behavior and cognition and obtain experience in behavioral observation and assessment. The behavioral data generated may be useful for colony management such as assessment of social or clinical problems with individual animals or arising within the groups. This project involves Behavioral Observation and Standardized Behavioral Assessment of the macaques and baboons in the social groups on the 7th floor of the NPRC Seattle Colony, as well as the infant and juvenile macaques and baboons in the Infant Primate Research Laboratory (IPRL).

Behavioral observations are scheduled so as not to conflict or interfere with regular management activities or other projects. There is no physical contact, capture, transfer or movement of animals required as part of this protocol. Standardized behavioral assessment utilizes an assessment apparatus that consists of a panel with a rear projection screen/computer monitor that can be positioned outside of a cage or a small open field enclosure. A set of computerized visual stimuli depicting a range of stimuli are presented to the group to elicit behavioral response. The animals' responses are recorded via closed-circuit TV camera mounted below the screen/monitor. During testing, the panel is placed in front of the cage (NPRC) or monkeys are placed individually in the open-field enclosure (IPRL). A 10-min acclimation period precedes the stimulus presentation. Each stimulus is then presented sequentially for 30 sec with a 2-min inter-stimulus interval. Subject's duration of attention and any behavioral responses directed toward the stimulus are recorded. The order of testing and stimulus presentation is randomized for each session.

PRIMATE IMAGING USING POSITRON EMISSION TOMOGRAPHY AND MAGNETIC RESONANCE IMAGIN (0316)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
MINOSHIMA, SATOSHI	MD, PHD	A	RADIOLOGY	
names	BSE	C	NPRC	
	PHD	C	PHYSIOL & BIOPHYS	
	OTH	A	RADIOLOGY	
1	PHD	A		FUJISAWA PHARMACY, JAPAN

AXIS I CODES: 1A, 9, 21 **AXIS II CODES:** 46, 63C, 63E, 80

ABSTRACT

This new Core project is established in the Neuroscience Division of the Washington National Primate Research Center. During the second year of the funding (2003-2004), we have developed further infrastructure to support researchers who wish to use imaging for their research investigations. To facilitate routine imaging of non-human primates, we have established a contract with PETNET, Inc., for the delivery of a common radiotracer, [F-18]FDG. In addition to more specialized radiotracer production by the Radiochemistry in the Department of Radiology, this contract permits more reliable and flexible scheduling of PET imaging for investigators. The Core activity also has facilitated magnetic resonance imaging (MRI) research of non-human primates in collaboration with the Department of Radiology. This includes new technology developments for 1) MR track tracing for the monkey brain connectivity and 2) neuroprogenitor cell tracking using MR-contrast cell labeling techniques. Both methods were initially tested in rodents prior to the non-human primate applications in our newly established wet laboratory adjacent to the PET Imaging Suite. On-going projects that utilize or has utilized the PET Imaging Core include 1) Imaging of Neurogenesis in monkey brains; 2) Imaging of dopaminergic neuronal degeneration in non-human primate models of Parkinson's disease; 3) Imaging of brain metabolism in HIV/SIV infected juvenile monkeys; 4) Imaging investigation of neuronal connectivity in rat and monkey brains; 5) Effects of insulin in the human memory system; and 6) Mathematical modeling of radiotracer kinetics in the non-human primate brain. The Core continues to support new imaging research projects through collaborations with multi-disciplinary investigators.

LONG-TERM SURVIVORS OF SIV/HIV INFECTION (0307)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.200% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
MORTON, WILLIAM R	VMD	C	NPRC	
[illegible]	DVM	C	NPRC	

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

ABSTRACT

Animals assigned to this project have been sucessfully infected with a primate lentivirus. The purpose is to continue health, virologic and immunologic monitoring for an extended period of time. The current animals have been infected with HIV-1 over 11 years at this time, and continue to demonstrate seropositive responses to HIV-1 proteins.

IN VIVO EVALUATION OF PRIMATE LENTIVIRUSES (0329)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.200% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
MORTON, WILLIAM R	VMD	C	NPRC	
L names	DVM	C	NPRC	
nd	PHD	C	PHARMACEUTICS	

AXIS I CODES: 1A, 7B **AXIS II CODES** 31, 64, 66, 83

ABSTRACT

This project was initiated to determine the in vivo infectivity and pathogenicity of several challenge stocks of SIVmne: CL 8, an infectious and pathogenic molecular clone; 170 wk, an isolate from the late stage of in vivo infection of CL 8; and two chimeras of these two viruses: 8/170, containing the 3' half of the viral genome of 170wk (vpr, tat, rev, env, nef); and 170/8, containing the 3' half of the viral genome of CL 8. These viruses are needed for the study of determinants of SIV vaccine protection.

As a pilot study to determine the infectivity of the chimeric viruses, we inoculated intravenously one Macaca nemestrina with each of the two chimeras. Both animals became infected with high peak viremias (107-108), which declined to set points between 105 and 106 copies/ml plasma. Peripheral blood CD4+ $\overline{T}$ cells declined to 108 copies/ml plasma) and set-point (107 - 108 copies/ml plasma) viral loads. Three animals developed clinical signs of AIDS and were euthanized. These results confirm the different phenotypes of the SIV isolates needed as challenge viruses. Additional animals will be inoculated with lower doses to determine the 50% infectious dose.

LOCAL IMMUNE RESPONSE IN CHLAMYDIA SALPINGITIS (0272)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
PATTON, DOROTHY L	PHD	A	OB-GYN	

AXIS I CODES: 1A, 7A, 23 **AXIS II CODES** 64, 66, 83, 93

ABSTRACT

These experiments are designed to test the immunomodulatory roles of cytokines (specifically IL-10 in this year of the study) in chlamydial PID. Animals in this experiment underwent multiple inoculations with three different serovars of C. trachomatis, in an effort to produce more chronic disease and lesion development in pocket tissues. The pockets of two animals were challenged with chlamydial inoculation delivered in the presence of IL-10 (100ng IL-10/50 microliter inoculation), and subsequently "boosted" with repeat inoculations of IL-10 alone. The pockets of two separate animals were challenged with the same dose Chlamydia trachomatis, in the absence of exogenous IL-10, followed by SPG (growth media) "boosts".

Pockets were then removed on days 0, 17, 21, 35 and 50 for analysis. We anticipate that IL-10 may reduce the incidence of fibrosis after multiple infections, but IL-10 may also increase the numbers of chlamydia present. These studies might demonstrate the effects of exogenous IL-10 on chlamydial infection. If antigen clearance is enhanced, or immunopathology decreased, further studies of cytokine manipulation therapy will be warranted.

STD PREVENTION - PRIMATE UNIT (0274)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.200% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
PATTON, DOROTHY L	PHD	A	OB-GYN	

AXIS I CODES: 1A, 2, 7A, 23 **AXIS II CODES:** 31, 64, 66, 83, 93, 94

ABSTRACT

The Sexually Transmitted Disease Prevention–Primate Unit (STDP-PU) contract has been established as a means to comparatively assess topical microbicide products vis-à-vis safety to cervical/vaginal tissues after repeated use, and efficacy in preventing cervical chlamydial infection.

The contract is designed to assess first, effects that a formulated microbicide product has on the surface tissues and microenvironment of the cervix and vagina (modified colposcopy, cervical gram stain, pH, vaginal flora), thirty minutes and 24 hours after each application when applied daily for four days. Cervical and vaginal biopsies will be collected 24 hours after the final application to assess the cellular immune response induced by repeated use. This experiment also tests for tissue and flora recovery within one week following final application.

After a product has been shown not to induce deleterious outcome after repeated use, it will be assessed for its ability to prevent chlamydial infection of the cervix. In this experiment, a single dose of the formulated microbicide product is applied to each of six animals, followed (at thirty minutes) by a cervical challenge with Chlamydia trachomatis. Detection of viable chlamydial organisms and DNA, as well as serum antibody to chlamydia will be attempted for seven weeks post inoculation. In addition, a cervical biopsy will be collected at seven days post-inoculation, which will be assessed for presence of chlamydial antigen in the cervical tissue.

CHLAMYDIA TRACHOMATIS + SHIV: CO-INFECTION MODEL DEVELOPMENT (0275)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.200% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
PATTON, DOROTHY L	PHD	A	OB-GYN	
[redacted]	DVM, PHD	C	NPRC	

AXIS I CODES: 1A, 7A, 7B, 23 **AXIS II CODES** 31, 64, 66, 77, 83, 93

ABSTRACT

In humans, it is now widely believed that the presence of other sexually transmitted infections greatly facilitate the transmission and acquisition of HIV between sexual partners. As an example, chlamydia induced endocervical infection causes inflammation of the lower reproductive tract, which may allow for more efficient exchange of infectious viral particles, thereby enhancing HIV infection. Using this potential mechanism for enhanced viral uptake, we plan to "prime" monkeys with a chlamydial infection, then attempt to infect them by mucosal challenge with SHIV.

We intend to develop a co-infection model in the pig-tailed macaque, in which a reproducible SHIV infection rate (80-100%) is achieved after a single mucosal challenge in animals previously infected with Chlamydia trachomatis. Upon successful development of this co-infection model, we expect to use it for efficacy-testing of topical microbicide products, in preventing SHIV infection. To evaluate the ability of a topical microbicide product to prevent viral uptake, we will expose chlamydia infected animals to a topical microbicide product, then challenge with SHIV. Such pre-clinical testing will greatly aid in the process of screening products for enrollment in clinical studies.

NON-HUMAN PRIMATE MODEL FOR RECTAL AND VAGINAL TOPICAL MICROBICIDE USE (0276)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.200% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
PATTON, DOROTHY L	PHD	A	OB-GYN	
[redacted]	PHD	A	OB-GYN	U PITTSBURGH, PA USA

AXIS I CODES: 1A, 2, 23, 28(RECTUM) **AXIS II CODES:** 31, 64, 83, 93, 94

ABSTRACT

Topical microbicides represent an important potential strategy for preventing the transmission of HIV/STD. It is desirable that a topical microbicide product be effective in preventing HIV and STD infections while not irritating the mucosal surface or adversely affecting normal flora of the vagina or rectum, after single and repeated use.

It is essential that the in vivo activity of developing topical microbicidal products be evaluated prior to recommendations for widespread intravaginal or rectal use. Because clinical trials are too cumbersome and expensive for screening purposes, animal models need to be used.

The primary goal of this study is to develop a combination topical microbicide product. That is to say, a product which will be composed of more than one active (antimicrobial) compound, providing more than one mode of action against HIV and other STI.

As the proposed combination topical microbicide formulation evolves, we will assess safety of intermediary formulated products in the rectal and vaginal environments using our established animal model for topical microbicide safety testing.

These proposed studies are key to bridging the gap between laboratory and clinical studies aimed at preventing the spread of HIV/STI.

FUNCTIONAL ORGANIZATION OF CERVICAL INTERNEURONS (0304)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
PERLMUTTER, STEVEN I I	PHD	A	PHYSIOL & BIOPHYS	
	PHD	C	PHYSIOL & BIOPHYS	
	PHD	A	PHYSIOLOGY & BIOPHYSICS	
	PHD	A	PHYSIOLOGY & BIOPHYSICS	

AXIS I CODES: 1A, 20, 21 **AXIS II CODES:** 82, 92(MOTOR SYSTEM)

ABSTRACT

During the period covered by this report, studies were conducted in two areas.

1. The role of inhibition in shaping spinal motoneuronal and interneuronal activity during voluntary movement was studied. Recordings were made in a behaving monkey making multi-dimensional movements of the wrist. Neural activity was recorded from individual spinal neurons with a multi-barrel electrode containing inhibitory neurotransmitters and their antagonists. The activity of many interneurons was affected by local iontophoresis of these drugs. Iontophoresis of both glycine and GABA produced widespread inhibition of interneurons, which could often be blocked by the simultaneous ejection of the antagonists to the neurotransmitters, strychnine or bicuculline, respectively. Ejection of the antagonists themselves often evoked increased discharge of the interneurons. Interestingly, the preferred directions of most interneurons for wrist movements in different directions were not significantly effected by application of the inhibitory neurotransmitters or their antagonists. This suggests that inhibition does not contribute significantly to the spatial tuning of spinal interneurons.

2. Neural activity in the C3-C4 spinal segments was recorded in another monkey trained to make both simple flexion and extension movements of the wrist and free-from reaching movements to retrieve food pellets. Many neurons in these segments exhibited activity that was strongly modulated during one or both of the forelimb tasks. This was not expected since the forelimb is innervated by nerves originating in the C5-T1, not C3-C4, spinal segments. We found some evidence for a population of C3-C4 premotor interneurons that produce post-spike effects in spike-triggered averages of EMG of arm muscles. These neurons appear to make an important contribution to forelimb movements in the cat, and there has been uncertainty as to their role in primates.

These studies will elucidate the contribution of spinal cord circuits to the control of voluntary movements in normal, behaving primates. This knowledge will provide the framework in which to understand, and overcome, the motor deficits associated with central nervous system injury or disease.

ROLE OF CEREBELLAR NUCLEI IN EYE MOVEMENT CONTROL AND ADAPTATION (0296)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
ROBINSON, FARREL R	PHD	A	BIOLOGICAL STRUCTURE	
L name d	PHD	C	PHYSIOL & BIOPHYS	

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

ABSTRACT

We use eye movements to study the cerebellum's role in movements. Cerebellar damage leaves movements, including eye movements, slow, inaccurate and variable. It also abolishes the ability to adjust, or adapt, motor commands, including those for eye movements, that consistently result in inaccurate movements. The movement adaptation produced by the cerebellum is necessary when growth, aging, trauma, or disease change our bodies or brains so that the commands that previously caused accurate movements no longer do so. We do three types of experiments. 1) We record the activity of neurons in an eye movement-related part of the cerebellar nuclei as monkeys make eye movements. 2) We measure eye movement abnormalities after we temporarily anesthetize an eye movement-related part of the cerebellum by injecting drugs into it. 3) We measure adaptation of eye movements when we make them seem to be inaccurate. We do this by moving the target toward which a monkey is making a rapid eye movement, called a saccade. When the eye movement ends it seems to have overshot the target. If a monkey tracks ~1000 target movements like this its saccades become significantly smaller.

Recent results told us 1) show well the brain compensates for movement errors of different sizes, 2) that signals carried by nerve fibers, called parallel fibers, running horizontally across the surface of the eye movement part of the cerebellum, help stop end eye movements properly so that they do not overshoot, 3) that there are two adaptation processes in the brain for making eye movements accurate. One type is relatively short-term and corrects eye movements over several hours. This is the type that has been studied extensively in the past. The second is longer-term and makes longer lasting corrections in eye movements over ~10 days. This type has been studied very little previously.

OLFACTORY CONDITIONING OF FLAVORS IN MACACA NEMESTRINA (0277)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
SACKETT, GENE P	PHD	C	PSYCHOLOGY	

AXIS I CODES: 1A, 9, 21, 25C **AXIS II CODES:** 36, 60, 67, 78

ABSTRACT

Olfactory conditioning in human infants can enhance ingestion of new and aversive solutions, thereby aiding medicine consumption and diet transitions. Olfactory conditioning is also useful for studying long term memory. Preliminary to a study of olfactory conditioning, we assessed scent preference/aversion in 5 nursery raised infants ranging in age from 5-10 months. The method uses 10-cm diameter circles with a .5-in center hole, cut from coffee filters, soaked for 60-sec in pure extracts of lemon, almond, or vanilla. Two bottles containing 500 ml of water are attached to the left and right rear cage wall, at "lixit" height (turned off) 1-ft from the cage floor. The circles were randomly placed on the bottles, 2-in from the spout end, from 11:00-14:45 hours on each of 21 test days. Baseline sessions used unscented bottles. Test sessions paired each scent against water, as well as each against the other two scents. Amount of water consumed from each bottle was recorded. Infants consumed more water paired with almond and vanilla than at baseline, demonstrating that these scents enhanced ingestion. Water paired with lemon was at or below baseline, suggesting a relative aversion to this scent. We conclude that some scents can enhance the intake of water by infant macaques. These may be useful in olfactory conditioning to study memory and for enhancing substance palatability.

SLEEP AND ABNORMAL BEHAVIOR (0279)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
SACKETT, GENE P	PHD	C	PSYCHOLOGY	

AXIS I CODES: 1A, 9, 21 **AXIS II CODES** 36, 77, 85

ABSTRACT

About 3-4% of macaque monkeys that are housed for long periods of time as juveniles and adults in single cages develop high levels of abnormal behaviors. These are often expressed in stereotyped locomotor behavior. In some cases this may include self-injurious behavior (SIB) alone or accompanying stereotypies. To date, it has not been possible to predict which animals will develop serious levels of these behaviors. In humans, a few studies have found that juveniles and adults with self-injurious behavior exhibit sleep disturbances, including abnormal EEG patterns and frequent night waking. In addition to being a correlate of SIB, it is possible that lack of sleep may be an actual cause. This study aimed to determine whether monkeys with self-injurious behavior have abnormal sleep patterns. A portable computer and video camera system was developed to time sample night behavior and store the images in a computer file. Movement detection software continuously monitors changes in spatial location in the animal's cage, storing the onset time and duration of movement bouts.

10 adults were studied for 4-7 nights in SIB:Non-SIB pairs monitored at the same time. SIB was observed at night in 4 of the 5 SIB monkeys. These monkeys also had more night waking and took longer to become quiet at lights out. One control monkey, who never exhibited SIB in the daytime, had the next highest amount of night self-biting among the 10 animals. It is clear that monkeys with SIB have a different pattern of night movement, which includes SIB itself. Our next step will be to see if movement patterns on individual evenings are correlated with day time abnormal behavior.

DEVELOPMENT OF MONKEYS PRODUCED BY EMBRYO SPLITTING AND INTRACYTOPLASMIC SPERM I (0280)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
SACKETT, GENE P	PHD	C	PSYCHOLOGY	
[illegible]	BS	A		UNIVERSITY OF PITTSBURGH, PA USA

AXIS I CODES: 1A, 15, 21, 23, 25B **AXIS II CODES:** 36, 41, 44, 58, 60, 64, 65, 74E, 77

ABSTRACT

Two techniques of assisted reproductive technology (ART) in primate research involve production of identical twins through embryo splitting (ES) at the 4 cell stage and intracytoplasmic sperm injection (ICSI) in which mature or immature sperm are directly injected into the egg to produce fertilization. We studied ICSI (n=6) and ES (n=5) monkeys in our Infant Primate Research Laboratory, along with 5 in vitro fertilization (IVF) and 4 Artificial Insemination (AI) monkeys from birth through 24 months of age.

The monkeys were assessed on a broad battery of growth, behavior, and physiological development measures designed to identify potential areas of moderate to severe abnormalities in growth, social, or cognitive development. After nursery rearing with daily socialization from 1-12 months, the animals were group housed in large gang cages for the next year. The data are currently being analyzed and prepared for publication. Three findings appear to be warranted by the 1-12 month results. Relative to artificial controls produced through natural reproduction, ART monkeys (1) are accelerated in early motor and sensory development and in maturation of very basic cognitive skills requiring object permanence and recognition memory, (2) do not perform as well as controls in a more difficult concept learning set task, and (3) exhibit a hyperactive pattern of social behavior relative to natural reproduction controls. Social behavior from months 13-24 are currently under analysis.

TOUCHSCREEN COMPUTER METHODS TO STUDY LEARNING IN INFANT MONKEYS (0281)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
SACKETT, GENE P	PHD	C	PSYCHOLOGY	
[illegible]	PHD	A	PSYCHOLOGY	
	BS	A	PSYCHOLOGY	

AXIS I CODES: 1A, 9, 21, 25B **AXIS II CODES** 36, 41, 60

ABSTRACT

Contemporary behavioral and neuroscience research on learning, perception, memory, and problem solving uses video and computer technology as primary stimulus presentation, problem setup, and response measurement techniques. Although some of this technology has been applied in studying human infants and young children, there has been almost no work on infant monkeys. In part, this is because young primates have many behaviors that compete with the attention required to perform well on computer tasks, e.g., playing with the apparatus, not looking at the video monitor. The project developed a battery of tasks and training techniques for testing infants starting at 3-9 months of age and young monkeys between 1 and 2 years of age.

Software was written for touch screen training, using a basic shaping technique. 12 infants, from 4-9 months of age at the start of testing, were trained to consistently touch a square on the screen, with a unique tone and apple sauce delivered after the touch. Software was also written for a simple 2-choice discrimination task, reversal of the 2-choice task, 6-trial per problem learning set formation, nonmatching-to-sample, and delayed nonmatching-to-sample tasks. All monkeys have performed well through learning set, and older monkeys are doing the nonmatching with delay task. We will soon compare these performances with that of our Infant Primate Laboratory monkeys (n=150) doing the same tasks using standard Wisconsin General Test Apparatus (WGTA) procedures. Software is also being prepared to study more complex spatial learning, tracking, counting, and uncertainty assessment procedures. In current work we will validate these procedures and identify the earliest age at which monkeys can be trained to perform in the touch screen environment. We expect to apply these techniques with monkeys produced by embryo splitting and intracytoplasmic sperm injection as they become available for study.

VISUAL PERCEPTION LABORATORY (0189)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
SHADLEN, MICHAEL N	MD, PHD	C	PHYSIOL & BIOPHYS, HHMI	
	BS	G	NEUROBIOL&BEHAV	
	PHD	A	PSYCHOLOGY	VANDERBILT UNIVERSITY, TN USA
	PHD	A	BRAIN AND COGNITIVE SCIENCES	MIT, MA USA
		A	NEUROBIOLOGY & BEHAVIOR	
	BS	A		STANFORD UNIVERSITY, CA USA
	PHD	A	HHMI	
		A		U OF CALIFORNIA DAVIS, CA USA
	PHD	A	NEUROSCIENCE	UNIV. OF PENNSYLVANIA, PA USA
		G	NEUROBIOLOGY & BEHAVIOR	
		A	NATIONAL EYE INSTITUTE	NATIONAL INSTITUTE OF HEALTH, MD USA
	PHD	A	PHYSIOLOGY & BIOPHYSICS	
	PHD	C	PHYSIOL & BIOPHYS	
	MD, PHD	G		
	MD	A		NIAVARAN, IRAN
	PHD	G	NPRC	
	PHD	A		MIT, MA USA
	PHD	G	PHYSIOL & BIOPHYS	
	PHD	A		CALIFORNIA INSTITUTE OF TECHNOLOGY, CA USA
	PHD	G	MED SCIENCES	
		A		NATIONAL BRAIN RESEARCH CENTER, INDIA
	PHD	A	PSYCHOLOGY	
	PHD	A	BIOLOGICAL STRUCTURE	
	BA	A	NEUROBIOL&BEHAV	
	PHD	A		
	MS	G	PHYSIOL & BIOPHYS	
	PHD	A	PSYCHOLOGY	VANDERBILT UNIVERSITY, TN USA
	PHD	A		UNIVERSITY OF MELBOURNE, AUSTRALIA
	PHD	A	CENTER FOR NEUROSCIENCE	U OF CALIFORNIA DAVIS, CA USA
	PHD	A	NEUROLOGY AND PSYCHOLOGY	KU LEUVEN MEDICAL SCHOOL, BELGIUM

AXIS I CODES: 1A **AXIS II CODES**88

ABSTRACT

To comprehend the neural basis of visual perception, it is necessary to determine how information from sensory regions of the brain influences the neural circuitry that governs behavior. The brain acquires visual information and interprets this information to decide its significance. A decision process thus intervenes between visual sensation and visually guided behavior. In the past six years, neurons have been identified in the parietal and frontal lobes of the monkey that represent the formation of a perceptual decision about the direction of visual motion in a simple discrimination task. These neurons associate visual information with a planned behavioral response. They thus provide an unrivaled opportunity to study the formation of a decision at the neural level. Preliminary findings have shown that decisions about the direction of visual motion benefit from the integration of information as a function of time. The proposed experiments test the hypothesis that neurons in the association cortex compute the time integral of appropriate sensory information from the visual Four specific aims are planned. 1) Microstimulation of area MT will elucidate how changes in the representation of direction influence the perception of direction and the time required to reach a decision. 2) Neural recordings in area LIP will reveal the mechanism of the accumulation of motion information toward a decision. 3) Neural recordings in area LIP combined with behavioral manipulations of reward and prior bias will reveal the integration of psychological variables with visual information in decision formation. 4) Microstimulation of area LIP will determine the role of this association area in decision formation. Understanding the neural machanisms that underlie a visual decision will help to elucidate the neural basis of cognition and its disorders and provide the means to promote recovery of both sensory and intellectual function in the face of neurological disease.

NEURAL MECHANISMS OF VISUAL PERCEPTION (0297)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
SHADLEN, MICHAEL N	MD, PHD	C	PHYSIOL & BIOPHYS, HHMI	
	PHD	A		COLD SPRING HARBOR LABORATORIES, NY USA
	PHD	G	PHYSIOLOGY AND BIOPHYSICS	
	PHD	A		UNIVERSITY OF PENNSYLVANIA, P USA
		G	NEUROBIOLOGY & BEHAVIOR	
	PHD	G	PHYSIOLOGY AND BIOLOGY	
	MD, PHD	G		
		G	NEUROBIOLOGY, BIOMEDICAL ENGIN	
	PHD	G	PHYSIOL & BIOPHYS	
	PHD	A	PSYCHOLOGY	
	BA	A	NEUROBIOL&BEHAV	
	PHD	A		BRANDEIS UNIVERSITY, MA USA
	PHD	G	PHYSIO BIO	

AXIS I CODES: 1A **AXIS II CODES:** 88

ABSTRACT

We proposed three experiments that test specific hypotheses about the neural mechanisms that govern the conversion of sensory evidence in visual cortex to a decision about the direction of motion.

1. To measure the effect of stimulus strength and duration on direction discrimination in combination with microstimulation of area MT. A paper describing our findings was published this year (Ditterich et al., 2003).

2. To measure the effect of stimulus strength and duration on direction discrimination and on neural activity in area LIP. Data collection was completed on this project in year 1. The main report was published last year (Roitman and Shadlen, 2002). A paper describing theoretical implications was published in Neuron (Gold and Shadlen, 2003), and a computational modeling paper was published in Cerebral cortex (Mazurek et al., 2003).

3.To measure the effect of response bias on direction discrimination and on neural activity in area LIP. We have completed behavioral measurements in 2 monkeys. Electrophysiology is in progress. We have made significant progress on two related studies, which demonstrate that elapsed time and the anticipation of behaviorally relevant cues are represented by single neurons in area LIP (Leon and Shadlen, 2003; Janssen and Shadlen, 2003).

Building on a foundation of visual psychophysics and physiology, we find ourselves in the fortunate position to narrow the gap between sensation and behavior. Nearly all non-reflexive behaviors require the brain to draw upon its sensory cortex to guide motor and premotor circuitry. Thus, the neural mechanisms underlying decision-making will lend insight into many aspects higher cognitive function. Neurological diseases affecting higher brain function are likely to involve the structures targeted in our studies. Our efforts will furnish new insights into the causes and treatments for disorders affecting visual perception and cognition.

PROTECTION FROM SHIV-INFECTION BY CTL AND ANTIBODIES (0317)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.200% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
STAMATATOS, LEONIDAS	PHD	A	PATHOBIOLOGY	SBRI, WA USA
[illegible]	PHD	A	PATHOBIOLOGY	SBRI, WA USA

AXIS I CODES: 25 **AXIS II CODES:** 31, 65, 91

ABSTRACT

Our studies aim at developing vaccine strategies that will prevent the establishment of HIV-infection. Vaccination strategies that only elicit cellular antiviral responses are not capable of sterilizing immunity, but can reduce the plasma viral load during the chronic phase of infection; prevent the rapid elimination of CD4+ T lymphocytes; and delay the development of disease. Vaccination methodologies that principally elicit neutralizing antibodies also offer protection (and in certain cases sterilizing immunity), but only against the homologous virus. This is due to the inability of currently used envelope immunogens to elicit cross-reactive neutralizing antibodies. The proposed studies are based on our observation that the partial elimination of the V2 loop from the SF162 envelope increases the exposure of conserved neutralization epitopes. Macaques immunized with this modified envelope, termed SF162-delta-V2, but not with the unmodified SF162 envelope, generate antibodies that neutralize several heterologous primary HIV-1 isolates. We propose that the antibodies elicited by the SF162-delta-V2 envelope immunogen will offer protection from heterologous viral challenge, while those elicited by the unmodified SF162 envelope immunogen will offer protection only from the homologous viral challenge. To test this hypothesis macaques will first be immunized with DNA vectors expressing the SIVmac239 Gag and Pol and either the SF162 or SF162-delta-V2 envelope proteins, to elicit cellular responses against multiple antigens and subsequently immunized with the corresponding purified envelope protein to increase the titer of neutralizing antibodies. The animals will then be challenged with the homologous SHIVSF162P4 or the heterologous SHIV89.6P viruses.

T CELL REGENERATION IN PRIMATES (0282)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
STOREK, JAN	MD, PHD	A	MEDICINE/ONCOLOGY	FRED HUTCHINSON CANCER RES CTR, WA USA
L names	MD	A	HEMATOL/ONCOL	
	MD	A	MEDICINE	

AXIS I CODES: 1A, 17, 19 **AXIS II CODES:** 64

ABSTRACT

After hematopoietic cell transplantation (e.g., bone marrow transplantation) patients are susceptible to frequent infections due to very slow recovery of CD4 T cells. We studied whether the recovery of CD4 T cells can be hastened using interleukin-7 (IL7). By comparing4 IL7-treated and 3 placebo-treated baboons, we found that IL improved the recovery of CD4 T cells. This information may contribute to treatments that prevent infection in humans who have had bone marrow transplants in the future.

HEMOLYSIN AND IMMUNOBIOLOGY OF CHANCROID (0289)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.000%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
TOTTEN, PATRICIA	PHD	A	INFECTIOUS DISEASES	HARBORVIEW MED CTR, WA USA
L nones	PHD	A	BIOSTATISTICS	
	PHD	A	MEDICINE	
1	PHD	A	EPIDIMIOLOGY	

AXIS I CODES: 1A, 7A, 18 **AXIS II CODES:** 64, 66, 77, 83

ABSTRACT

H. ducreyi is the causative agent of chancroid, a disease characterized by genital ulcers, and in 50% of cases, inguinal lymphadenopathy. The occurrence of chancroid outbreaks in the United States coupled with its association with the heterosexual transmission of HIV in Africa makes understanding the pathogenesis of this disease imperative so that rational intervention strategies can be devised. We have developed a primate model for chancroid that measures the effect of disease progression through the pustular, ulceral, and resolution stages of disease at a genital site in an animal closely related to humans. We also hypothesize that an H. ducreyi protein, hemolysin, is essential for disease progression and that immunization with hemolysin will prevent disease. Thus, we will use our recently developed primate model to: (1) investigate the local and systemic response to infection, (2) determine the effect of hemolysin on the survival of, and immune response to, this organism, and (3) analyze the contribution of H. ducreyi hemolysin to disease progression. These studies will provide a better understanding of the role of the H. ducreyi hemolysin in the pathogenesis and immunobiology of chancroid and will provide a groundwork on which to base future strategies for vaccine development for chancroid.

IN VIVO ADAPTATION OF SHIVSF162P3 IN PIGTAILED MACAQUES (0324)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.200% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
TSAI, CHE-CHUNG	DVM, PHD	C	NPRC	
	PHD	A	DAIDS	NIAID, NIH, MD USA
	BVS, PHD	C	NPRC	
	PHD	A	DAIDS	NIAID, NIH, MD USA
	DVM, PHD	A	PHYSIOLOGY BIOLOGY	

AXIS I CODES: 1A, 1D, 6, 7B, 17, 19, 23 **AXIS II CODES** 31, 56, 66, 83

ABSTRACT

The majority of new HIV infections are acquired through sexual transmission. Moreover, the vast majority of children with HIV/AIDS are vertically or horizontally infected by their mothers. CCR5-using viruses are frequently associated with sexual transmission of HIV in humans. A pathogenic CCR5-using SHIV (chimeric SIV/HIV) virus would be useful for testing mucosal transmission in the macaque model. In this study, we describe the in vivo adaptation of the parental SHIV162P3 in four pigtailed macaques. The name of SHIV162 Pt refers to adaptation to the pigtailed macaque. Our results showed that SHIV162Pt appears to be adapted and increased its infectivity and pathogenesis in pigtailed macaques. This pathogenic CCR5-using SHIV162Pt would further establish its ability for mucosal transmission in the macaques. Ultimately, this virus stock can be used to improve macaque model for evaluation of topical microbicide candidates.

SPL7013 GELS AS MICROBICIDE INHIBIT VAGINAL TRANSMISSION OF SHIV89.6P IN MACAQUE (0325)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.200% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
TSAI, CHE-CHUNG	DVM, PHD	C	NPRC	
	PHD	A	DAIDS	NIAID, NIH, MD USA
	BVS, PHD	C	NPRC	
	PHD	A	DAIDS	NIAID, NIH, MD USA
	DVM, PHD	A	PHYSIOLOGY BIOLOGY	
	PHD	A	PRODUCT/DRUG DEVELOPMENT	STARPHARMA PTY LTD, AUSTRALIA

AXIS I CODES: 1A, 2, 6, 7B, 12, 17, 19, 23 **AXIS II CODES:** 31, 56, 66, 69, 83, 94

ABSTRACT

SPL7013 potently inhibits strains of HIV-1, SIV, and SHIV in vitro. We evaluated the in vivo efficacy of SPL7013 gel in a mucosal challenge model by exposing female pigtailed macaques to SHIV89.6P. All control macaques except for one in the placebo group were infected within 2 weeks PI and showed high plasma viremia, cell-associated viremia, and dramatic CD4+ cell decline within 4 weeks PI. In contrast, macaques treated with SPL7013 showed a dose-dependent resistance to virus challenge. Five of six macaques treated with 3% SPL7013 and two of six macaques treated with 1% SPL7013 gels were protected from vaginal transmission of SHIV89.6P. Neither SPL7013 nor placebo gels produced any adverse effects in any macaque following the single application in the study. Taken together the results of present and previous studies suggest that SPL7013 can inhibit vaginal transmission of SHIV in a dose-dependent manner; while 5% and 3% SPL7013 gels are effective in blocking transmission, 1% is only marginally effective.

CYNOVIRIN-N AS A MICROBICIDE INHIBITS VAGINAL TRANSMISSION OF SHIV89.6P IN MACAQ (0326)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.200% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
TSAI, CHE-CHUNG	DVM, PHD	C	NPRC	
	PHD	C	NPRC	
	PHD	A	USA CANCER RESEARCH	UNIVERSITY OF SOUTH ALABAMA, AL USA
	BVS, PHD	C	NPRC	
	PHD	A	CENTER FOR CANCER RESEARCH	NCI, MD USA
	DVM, PHD	A	PHYSIOLOGY BIOLOGY	
	PHD	A	INFECTIOUS DISEASES	ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, UK

AXIS I CODES: 1A, 2, 6, 7B, 12, 17, 19, 23 **AXIS II CODES:** 31, 56, 66, 69, 83, 94

ABSTRACT

The cyanobacterial protein cyanovirin-N (CV-N) potently inactivates diverse strains of HIV-1 and other lentiviruses due to irreversible binding of CV-N to the viral envelope glycoprotein gp120. In this study, we show that recombinant CV-N effectively blocks HIV-1Ba-L infection of human ectocervical explants. Furthermore, we demonstrate the in vivo efficacy of CV-N gel in a vaginal challenge model by exposing CV-N-treated female macaques (Macaca fascicularis) to a pathogenic chimeric SIV/HIV-1 virus, SHIV89.6P. All of the placebo-treated and untreated control macaques (8/8) became infected. In contrast, 15 of 18 CV-N-treated macaques showed no evidence of SHIV infection. Further, CV-N produced no cytotoxic or clinical adverse effects in either the in vitro or in vivo model systems. Together these studies suggest that CV-N is a good candidate for testing in humans as an anti-HIV topical microbicide.

CYNOVIRIN-N AS A MICROBICIDE PREVENTS RECTAL TRANSMISSION OF SHIV89.6P IN MACAQU (0327)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.200% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
TSAI, CHE-CHUNG	DVM, PHD	C	NPRC	
	PHD	A	USA CANCER RESEARCH	UNIVERSITY OF SOUTH ALABAMA, AL USA
	BVS, PHD	C	NPRC	
	PHD	A	CENTER FOR CANCER RESEARCH	NCI, MD USA
	DVM, PHD	A	PHYSIOLOGY BIOLOGY	

AXIS I CODES: 1A, 2, 6, 7B, 12, 17, 19, 23 **AXIS II CODES:** 31, 56, 66, 69, 83, 94

ABSTRACT

Cyanovirin-N (CV-N), an 11-kDa cyanobacterial protein, potently inactivates diverse strains of HIV-1, HIV-2, and simian immunodeficiency virus (SIV) and also prevents virus-to-cell fusion, virus entry, and infection of cells in vitro. These properties make CV-N an attractive candidate for use as a topical microbicide to prevent the sexual transmission of HIV. We evaluated the efficacy of gel-formulated, recombinant CV-N as a topical microbicide in male macaques (Macaca fascicularis) that were rectally challenged with a chimeric SIV/HIV-1 virus known as SHIV89.6P. All of the untreated macaques were infected and experienced CD4+ T cell depletion. In contrast, none of the macaques that received either 1% or 2% CV-N gel showed evidence of SHIV89.6P infection. Neither CV-N nor placebo gels produced any adverse effects in any macaque following the rectal application. These results indicate that CV-N gel as a topical microbicide can prevent rectal transmission of SHIV in macaques. These studies encourage clinical evaluation of CV-N as a topical microbicide to prevent sexual transmission of HIV in humans.

BEHAVIORAL AND PHYSIOLOGICAL CONSEQUENCES OF LOSS (0301)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.200% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
WORLEIN, JULIE M	PHD	C	NPRC	
[illegible]	PHD	A	PSYCHIATRY	U COLORADO, CO USA

AXIS I CODES: 1A, 1D, 7B, 15, 17 **AXIS II CODES:** 31, 36, 64, 66

ABSTRACT

There is considerable variability in the rate of progression following infection with HIV in humans. This study investigates the impact of developmental history on disease progression following infection with SIV in a nonhuman primate model. Although a single stressful event encountered early in development (a 2-week maternal separation at 6 months of age) has been shown to impact both behavioral and immunological profiles into adulthood in macaques, it is not known whether these changes have any functional consequences in terms of disease progression. During the past year behavioral profiles, blood profiles, virology, antibody responses, salivary cortisol and dehydroepiandrosterone (DHEA) were followed and necropsy results obtained from subjects with known developmental histories. Data from completed protocols are now available on 19 young adult animals; 11 who underwent a stressful event (maternal separation) at 6 months of age, (SEPS) and 8 who did not undergo a maternal separation and served as controls (CONS). To date we have found that nonseparated control animals produce more antibodies in response to SIV infection than SEPS. Females (regardless of experimental condition) carry a significantly higher viral load after infection than males. We have also found that females have a higher CD4+/CD8+ ratio than males prior to infection, but a lower ratio after infection. In addition, males have higher DHEA levels than females and also a higher DHEA/CORT ratio. These data suggest that higher DHEA levels may serve as a protective factor in males. We have also found that animals with extremely high number of CD16+ lymphocytes prior to and after infection are more susceptible to rapid disease progression and CNS involvement. In addition, we have documented changes in behavioral profiles following infection. These data have implications for predicting response to disease infection in humans and suggest that both developmental history and gender impact disease progression.

DEVELOPMENTAL NEUROAIDS (0302)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.200% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
WORLEIN, JULIE M	PHD	C	NPRC	

AXIS I CODES: 1A, 1D, 7B, 17, 21 **AXIS II CODES** 31, 36, 60, 63E, 64, 66, 77

ABSTRACT

The effects of HIV on cognitive and motor development in infants and children are often devastating. It is difficult to study neurobehavioral sequelae in humans due to a number of confounding factors present in HIV infected populations (maternal drug use, lack of prenatal care, low socioeconomic status, foster care, long periods of hospitalization, etc.). These factors can be avoided by using a nonhuman primate model. The specific aims of this study are to develop nonhuman primate models of neuroAIDS, develop new behavioral and neuroimaging testing procedures for lentivirus infected infants, to assess behavioral changes in infected infants and to provide noninfected social partners for infected infants (these infants also provide control data on behavioral measures). We have developed and confirmed a nonhuman primate model of pediatric neuroAIDS using HIV-2287 . by showing that controls are different from infected infants in a number of behavioral measures including performance on cognitive tasks, gross motor development and visual acuity. In the past year, in collaboration with Dr. Satoshi Minoshima we have also piloted neuroimaging data using both [18F]2-fluoro-2-deoxy-D-glucose (FDG) and [11C] (DTBZ) PET imaging. These data show that infected infants differ from controls in glucose uptake and that the basal ganglia (a primary site of lentivirus infection) are compromised in infected infants. In addition we have piloted new behavioral testing procedures using automated computerized testing. These procedures can be used to test the efficacy of pharmaceutic regimens on central nervous system effects of lentivirus infection.

PILOT SUBPROJECTS

SAFETY AND EFFICACY OF RECOMBINANT ERYTHROPOIETIN (REPO) AS A RESCUE AGENT FOR A (0298)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
JUUL, SANDRA	MD, PHD	A	PEDIATRICS	

AXIS I CODES: 1A

AXIS II CODES: 60, 63C, 77, 92(NEUROPROTECTION)

ABSTRACT

Birth asphyxia occurs in 3-9 of every 1000 live-born infants. About 10 percent of these patients die during their first week of life, and 30 to 40% of the survivors are left with severe and life-long neurodevelopmental handicaps. Despite advances in perinatal medicine, no pharmacologic treatment strategies have yet been found that will lessen the harmful effects of hypoxia on subsequent neurodevelopment. Although some irreversible damage occurs acutely during an asphyxial event, much of the damage to the neonatal brain occurs in the hours immediately following the event. Thus an intervention during this period (3 to 6 hours) might be efficacious in reducing the severity of ongoing brain damage. Indeed, studies in adult rats have demonstrated that the administration of high dose erythropoietin (Epo) up to 6 hours following injury can reduce the brain damage caused by asphyxia, bleeding, or trauma by 50-70%. If a comparable 50% reduction in brain damage of human neonates following birth asphyxia were obtained using high dose Epo therapy, this treatment could save up to 1 million lives annually world wide while substantially lessening the financial and emotional consequences of asphyxia. Non-human neonatal primates provide a superior model of perinatal asphyxia, because their brain structure is much closer to the human neonate than other lower mammals. This allows for the use of sophisticated behavioral assessments to assess their neurodevelopment, as well as imaging techniques. The specific aims of this project are to: 1) establish a model of perinatal asphyxia in the non-human primate, 2) determine whether high dose rEpo will diminish the structural brain damage caused by lack of oxygen preceding birth (perinatal asphyxia) in near-term pigtailed macaques, and 3) determine whether high dose rEpo will decrease the developmental problems caused by perinatal asphyxia in near-term pigtailed macaques.

GENE EXPRESSION CONTROL OF RECONSTRUCTED INFLUENZA (0300)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KATZE, MICHAEL G	PHD	C	MICROBIOLOGY	
[illegible]	PHD	A	MICROBIOLOGY	MNT SINAI SCHOOL OF MED, NY USA
[illegible]	PHD	A	INFLUENZA BRANCH	CENTERS FOR DISEASE CONTROL, GA USA

AXIS I CODES: 1A **AXIS II CODES:** 66

ABSTRACT

Flu viruses are consistently responsible for an average of 20,000 deaths and 114,000 hospitalizations per year. To a great extent, these viruses always stay one step ahead of the available vaccines and people's immunity year after year because they have the ability to either mutate part of their genetic material, or to be transmitted from one species to another. That same genetic variability explains why, occasionally, a flu virus emerges that causes great mortality over several countries: the most famous example is the virus that caused the 1918 pandemic, which resulted in the death of 20-40 millions people worldwide, and therefore killed more people than the "great war". Not only did the 1918 virus caused great morbidity and mortality, but it tended to affect young adults the most, as opposed to other flu viruses which tend to affect the very young or very old instead. For these reasons, and because of its ease of transmission, influenza is high on the list of emerging bio-terrorism agents. Scientists have therefore been very interested in finding out what makes the 1918 virus different from all others, and extensive preliminary research of cells infected in culture has shown that a non-structural protein of the virus (NS1) may be to blame. NS1 down regulates the innate (or first-line) immune response to viral infection, and also prevents the cell from slowing down protein synthesis, which it does in an attempt to prevent replication of the virus. Thanks to recovery of genetic material from cadavers who died from the 1918 pandemic, the original NS1 gene was isolated and made available to incorporate into other flu viruses to study its function independently from the rest of the genes of the 1918 virus. So far, it appears that NS1 is very species-specific, so it is important to study it in a species that is as close to humans as possible. It also seems that its presence and actions affect many genetic processes at the same time, so it is important to study these processes in a context as close to natural conditions as possible. We therefore propose, in the larger stud to follow this series of pilot studies, to compare the clinical course, pathology, and gene expression patterns in several tissues of macaques infected with a mildly pathogenic human strain (the Texas strain) of the flu and the same recombined with one or several genes from the 1918 pandemic. If the virus fitted with the 1918 NS1 gene(s) is significantly more pathogenic than the other, then we will confirm and qualify the importance of the NS1 gene. In addition, with the use of array technology, we will be able to compare the expression of over 13,000 genes during infection in, amongst others, epithelial lung cells, and make important strides in understanding the mechanism of action of the NS1 protein at the genetic level.

SCREENING FOR ANTIVIRAL CONTRACT ANIMALS (0323)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.200% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
TSAI, CHE-CHUNG	DVM, PHD	C	NPRC	
	DVM	C	NPRC	
	BVS, PHD	C	NPRC	
	DVM, PHD	A	PHYSIOLOGY BIOLOGY	

AXIS I CODES: 1A, 1D, 6, 7B, 17, 19 **AXIS II CODES:** 31, 56, 66

ABSTRACT

This project is used to screen macaques for the use in experiments related to the AIDS Therapies contract. It is not itself a research project, but rather is designed to assess the usefulness of macaques for experimental projects. Although macaques used for research were pre-screened negative for SRV, STLV and SIV antigen and antibodies, we have to test their peripheral blood mononuclear cells (PBMCs) that are proven susceptible to SIV or SHIV replication in vitro before the start of any research projects. In 2001, PBMCs obtained from 42 cynomolgus macaques, 22 pigtailed macaques, and 6 Chinese rhesus macaques were tested for susceptibility to SIV or SHIV replication in vitro using coculture techniques, SIV p27 antigen capture ELISA and immuno-flourescence assay. All of the macaques tested were negative for these viruses. These virus- and antibody-free macaques were also tested for their PBMC susceptible to SIV or SHIV replication, and then assigned to the new project or housed separately before they entered clinical trials or other transmission studies with SIV or SHIV. This is on going project that will continue in the coming years.

COLLABORATIVE SUBPROJECTS

DEVELOPMENTAL NEUROTOXICOLOGY PROGRAM (0337)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
BURBACHER, THOMAS M	PHD	C	ENVIRONMENTAL HEALTH	

AXIS I CODES: 1A, 2, 21, 25A, 25B, 25D **AXIS II CODES**36, 41, 54A, 60, 71

ABSTRACT

During 2003,the Developmental Neurotoxicology Program has concentrated on developing the Positron Emission Tomography (PET) procedures to be used with complex reaction time tests. This collaborative project is being done in conjunction with the Neuroscience Core, the PET Imaging Laboratory and the Instrument Development Laboratory. To this end, we have:

1. modified our testing chairs so that the legs of animals are restrained for radioactive infusion during testing,

2. modified our testing chambers for certification of radioactive use,

3. completed training and certification for use of radioactivity by three staff members, including Dr. Burbacher,

4. updated the software for data collection, summary and analysis of our complex reaction time procedures,

5. initiated retraining of the animals on the complex reaction time procedures, and

6. updated protocols to include radioactive infusion and PET procedures in collaboration with Dr. Satoshi Minoshima.

The laboratory also continues to offer training opportunities for students in the area of nonhuman primate operant training and testing. During the year, three undergraduate students have participated in the studies. Finally, personnel in our laboratory continue to actively assist investigators and research staff with the design of new operant procedures. The flexibility and versatility of the computer-driven test chambers allows for the study of many important behavioral processes. Given the individual needs of the investigator, operant test procedures can be designed to provide a means of testing both subtle and frank effects of experimental treatments. During the last year, operant procedures have been developed for several of the early WGTA learning measures. Eventually these operant procedures may replace the more labor intensive WGTA test procedures.

NEURAL CONTROL OF LIMB MOVEMENT (0333)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
FETZ, EBERHARD E	PHD	C	PHYSIOL & BIOPHYS	
	MD	A	PHYSIOL & BIOPHYS	
	PHD	G	PHYSIOL & BIOPHYS	
	MD	A		
	PHD	A	PHYSIOLOGY & BIOPHYSICS	
	PHD	G	PHYSIOLOGY AND BIOLOGY	
	MD	A	PHYSIOLOGY	GIFU UNIVERSITY, JAPAN
	PHD	G	NPRC	
		A	PHYSIOLOGY & BIOPHYSICS	
	MD, PHD	A	NEUROBIOLOGY	DUKE UNIVERSITY, NC USA
	MD, PHD	A	MEDICINE, PHYSIOLOGY	UNIVERSITY OF COPENHAGEN, DENMARK
	MD	A	NEUROL SURG	
	PHD	A	PHYSIOL & BIOPHYS	
	PHD	A	PHYSIOL & BIOPHYS	
	PHD	A	PHYSIOL & BIOPHYS	
	BS	C	NPRC	
	MD, PHD	A	NEUROLOGY	U OF CALIFORNIA SAN FRANCISCO CA USA
	PHD	G	PHYSOLOGY AND BIOLOGY	

AXIS I CODES: 21 **AXIS II CODES**92(NEUROSCIENCE)

ABSTRACT

The Fetz laboratory is investigating the neural mechanisms controlling voluntary hand and forelimb movements in primates. Of particular interest are premotor neurons in motor cortex and spinal cord that generate output effects on muscles, as detected by postspike effects in spike-triggered averages of EMG activity. We have documented the activity of spinal interneurons during a repertoire of multidirectional wrist movements designed to test their roles in producing different muscle synergies. The spatial tuning of spinal neurons tends to be broader than that of cortical neurons. We have also found that in monkeys performing instructed delay tasks spinal neurons, like previously documented cortical neurons, modify their activity in preparation for instructed movements. This is the first evidence that in awake monkeys spinal interneurons show response properties similar to those of cerebral cortex neurons under comparable behavioral conditions.

TRANSPLANTATION & STEM CELL BIOLOGY CORE (0242)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.900%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
GAUR, LAKSHMI	PHD	A		PUGET SOUND BLOOD CENTER, W/ USA
L	MD	A	HEMATOL/ONCOL	
	PHD	C	NPRC	
	MD	A	IMMUNOLOGY	HARVARD, MA USA
	PHD	A	MICROBIOLOGY	UNIVERSITY OF MIAMI, FL USA
	MD	A	MEDICINE	
	PHD	A	MEDICINE	
names	MD, PHD	A	UNKNOWN	VIRGINIA MASON HOSP, WA USA
	PHD	A	OB-GYN	
	MD	A		FRED HUTCHINSON CANCER RES CTR, WA USA
	PHD	A	PATHOLOGY	HARVARD, MA USA
	MD	A	OB/GYN	
	PHD	A	GENETICS	
		A	MEDICINE	

AXIS I CODES: 1A **AXIS II CODES:** 88

ABSTRACT

The goals of the Immunogenetics Core are to provide accurate, state of the art typing of major histocompatibility complex (MHC) alleles as well as make reagents available for paternity testing for both macaques and baboons with the UW-RPRC and its affiliated colonies. Accurate MHC typing is essential for all experiments involving cell and tissue transplantation, AIDS/SIV virology, vaccine studies, and immunology. Further, it is crucial to discern the familial relationships between donors and recipients in transplantation studies. Most important, the MHC typing is essential in identifying animals with desired alleles for various researchers to enable selective breeding by the primate center breeding as a part of Transplantation and Stem Cell Biology Research Resources. We had continued our efforts to improve class I and class II MHC typing by updating the oligoblots with newly identified alleles. We are currently working with One Lambda Inc, Los Angeles to develop high throughput typing for macaques using our probe primer combination in their luminex based typing methods. We have identified a number of class I alleles which are currently being analyzed for proper nomenclature. Along with the newly identified class II alleles, this information is essential in selecting animals with desired haplotypes for various programs such as AIDS/SIV virology, as well as diversify the resource animals by breeding the under represented haplotypes. In the past year the transplantation and stem cell biology core has provided ongoing support for post-natal and pre-natal (fetal) stem cell transplantation models at the WNPRC. The core has assisted in animal acquisition, training, management and procedures.

DIVISION OF AIDS-RELATED RESEARCH (0243)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.700% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
HU, SHIU-LOK	PHD	C	PHARMACEUTICS	
	PHD	C	NPRC	
	PHD	A	VACCINE RESEARCH CTR.	EMORY UNIVERSITY, GA USA
	PHD	A		LONDON SCHOOL OF PHARMACY, UK
	PHD	A	YERKES NPRC	EMORY UNIVERSITY, GA USA
	PHD	G	PATHOBIOLOGY	
	DVM	C	NPRC	
	PHD	A	BIOLOGY	EMORY UNIVERSITY, GA USA
	PHD	A		UNIVERSITY OF SOUTHAMPTON, UK
	PHD	A		CHIRON CORP., CA USA
	MD, PHD	A		NCI, MD USA
	PHD	A		VAX-GEN, INC., CA USA
	PHD	A		SCRIPPS RESEARCH, CA USA
	PHD	A	IMMUNOLOGY	SCRIPPS RESEARCH, CA USA
	PHD	A	PATHOBIOLOGY	NORTHWEST BIOTHERAPEUTICS, WA USA
	PHD	A	MOLECULAR BIOTECHNOLOGY	
	PHD	A	CHEMISTRY	INDIANA UNIVERSITY, IN USA
	PHD	A	MEDICINE	HARVARD, MA USA
	PHD	A		AARON DIAMOND AIDS RSCH CTR. NY USA
	PHD	C	MICROBIOLOGY	
	PHD	A		RXKINETICS, CO USA
	MD	A	LABORATORY MEDICINE	
	MD	A	MEDICINE	
	PHD	A	MICROBIOLOGY	NENPRC, MA USA
	PHD	A		CHIRON CORP., CA USA
	PHD	A		LONDON SCHOOL HYG./TROP. MED., UK
	MD, PHD	A		VRC/NIH, MD USA
	PHD	A	VACCINE DEVELOPMENT	IAVI, NY USA
	PHD	A		VAXGEN, INC., CA USA
	PHD	C	NPRC, PATHOBIOLOGY	
	PHD	A		GENE THERAPY SYSTEMS INC, CA USA
	PHD	C	NPRC	
	PHD	A	MATHEMATICS	UNIVERSITY OF FLORIDA, FL USA

	PHD	A		PUGET SOUND BLOOD CENTER, W/ USA
	PHD	C	NPRC	
	MD	A	MEDICAL ONCOLOGY	
		A		DEF. SCI. TECH. LAB, UK
	PHD	A	PATHOBIOLOGY	SBRI, WA USA
	PHD	A		IDEC PHARM., CA USA
	PHD	A		IDEC, CA USA
	PHD	A	PHARMACEUTICS	
	MD	A		UNIVERSITY COLLEGE, LONDON, UK
	MD	A	NE-NPRC	HARVARD UNIVERSITY, MA USA
	PHD	C	IMMUNOLOGY	
	PHD	C	MICROBIOLOGY	
	MD	A	MEDICINE	
	PHD	A		SWFBR, TX USA
	PHD	A		UNITED BIOMED., NY USA
NAM CS	PHD	A	IMMUNOLOGY	ROSWELL PARK CANCER INST., NY USA
	MD	A	UNKNOWN	UCSF, CA USA
	PHD	A	MICROBIOLOGY	OSEL, INC., CA USA
	MD	A		NCI, MD USA
	PHD	A	PATHOBIOLOGY	
	PHD	A	COMP. MED.	UC DAVIS, CA USA
	PHD	A	TROP. MED.	TULANE, UHSC, LA USA
		A		INT. THERAPEUTICS, WA USA
	MD, PHD	A		FHCRC, WA USA
	MD	A	MEDICINE	
	PHD	A		DUKE UNIVERSITY, NC USA
	PHD	C	NPRC	
	VMD	C	NPRC	
	PHD	A		CORIXA, WA USA
	PHD	A	MICROBIOLOGY	
	PHD	A	PHARMACEUTICS.	UNIVERSITY OF KENTUCKY, KY USA
	PHD	A		IMPER. COLLEGE, UK
	PHD	A	MICROBIOLOGY	
		A	IMMUNOLOGY	CNRS, FRANCE
	PHD	A	OB-GYN	
	MD	A	PATHOLOGY	OR. HEALTH SCI. UNIVERSITY, OR USA
	PHD	A	MATHEMATICS	UNIVERSITY OF FLORIDA, FL USA
	MD	A	PEDIATRICS AND MICROBIOLOGY	CHILDREN'S HOSPITAL, LA USA
	PHD	A		CHIRON CORPORATION, CA USA
	MD, PHD	A	PHARMACEUTICS	CHIRON, ITALY
	PHD	A		DANA FARBER, MA USA

PHD	A		INBIOS, WA USA
PHD	A	EPIDEMIOLOGY	
PHD	A		EMORY UNIVERSITY, GA USA
MD	A	PEDIATRIC INFECTIOUS DISEASE	TULANE UNIVERSITY, LA USA
PHD	A	GENETICS	SWFBR, TX USA
PHD	A	PATHOLOGY	YALE UNIVERSITY, CT USA
MD, PHD	A	DEPT. OF MEDICINE	HARVARD MEDICAL SCHOOL, MA USA
PHD	A	PHARMACEUTICS	
PHD	A		LA JOLLA INST ALLERGY/IMMUNOLOGY, CA USA
PHD	C	PHARMACEUTICS	
PHD	A		SCRIPPS INST., CA USA
PHD	A	PATHOBIOLOGY	SBRI, WA USA
MD	A		BIOJECT, OR USA
PHD	A		UNIVERSITY OF LEEDS, UK
PHD	A		DEF. SCI. TECH. LAB, UK
PHD	A		PSIMEDICA, UK
DVM, PHD	C	NPRC	
PHD	A	PHARMACEUTICS	
PHD	A		INST ANIMAL SCIENCE/HEALTH, NETHERLANDS
PHD	A		GLAXOSMITHKLINE, BELGIUM, BELGIUM
MD	A		BASTYR UNIVERSITY, WA USA
PHD	A	MICROBIOLOGY, IMMUNOLOGY	EMORY UNIV, GA USA
PHD	C	NPRC	
PHD	A	MICROBIOLOGY	LONDON SCHOOL, UK
PHD	A	PARMACY	NATIONAL UNIVERSITY, TAIWAN
MD	A	LABORATORY MEDICINE	

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

ABSTRACT

The overall objective of the AIDS-Related Research Division is to develop and provide scientific expertise and resources to enable efficient and productive use of non-human primates for research aimed at the understanding, treatment, and prevention of AIDS. Currently, the Division conducts three major areas of AIDS-related research through its Core and Affiliate Research Resources: (1) Pathogenesis of HIV and related primate lentiviruses; (2) Design, evaluation, and improvement of candidate vaccines against AIDS; and (3) Evaluation of novel therapeutic and vaccination approaches against AIDS. Highlights include: (1) development of the HIV-2/287 model for neonatal transmission; (2) vaccines against mucosal infection and infection of neonates; (3) further understanding of the mechanisms involved in the generation and maintenance of immunological memory; and (4) structural and functional characterization of novel adjuvants.

In addition to fulfilling its research and training missions, the Division also provides services and resources for in-house and outside investigators. The Virology/Immunology Core provides services, standardized virus stocks, reagents and assays for tissue processing, viral load determination, lymphocyte immunophenotyping, hematology, and serology. The Animal Model and Resource Core provides expertise and non-human primate resources for AIDS

research at WaNPRC. In the past year, this Division provided such expertise and resources for 35 investigators (including 5 in-house investigators and 30 outside Research Affiliates and collaborators), pursuing 44 funded projects, involving a total of 666 animals.

GENOMICS DIVISION (0240)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.700% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
KATZE, MICHAEL G	PHD	C	MICROBIOLOGY	
	PHD	A		INSTITUTE FOR SYSTEMS BIOLOGY WA USA
	PHD	C	NPRC	
	BS	G	MICROBIOLOGY	
		A		ARIAD PHARMACEUTICALS, MA USA
	PHD	A	MICROBIOLOGY	
	MD	A	PATHOLOGY	
	MS	A	MICROBIOLOGY	
	BA	A	MICROBIOLOGY	
		A	CENTRE FOR CELL-MATRIX RESEARC	U OF MANCHESTER, UK
	PHD	A	MICROBIOLOGY	
	MS	G	MICROBIOLOGY	
		A	CANCER IMMUNOLOGY AND AIDS	DANA FARBER CANCER INSTITUTE MA USA
	PHD	A	PATHOBIOLOGY AND IMMUNOLOGY	ORNPRC, OR USA

AXIS I CODES: 1D, 7B, 9 **AXIS II CODES:** 31, 59, 66, 68

ABSTRACT

The Genomics Division provides a national resource for the development of nonhuman primate genomic materials and for the incorporation of functional genomics into nonhuman primate research. The Division consists of four units—Genomic Resources & Virology, Microarray Resources, Proteomic Resources, and Bioinformatic Resources—which encompass the latest advances in genome-based and information technologies. A variety of resources are being provided to the research community, including macaque cDNA libraries and an expressed sequence tag (EST) database of macaque nucleotide sequences. To date, over 9,500 sequences have been generated, representing approximately 3,600 unique genes. A manuscript describing the sequence analysis has been submitted for publication. A prototype microarray that contains over 5,000 macaque cDNAs has been constructed and is being used together with human cDNA microarrays for gene expression studies. Our current emphasis is on profiling the response of human T-cell lines and macaque peripheral blood mononuclear cells to infection with wild type or mutant forms of simian immunodeficiency virus (SIV). Our characterization of SIV infection serves to drive resource development and to enhance our understanding of an important and widely used model in AIDS research. The Proteomics unit, which uses state-of-the-art isotope-coded affinity tag (ICAT) and mass spectrometry technologies for quantitative protein profiling, has recently completed an experiment in which mock- and HIV-infected CEM x 174 cells were partitioned into cytosolic, nuclear, and microsomal fractions, differentially labeled with ICAT reagent, and analyzed by mass spectrometry. Data analysis is in progress, and this information will be integrated with gene expression data. This combination of nonhuman primate genomics, microarrays, and proteomics is unique to the WaNPRC and provides an exceptional opportunity to integrate these data types and to explore the cellular response to SIV infection in unprecedented detail. Information resulting from EST sequencing, microarray, and proteomic analyses is fed into the Bioinformatics unit, which is working to develop an integrated database for data archiving, analysis, and distribution to the research community.

THE WWAMI RCE FOR BIODEFENSE AND EMERGING INFECTIOUS DISEASE (0339)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 0.450%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
MILLER, SAMUEL I.	MD	A	MEDICINE	
	PHD	A		INSTITUTE FOR SYSTEMS BIOLOGY WA USA
	PHD	A		UNIVERSITY OF IDAHO, ID USA
	PHD	A		UNIVERSITY OF IDAHO, ID USA
	PHD	A	MEDICINE	
	PHD	A	MICROBIOLOGY	
names	MD	A	MEDICINE	
	PHD	A	GENOMICS	FHCRC, WA USA
	MD	A	MEDICINE/INFECTIOUS DISEASE	
	MD	A	PEDIATRICS/MEDICINE	
	PHD	A	GENETICS	
	VMD	C	NPRC	
	MD	A	GENOME SCIENCE	
	MD, PHD	A	ANTIGEN DISCOVERY	CORIXA CORPORATION, WA USA
	PHD	A	GENOMICS	FHCRC, WA USA
	MD	A	MEDICINE	HARBORVIEW MEDICAL CENTER, WA USA
	PHD	A	EPIDIMIOLOGY	
1	PHD	A		VETERANS ADMINISTRATION MEDICAL CENTER, ID USA

AXIS I CODES: 1A, 2, 5, 12 **AXIS II CODES**54A, 66, 81

ABSTRACT

The WWAMI RCE will develop a strong program of basic research, education, and training in biodefense and emerging infectious diseases with a focus on Gram-negative pathogens. The objectives are: 1. Development of a regional program supported by modern biotechnology platforms, including proteomics, genomics, and bioinformatics dedicated to studying the biology and pathogenesis of Gram-negative bacterial agents of relevance to biodefense and emerging infectious diseases. The WWAMI RCE will initially focus on Yersinia pestis (YP), Francisella tularensis (FT), and Burkholderia pseudomallei (BP). 2. Development of a regional program to understand in greater detail the pathophysiology of airway infection and inflammation by Gram-negative pathogens. Animal models of airway infection will be utilized, including non-human primates and rodents. 3. Development of a regional program that will study differences in human susceptibility to Gram-negative bacterial agents of relevance to biodefense and emerging infectious diseases. Initial studies will define variability in the response of normal humans of varying genetic backgrounds to LPS from YP, FT, and synthetic LPS derived compounds. 4. Translate information obtained into preclinical testing of vaccine candidates and therapeutics that can be useful in protection against Gram-negative agents of relevance to biodefense and emerging infectious diseases. The initial focus will be on the development of vaccines for YP and the use of synthetic LPS derived compounds as adjuvants and innate immune stimulators that broadly protect against a variety of infectious agents. 5. Utilize the extensive WWAMI regional program in education and training to recruit new investigators and educate trainees about the field of biodefense and emerging infectious diseases. 6. Development of a regional plan to interface with the regional public health network to utilize WWAMI RCE resources in a national emergency.

WANPRC SEMINAR SERIES (0188)

NPRC UNIT: RESEARCH RESOURCES

%NPRC $: 1.200% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
MORTON, WILLIAM R	VMD	C	NPRC	
	FRAC, MD	A	MICROBIOLOGY AND IMMUNOLOGY	UNIVERSITY OF MELBOURNE, AUSTRALIA
	MD	A	UNKNOWN	UCSF, CA USA
	MD, PHD	A		FHCRC, WA USA
	DVM, PHD	A	CALIFORNIA NPRC	U OF CALIFORNIA-DAVIS, CA USA
	PHD	A	INSTITUTE OF VIROLOGY	PHILLIPS UNIVERSITY OF MARBURG, GERMANY
	PHD	A	INST OF VIROLOGY & IMMUNOLOGY	U OF CALIFORNIA-SAN FRANCISCO CA USA
	PHD	A	VACCINE DELIVERY	CHIRON CORPORATION, CA USA
	PHD	A	MICROBIOLOGY	
	MD	A	PATHOLOGY	OR. HEALTH SCI. UNIVERSITY, OR USA
	PHD	A	MICROBIOLOGY	BEN GURION UNIVERSITY, ISRAEL
	MD, PHD		MEDICINE	HARVARD MEDICAL SCHOOL, MA USA
	PHD	A	VETERINARY SCIENCES	U OF TEXAS, TX USA
	MD	A	INTERNAL MEDICINE	U OF IOWA, IA USA
	MD, PHD	A	CELLULAR PATHOLOGY	ARMED FORCES INSTITUTE OF PATHOLOGY, DC USA
	PHD	A	MICROBIOLOGY	LONDON SCHOOL, UK

AXIS I CODES: 7B **AXIS II CODES:** 31, 51, 55

ABSTRACT

The Washington National Primate Research Center hosted several seminars given by scientists who perform cutting edge research. Below are the seminars given during the current fiscal year:

"The Role of Viral Genetics and Hormones in HIV Transmission and Pathogenesis"
"Neutralizing antibodies: potent line of defense against acute and chronic AIDS virus infection"
"Characterization of the 1918 'Spanish' Influenza and lessons for the future."
"Innate and Adaptive Immune Mechanisms contributing to attenuated primate lentiviral vaccine -induced protection in rhesus monkeys challenged intravaginally with SIV"
"HIV/AIDS: The Importance of Innate Immunity in Preventing HIV Infection and Pathogenesis"
"Immunogenicity and Efficacy of DNA and fowlpoxvirus HVI vaccines in macaques"
"Vaccine adjuvants and delivery systems"
"Using Positive Reinforcement Training Techniques to Enhance the Well-being of Primates in Research Settings"
"Replication and Transcription of Filoviruses"
"Therapy and Protection of West Nile Virus Infection"
"CD8+ T cells and HIV infection"
"The plague genome sequence - add DNA, stir and reduce"

"New Insights into Lentiviral Pathogenesis"

"GB Virus C: A common, nonpathogenic persistent human flavivirus that influences HIV disease progression"

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RESEARCH SERVICES

NAME	NON-HOST INSTITUTION: STATE, COUNTRY	# SPECIES: SPECIMEN
ANDREWS, ROBERT G.	FRED HUTCHINSON CANCER RESEARCH CENTER: WA	MACACA NEMESTRINA: TISSUES MACACA NEMESTRINA: CELLS
	FRED HUTCHINSON CANCER RESEARCH CENTER: WA	PAPIO CYNOCEPHALUS: CELLS
	JOHNSON AND JOHNSON: CA	MACACA NEMESTRINA: ORGANS
	TRIAD TECHNOLOGY CENTER: MD	PAPIO CYNOCEPHALUS: OTHERS MACACA FASCICULARIS: TISSUES
	LDS INC.: MN	MACACA FASCICULARIS: ORGANS
	LDS INC.: MN	MACACA NEMESTRINA: ORGANS
	LDS, INC: MN	PAPIO CYNOCEPHALUS: ORGANS
	KANSAS UNIVERSITY MEDICAL CENTER: KS	MACACA FASCICULARIS: TISSUES
	KANSAS UNIVERSITY MEDICAL CENTER: KS	MACACA NEMESTRINA: ORGANS
	KANSAS UNIVERSITY MEDICAL CENTER: KS	MACACA NEMESTRINA: TISSUES
	JOHNSON AND JOHNSON: CA	MACACA NEMESTRINA: TISSUES
	MEDICAL COLLEGE OF WISCONSIN: WI	MACACA NEMESTRINA: ORGANS
	CSDB/NIDCR/NIH: MD	MACACA FASCICULARIS: ORGANS
	CSDB/NIDCR/NIH: WI	MACACA FASCICULARIS: TISSUES
	CSDB/NIDCR/NIH: MD	MACACA NEMESTRINA: ORGANS
	CSDB/NIDCR/NIH: MD	MACACA NEMESTRINA: TISSUES
	U OF ALABAMA-BIRMINGHAM: AL	MACACA FASCICULARIS: ORGANS
	PUGET SOUND BLOOD CENTER: WA	MACACA NEMESTRINA LEONINA: CELLS
	PUGET SOUND BLOOD CENTER: WA	MACACA NEMESTRINA: ORGANS
	PUGET SOUND BLOOD CENTER: WA	MACACA NEMESTRINA: TISSUES
		MACACA NEMESTRINA: CELLS MACACA FASCICULARIS: ORGANS MACACA FASCICULARIS: TISSUES MACACA FASCICULARIS: TISSUES MACACA NEMESTRINA: ORGANS MACACA NEMESTRINA: TISSUES
	FRED HUTCHINSON CANCER RESEARCH CENTER: WA	PAPIO CYNOCEPHALUS: CELLS
	FRED HUTCHINSON CANCER RESEARCH CENTER: WA	PAPIO CYNOCEPHALUS: TISSUES
	SCIMEDX CORP: NJ	MACACA FASCICULARIS: ORGANS
	SCIMEDX CORP: NJ	MACACA FASCICULARIS: TISSUES

SCIMEDX CORP: NJ	MACACA NEMESTRINA: ORGANS
SCIMEDX CORP: NJ	MACACA NEMESTRINA: TISSUES
SCIMEDX CORP: NJ	PAPIO CYNOCEPHALUS: ORGANS
KALEIDOS PHARMA INC.: WA	MACACA FASCICULARIS: OTHERS
	MACACA FASCICULARIS: ORGANS
	MACACA NEMESTRINA: ORGANS
	MACACA FASCICULARIS: CELLS
	MACACA FASCICULARIS: OTHERS
	MACACA MULATTA: CELLS
	MACACA NEMESTRINA: CELLS
	MACACA NEMESTRINA: OTHERS
	PAPIO CYNOCEPHALUS: CELLS
	MACACA NEMESTRINA: ORGANS
	MACACA FASCICULARIS: ORGANS
	MACACA NEMESTRINA: OTHERS
	MACACA NEMESTRINA: TISSUES
BATTELLE TOXICOLOGY NORTHWEST: WA	MACACA FASCICULARIS: OTHERS
PUGET SOUND BLOOD CENTER: WA	MACACA FASCICULARIS: ORGANS
PUGET SOUND BLOOD CENTER: WA	MACACA NEMESTRINA: TISSUES
PUGET SOUND BLOOD CENTER: WA	PAPIO CYNOCEPHALUS: ORGANS
	MACACA NEMESTRINA: TISSUES
	MACACA NEMESTRINA: TISSUES
	PAPIO CYNOCEPHALUS: ORGANS
	PAPIO CYNOCEPHALUS: TISSUES
PROCELL CORP: MD	MACACA FASCICULARIS: ORGANS
MOLECULAR TOXICOLOGY, INC: NC	MACACA FASCICULARIS: CELLS
MOLECULAR TOXICOLOGY, INC.: NC	MACACA FASCICULARIS: ORGANS
MEDICAL COLLEGE OF GEORGIA: GA	MACACA FASCICULARIS: OTHERS
U OF PENNSYLVANIA SCHOOL OF MEDICINE: PA	MACACA NEMESTRINA: OTHERS
FRED HUTCHINSON CANCER RESEARCH INSTITUTE: WA	PAPIO CYNOCEPHALUS: ORGANS
FRED HUTCHINSON CANCER RESEARCH INSTITUTE: WA	PAPIO CYNOCEPHALUS: TISSUES
AARON DIAMOND AIDS RESEARCH CENTER: NY	MACACA FASCICULARIS: ORGANS
AARON DIAMOND AIDS RESEARCH CENTER: NY	MACACA FASCICULARIS: TISSUES
BAYER CO. RESEARCH CENTER: CT	MACACA FASCICULARIS: ORGANS
BAYER CO. RESEARCH CENTER: CT	PAPIO CYNOCEPHALUS: ORGANS
BAYER CO. RESEARCH CENTER: CT	MACACA NEMESTRINA: TISSUES
BAYER CO. RESEARCH CENTER: CT	MACACA NEMESTRINA: ORGANS

CORIELL CELL REPOSITORIES: NJ	MACACA FASCICULARIS: OTHERS
CORIELL CELL REPOSITORIES: NJ	MACACA FASCICULARIS: ORGANS
CORIELL CELL REPOSITORIES: NJ	PAPIO CYNOCEPHALUS: ORGANS
CORIELL CELL REPOSITORIES: NJ	PAPIO CYNOCEPHALUS: TISSUES
CORIELL CELL REPOSITORIES: NJ	PAPIO CYNOCEPHALUS: CELLS
CORIELL CELL REPOSITORIES: NJ	MACACA FASCICULARIS: CELLS
CORIELL CELL REPOSITORIES: NJ	MACACA NEMESTRINA: TISSUES
CORIELL CELL REPOSITORIES: NJ	MACACA FASCICULARIS: TISSUES
CORIELL CELL REPOSITORIES: NJ	PAPIO CYNOCEPHALUS: OTHERS
CORIELL INSTITUTE FOR MEDICAL RESEARCH: NJ	PAPIO CYNOCEPHALUS: ORGANS
CORIELL INSTITUTE FOR MEDICAL RESEARCH: NJ	PAPIO CYNOCEPHALUS: TISSUES
ENDOCYTE, INC.: IN	MACACA FASCICULARIS: ORGANS
ENDOCYTE, INC.: IN	MACACA FASCICULARIS: TISSUES
GENZYME: MA	MACACA FASCICULARIS: CELLS
GTX, INC.: TN	MACACA NEMESTRINA: CELLS
HEPATOTECH INC.: NC	PAPIO CYNOCEPHALUS: ORGANS
HEPATOTECH INC.: NC	MACACA FASCICULARIS: CELLS
ICOS CORPORATION: WA	MACACA FASCICULARIS: OTHERS
ICOS CORPORATION: WA	MACACA FASCICULARIS: ORGANS
ICOS CORPORATION: WA	MACACA NEMESTRINA: ORGANS
ICOS CORPORATION: WA	MACACA NEMESTRINA: TISSUES
ICOS CORPORATION: WA	PAPIO CYNOCEPHALUS: ORGANS
MARDX DIAGNOSTICS: CA	PAPIO CYNOCEPHALUS: TISSUES
MARDX DIAGNOSTICS, INC.: CA	MACACA FASCICULARIS: ORGANS
MARDX DIAGNOSTICS, INC.: CA	MACACA FASCICULARIS: TISSUES
MARDX DIAGNOSTICS, INC.: CA	MACACA NEMESTRINA: TISSUES
MEDICA: CA	MACACA FASCICULARIS: ORGANS
MEDICA: CA	MACACA NEMESTRINA: ORGANS
MEDICA: CA	PAPIO CYNOCEPHALUS: TISSUES
MEDICA: CA	MACACA NEMESTRINA: TISSUES
MEDICA: CA	MACACA FASCICULARIS: TISSUES
MEDICA: CA	PAPIO CYNOCEPHALUS: ORGANS
PHENOPATH LABORATORIES: WA	MACACA NEMESTRINA: ORGANS
SCIMEDX CORP: WA	MACACA NEMESTRINA: ORGANS
SCIMEDX CORP: WA	PAPIO CYNOCEPHALUS: ORGANS
SCIMEDX CORP: WA	PAPIO CYNOCEPHALUS: TISSUES
SCIMEDX CORP: WA	MACACA NEMESTRINA: TISSUES
SKELETECH, INC.: WA	MACACA FASCICULARIS: OTHERS
TARGETED GENETICS CORP: WA	MACACA FASCICULARIS: TISSUES
TARGETED GENETICS CORP.: WA	MACACA FASCICULARIS: ORGANS

ZYMOGENETICS, INC.: WA	MACACA FASCICULARIS: ORGANS
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0275	‡ In press publication
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	‡ In press publication
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Books	
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‡ In press publication

In press publication

0333 In press publication

0296 In press publication

In press publication

0302 ‡ In press publication

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0242 ‡ In press publication

0312, 0333 ‡ In press publication

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[In press publication]

0309 ‡ [In press publication]

‡ [In press publication]

0301 ‡ [In press publication]

0302 ‡ [In press publication]

0243 ‡ [In press publication]

SOURCE OF INVESTIGATORS' SUPPORT

NON-FEDERAL

FOUNDATION

INVESTIGATOR ORGANIZATION	GRANT/CONTRACT	TOTAL FUNDING	SPID
DACEY, DENNIS M			
[private funding]		$ 35,000	0290,0292,0293,0294
FETZ, EBERHARD E			
[private funding]		$ 36,730	0315
[private funding]		$ 365,000	
JAGADEESH, BARATHI			
[private funding]		$ 20,000	0328
[private funding]		$ 75,000	0328
[private funding]		$ 75,000	0328
JUUL, SANDRA			
[private funding]	OPTIMIZING IRON STATUS IN THE PRETERM NEONATE	$ 3,000	
MINOSHIMA, SATOSHI			
[private funding]		$ 50,000	
ROBINSON, FARREL R			
[private funding]		$ 7,874	0296
SHADLEN, MICHAEL N			
[private funding]		$ 539,459	0297
	FOUNDATION	$ 1,207,063	

private funding

INDUSTRY

INVESTIGATOR ORGANIZATION	GRANT/CONTRACT	TOTAL FUNDING	SPID
KATZE, MICHAEL G			
[ ]		$ 98,656	
PATTON, DOROTHY L			
[ ]	MSA-02-315	$ 288,675	0275
	INDUSTRY	$ 387,331	

private funding

OTHER NON FEDERAL

INVESTIGATOR ORGANIZATION	GRANT/CONTRACT	TOTAL FUNDING	SPID
[name]			
[private funding]		$ 124,000	
MORTON, WILLIAM R			
[private funding]		$ 5,000,000	0188,0204

OTHER NON FEDERAL		$	5,124,000

FEDERAL

INVESTIGATOR ORGANIZATION	GRANT/CONTRACT	TOTAL FUNDING	SPID
FEDERAL - NON PHS			
BURBACHER, THOMAS M			
(Private funding)		$ 1,324,454	0309
FEDERAL - NON PHS		$ 1,324,454	
FEDERAL - PHS			
NIH	5R33CA093302-03	$ 563,814	
NIH	5R01AI055996-02	$ 419,155	
NIH	1U19AI057266-01	$ 1,618,735	
NIH	5R37AI030048-13	$ 342,000	
NIH	5R01AI049532-03	$ 427,388	
NIH	1R01AI055996-01	$ 266,489	
NIH	5R01HL063652-05	$ 266,000	
NIH	5U24DK058813-03	$ 492,500	
NIH	5R21AI053488-02	$ 160,000	
NIH	5R01AI057029-02	$ 629,365	
NIH	1R01AI057029-01	$ 242,997	
NIH	1R01NS039178	$ 431,897	0306
NIH	1P01AI146177-01	$ 14,778	
NIH	2P01AI026503-12	$ 1,679,694	
NIH	5R01CA087061-03	$ 294,774	
NIH	5U24RR018114-02	$ 956,922	
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NIH	5R01NS044565-02	$ 396,713	0334,0335
NIH	5R24HD039629-04	$ 958,711	
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NIH	5R01AI049342-02	$ 484,010	

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NIH	3P50HD033812-09S1	$	458,000	
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NIH	5P01AI052106-02	$	168,046	
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NIH	5R01NS040823-02	$ 352,287		
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NIH	5U19HD035465-07	$ 1,979,740		
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NIH	5R21NS041347-03	$ 192,476		
EVANS, DAVID T.				
NIH	1K22AI052751-01	$ 162,000	0308	
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NIH	R21HD042213-01	$	337,500	
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KANEKO, CHRIS R S				
NIH	5R01EY006558-16	$	410,669	0284
KATZE, MICHAEL G				
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NIH	5P30DA015625-02	$	1,820,909	
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NIH	5R01NS034189-09	$	542,920	
NIH	5R01DK055178-04	$	669,192	
NIH	5U19AI051728-02	$	922,666	
NIH	1R01HL074162-01	$	432,500	
NIH	1R21DK063324-01	$	173,000	
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NIH	5T32RR007019-22	$	331,723	
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NIH	5R24RR014555-05	$	703,649	
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MILLER, SAMUEL I.				
NIH	5U54AI057141-02	$	10,490,069	0339
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MINOSHIMA, SATOSHI				
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NIH	5R01NS035533-07	$	341,000	
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MORTON, WILLIAM R				
NIH	5P40RR001240-24	$	120,000	
NIH	1R13RR018632-01	$	71,413	
NIH	1G20RR018389-01	$	699,384	
NIH	N01AI015431-11	$	1,991,977	0283,0318,0321,0329
NIH	1G20RR014359	$	699,980	
NIH	1P01AI057005-01	$	834,370	
NIH	5R01AI047734-04	$	507,865	
NIH	1R21AI051147-01A2	$	212,152	
NIH	5R01NS036860-07	$	250,250	
NIH	1C06RR016540-01A1	$	2,000,000	
NIH	5P51RR000166-42	$	10,631,169	
NIH	5R21DK063423-02	$	438,750	
NIH	5R01AR037296-16	$	302,765	
NIH	2R01EY005603-19	$	197,015	
NIH	2T32MH020016-06	$	706,400	
NIH	5R01DE013810-03	$	358,050	
NIH	1R21AI060407-01	$	240,952	
NIH	5R01AI046254-06	$	306,289	
NIH	5R01AI052731-02	$	398,000	
NIH	5R01AI044595-06	$	352,032	
NOVAK, MELINDA				
NIH	5R24RR011122-07	$	365,010	
NIH	5R37HD017427-37	$	286,582	
NIH	5R01DC003944-05	$	289,019	
NIH	3T32NS007144-23S1	$	137,544	

NIH	3U54HG002043-05S1	$	125,854	
NIH	2U54HG002043-05	$	1,814,522	
NIH	5P50HG002351-03	$	3,040,000	
NIH	5R01CA051080-14	$	297,789	
NIH	5R01AI043844-04	$	538,412	
NIH	5R37AI038518-10	$	511,053	
NIH	5R01DE012939-03	$	109,080	
NIH	1K23NS045832-01	$	166,271	
PATTON, DOROTHY L				
NIH	5R01AI022082-14	$	331,887	0272
NIH	U19AI051661-01	$	204,592	0276
NIH	5P01AI039061-08	$	241,317	0273
NIH	N01AI095388-01	$	850,934	0274
PERLMUTTER, STEVEN I I				
NIH	5R01NS040867-04	$	320,000	0304,0313
NIH	1R01AI054292-01	$	692,773	
NIH	5R01EY000901-30	$	445,905	
NIH	5R01AI053193-02	$	432,500	
ROBINSON, FARREL R				
NIH	5R01EY010578-09	$	244,939	
NIH	1R03EY014590-01	$	160,000	0296
NIH	3P01AI043045-05S1	$	1,119,409	
NIH	5P01AI049364-03	$	3,892,120	
NIH	5R01AI046275-05	$	241,067	
NIH	5R01AI024030-16	$	297,000	
NIH	1R21AI052844-01A1	$	222,750	
NIH	5R24RR015383-04	$	317,120	
NIH	5R01RR008781-10	$	308,000	
NIH	5R01MH065462-02	$	396,000	
NIH	5R37AI040357-09	$	327,000	
NIH	5R01AI045510-06	$	623,174	
NIH	2R37AI040357-08	$	163,500	
NIH	2R01AI045510-05	$	637,975	
NIH	3R01CA091760-02S1	$	100,000	
NIH	5R01RR013154-07	$	380,000	
NIH	5R01CA091760-02	$	296,690	
NIH	5K02AI049275-03	$	98,658	

NIH	5P30DC004661-04	$ 794,489	
NIH	5R01DC003829-05	$ 413,701	
NIH	5R01DC000395-18	$ 353,562	
NIH	5T32HD007233-22	$ 248,551	
NIH	5R01AI052299-02	$ 335,250	
NIH	5R01AI022498-18	$ 242,281	
NIH	1R01AI056073-01	$ 95,359	
NIH	5R37AI034266-09	$ 689,455	
NIH	5P01AI048240-04	$ 1,966,903	
NIH	5R01RR014180-05	$ 739,280	
NIH	5R01DE012937-05	$ 386,329	
NIH	1R21AI054183-01	$ 497,060	
SACKETT, GENE P			
NIH	5R01MH064647-02	$ 357,194	0278
NIH	1R01AI054423-01A1	$ 384,223	
NIH	1R33GM068152-01	$ 279,657	
NIH	5R01NS041298-03	$ 584,494	
NIH	5R01AG021544-02	$ 315,000	
SHADLEN, MICHAEL N			
NIH	5R01EY011378-08	$ 193,300	0297
NIH	5R01AT000864-03	$ 384,904	
NIH	1R01HL062422	$ 340,595	
NIH	5R01HL054972-07	$ 265,300	
NIH	5R01LM007292-03	$ 632,991	
NIH	5R21DA015450-02	$ 155,870	
NIH	5R24RR005090-14	$ 453,048	
NIH	2R24RR005090-13A2	$ 433,737	
NIH	1F32EY015046-01	$ 56,308	
NIH	5R01DE013813-03	$ 848,261	
STAMATATOS, LEONIDAS			
NIH	5R01AI051217-03	$ 586,676	0317
NIH	5R21AI053810-02	$ 268,500	
NIH	5R01AI047708-05	$ 324,527	

NIH	5U01HL066947-04	$ 2,744,642	
NIH	1U01HG003161-01	$ 2,263,508	
NIH	5P01HL053750-10	$ 1,974,038	
NIH	5P01DK055820-04	$ 1,051,960	
NIH	5R37DK045365-12	$ 563,969	
NIH	2R01HL020899-26	$ 525,461	
NIH	5T32AI007044-28	$ 367,838	
NIH	2P01DK053369-06A1	$ 1,101,358	
NIH	1R01AI058740-01	$ 663,858	
NIH	5R01NS042874-02	$ 376,438	
NIH	2R01HD027142-10A1	$ 204,660	
NIH	5T32HD007453-10	$ 152,738	
NIH	1R01DK061517-01A1	$ 197,420	
NIH	2R01DC003696-06A1	$ 207,773	
STOREK, JAN			
NIH	5R01HL069710-03	$ 442,704	0282
NIH	5R01AI046108-05	$ 299,316	
NIH	5R37AA001455-28	$ 223,216	
NIH	2R01AA010836-06A2	$ 306,088	
NIH	5R01NS024328-17	$ 663,551	
NIH	5R01MH056661-07	$ 327,726	
NIH	5T32GM008806-03	$ 246,516	
NIH	2R01AR045203-06	$ 361,195	
NIH	2R01AR045113-06	$ 402,021	
NIH	5R01AI050619-03	$ 196,350	
NIH	5R01EY004470-21	$ 338,950	
NIH	5R01DC003805-05	$ 313,729	
NIH	5R01DC002739-08	$ 385,086	
NIH	1R01DC006305-01	$ 492,065	
NIH	5P41RR013642-06	$ 2,389,497	
NIH	5P20MH065166-02	$ 1,019,856	
NIH	5R01MH052083-08	$ 343,125	
NIH	5T32MH019950-08	$ 179,067	
NIH	5R01LM005639-08	$ 346,414	
NIH			
TOTTEN, PATRICIA			
NIH	5R01AI048634-02	$ 372,073	

NIH	5R01AI047880-02	$	341,100	0289
TSAI, CHE-CHUNG				
NIH	1N01AI015450	$	2,045,000	0323,0324,0325,0326
NIH	5R21MH063641-03	$	151,600	
NIH	5P50HD044404-02	$	1,123,222	
NIH	5R01GM054447-12	$	325,415	
NIH	5R01MH060974-10	$	282,298	
NIH	5R01EY002091-26	$	332,423	
NIH	5R01AI050217-02	$	510,808	
NIH	5R01MH062349-03	$	271,250	
NIH	3R01DA012881-04S1	$	80,803	
NIH	5R01NR001075-18	$	606,941	
NIH	5R01DA012881-04	$	1,013,739	
NIH	5K01AT000065-04	$	93,383	
NIH	5R01DC000396-18	$	304,344	
NIH	5R01EY004367-21	$	313,563	
NIH	2P30EY001319-29	$	629,909	
NIH	1R01EY014375-01	$	1,998,922	
NIH	5P20MH062009-04	$	1,127,541	
NIH	5R01EY012991-04	$	284,000	
NIH	5U01AA013499-02	$	318,907	
NIH	5R01HL065898-04	$	250,205	
NIH	5R01HD039454-04	$	269,657	
NIH	5R01HD018184-24	$	263,115	
NIH	5T32CA009537-17	$	275,485	
NIH	2T32AI007411-11	$	222,601	
NIH	5P30EY001730-28	$	349,177	
NIH	5R01CA075922-07	$	672,498	
NIH	5R01EY006837-17	$	402,400	
NIH	1R01EY014596-01	$	370,650	
	FEDERAL - PHS	$	235,855,294	
	FEDERAL	$	237,179,748	
TOTAL FUNDING:		**$**	**243,898,142**	

RESOURCE SUMMARY: SUBPROJECTS

The following only includes information associated with subprojects.

	Mgmt. A	Research B	Pilot C	Collab. D	Total (excludes
Number of Subprojects	18	61	3	7	89
Number of Investigators	302	153	8	167	541
Number of Published	25	67	1	34	120
Number In Press	7	17	1	10	33
%AIDS of NPRC Dollars	10.900%	35.100%	1.200%	4.600%	51.800%
%Non-AIDS of NPRC Dollars	9.650%	33.600%	1.800%	3.150%	48.200%
Total Percent of NPRC Funds Awarded	20.550%	68.700%	3.000%	7.750%	100.000%

RESOURCE SUMMARY: ADMINISTRATIVE

PERSONNEL	On Subprojects	Not On Subprojects
Core Personnel		
DOCTORAL LEVEL SCIENTISTS (C)	60	21
Core Personnel	60	21
Non-Core Personnel		
AFFILIATED (A)	450	30
GRADUATE STUDENT/POST DOCTORAL SCIENTIST (G)	27	7
Others	4	0
Non-Core Personnel	481	37
Personnel Total:	541	58

ACCESS BY NON-NPRC PERSONNEL

GEOGRAPHICAL USAGE BY INVESTIGATORS AT NON-HOST INSTITUTIONS

Foreign Investigators by Country	**57**
AUSTRALIA	3
BELGIUM	2
CHINA	2
DEMOCRATIC REPUBLIC OF CONGO	1
DENMARK	2
FRANCE	1
GERMANY	3
INDIA	2
INDONESIA	6
IRAN	1
ISRAEL	1
ITALY	1
JAPAN	5
NEPAL	1
NETHERLANDS	1
RUSSIA	3
SINGAPORE	3
TAIWAN	1
THAILAND	1
UK	17
USA Investigators by State	**221**
AL	4
AZ	1
CA	46
CO	2
CT	2
DC	3
FL	3
GA	9
IA	1
ID	3
IL	5
IN	2
KY	2
LA	5
MA	17
MD	23
MN	2
MO	2
NC	3
NH	1
NJ	7
NM	3
NY	10
OH	1
OK	2
OR	6
PA	8
TN	4
TX	9
VT	1
WA	33
WI	1
Total Investigators at Non Host Institutions:	**278**

RESEARCH SERVICES

Scientists Provided with Services	32
Services Provided	

RESEARCH SERVICES BY COUNTRY

Research Services to USA Investigators by State	**20**
AL	1
CA	2
GA	1
KS	1
MD	3
MN	1
NC	1
NJ	1
PA	1
WA	7
WI	2
Research Services to Host Investigators	**12**
Total Research Services:	**32**

INFRASTRUCTURE TABLE

GRANT REPORTED UNITS		**%NPRC USE**
ADMINISTRATIVE		26.600%
COLONY HEALTH		5.000%
PRIMATE RESOURCES		21.800%
RESEARCH RESOURCES		46.600%
	TOTAL NPRC:	**100.00%**

RESEARCH TABLE

UNITS GENERATED BY SUBPROJECTS		**%NPRC USE**
ADMINISTRATIVE		3.700%
COLONY HEALTH		8.000%
PRIMATE RESOURCES		5.500%
RESEARCH RESOURCES		82.800%
	TOTAL NPRC:	**100.000%**

RESOURCE SUMMARY: PUBLICATION/SUPPORT

PUBLICATIONS

	Cited	Not Cited	Total
Published			
Abstracts	38	0	38
Books	10	0	10
Journals	335	20	355
In Press			
Abstracts	8	0	8
Books	8	8	16
Journals	27	5	32
Total	426	33	459

INVESTIGATOR SUPPORT

NON-FEDERAL

		$ 5,124,000
FOUNDATION		$ 1,207,063
INDUSTRY		$ 387,331
	NON-FEDERAL	**$ 6,718,394**

FEDERAL

NON-PHS		
EPA		$ 1,324,454
	NON-PHS	**$ 1,324,454**
PHS		
AA		$ 2,172,386
AG		$ 1,168,260
AI		$ 110,310,395
AR		$ 1,065,981
AT		$ 478,287
CA		$ 5,411,222
DA		$ 3,738,289
DC		$ 3,553,768
DE		$ 2,911,036
DK		$ 7,001,187
ES		$ 5,430,079
EY		$ 9,604,986
GM		$ 2,130,580
HD		$ 15,769,917
HG		$ 7,243,884
HL		$ 8,449,981
LM		$ 1,282,587
MH		$ 8,911,955

NR		$	606,941
NS		$	8,139,290
RR		$	28,792,158
TW		$	1,682,125
	PHS	**$**	**235,855,294**
	TOTAL SUPPORT	**$**	**243,898,142**

COLONY STATISTICS

Base Breeding Colony Only

Note: These animals are supported by NCRR Comparative Medicine.

[1]Genus Species	May-03	[2]Live Births	[3]Other Additions	Exper. Use	[4]Other Reduct.	[5]Sold or Trans.	[6]Trans. in Center	Apr-04
MACACA FASCICULARIS								
Adult Females	12	0	0	0	0	0	11	1
Adult Males	3	0	0	0	0	0	1	2
MACACA MULATTA								
Infants/Juveniles	17	0	0	0	0	17	0	0
MACACA NEMESTRINA								
Adult Females	388	0	83	0	26	9	22	414
Adult Males	57	0	16	0	3	3	7	60
Infants/Juveniles	322	158	40	0	111	21	17	371
Gender Undetermined	3	0	5	0	0	0	0	8
PAPIO CYNOCEPHALUS								
Adult Females	211	0	20	0	7	5	1	218
Adult Males	31	0	1	0	2	7	0	23
Infants/Juveniles	252	91	0	0	61	0	5	277
Gender Undetermined	1	0	0	0	0	0	1	0
	1,297	**249**	**165**	**0**	**210**	**62**	**65**	**1,374**

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 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-04
MACACA FASCICULARIS								
Adult Females	151	0	16	33	0	0	0	134
Adult Males	67	0	4	18	1	0	0	52
Infants/Juveniles	4	0	1	1	3	0	0	1
Gender Undetermined	2	0	0	0	0	0	0	2
MACACA MULATTA								
Adult Females	49	0	3	0	1	0	0	51
Adult Males	51	0	19	6	0	0	0	64
Infants/Juveniles	29	0	0	3	5	0	0	21
Gender Undetermined	1	0	0	0	0	0	0	1
MACACA NEMESTRINA								
Adult Females	202	0	28	52	7	0	0	171
Adult Males	98	0	36	11	3	0	0	120
Infants/Juveniles	107	35	17	13	34	7	0	105
Gender Undetermined	20	0	0	3	1	0	0	16
PAPIO CYNOCEPHALUS								
Adult Females	25	0	1	8	0	0	0	18
Adult Males	5	0	6	1	0	0	0	10
Infants/Juveniles	18	0	5	7	6	0	0	10
Gender Undetermined	1	0	1	1	0	0	0	1
	830	**35**	**137**	**157**	**61**	**7**	**0**	**777**

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

AIDS-RELATED RESEARCH

SPID(s): 0282, 0283, 0305, 0306, 0307, 0308, 0317, 0318, 0319, 0320, 0321, 0322, 0323, 0324, 0325, 0326, 0327

The overall objective of the AIDS-Related Research Division is to develop and provide scientific expertise and resources to enable efficient and productive use of non-human primates for research aimed at the understanding, treatment, and prevention of AIDS. Currently, the Division conducts three major areas of AIDS-related research through its Core and Affiliate Research Resources: (1) Pathogenesis of HIV and related primate lentiviruses; (2) Design, evaluation, and improvement of candidate vaccines against AIDS; and (3) Evaluation of novel therapeutic and vaccination approaches against AIDS. Highlights include: (1) development of the HIV-2/287 model for neonatal transmission; (2) vaccines against mucosal infection and infection of neonates; (3) further understanding of the mechanisms involved in the generation and maintenance of immunological memory; and (4) structural and functional characterization of novel adjuvants.

In addition to fulfilling its research and training missions, the Division also provides services and resources for in-house and outside investigators. The Virology/Immunology Core provides services, standardized virus stocks, reagents and assays for tissue processing, viral load determination, lymphocyte immunophenotyping, hematology, and serology. The Animal Model and Resource Core provides expertise and non-human primate resources for AIDS research at WaNPRC. In the past year, this Division provided such expertise and resources for 35 investigators (including 5 in-house investigators and 30 outside Research Affiliates and collaborators), pursuing 44 funded projects, involving a total of 666 animals.

Publications:

E In press publication

E In press publication

TSAI, CHE-CHUNG;EMAU, PETER;JIANG, YONGHOU;TIAN, BAOPING;MORTON, WILLIAM R;GUSTAFSON, KIRK R;BOYD, MICHAEL R Cyanovirin-N gel as a topical microbicide prevents rectal transmission ofSHIV89.6P in macaques. AIDS Res Hum Retroviruses 19 535-41 2003

TSAI C-C, EMAU P, JIANG YH, TIAN BP, MORTON WR, GUSTAFSON KR, BOYD MR (2003). Cyanovirin-N gel as a topical microbicide prevents rectal transmission of SHIV89.6P in macaques. AIDS Res Hum Retroviruses 19 (7).

KINMAN, LOREN;BRODIE, SCOTT J;TSAI, CHE CHUNG;BUI, TOT;LARSEN, KAY;SCHMIDT, ANN;ANDERSON, DAVID;MORTON, WILLIAM R;HU, SHIU-LOK;HO, RODNEY J Y Lipid-drug association enhanced HIV-1 protease inhibitor indinavirlocalization in lymphoid tissues and viral load reduction: a proof ofconcept study in HIV-2287-infected macaques. J Acquir Immune Defic Syndr 34 387-97 2003

GRAY, RONALD H;LI, X*IANBIN;WAWER, MARIA J;GANGE, STEPHEN J;SERWADDA, DAVID;SEWANKAMBO, NELSON K;MOORE, RICHARD;WABWIRE-MANGEN, FRED;LUTALO, TOM;QUINN, THOMAS C Stochastic simulation of the impact of antiretroviral therapy and HIVvaccines on HIV transmission; Rakai, Uganda. AIDS 17 1941-51 2003

VISCIDI, RAPHAEL P;AHDIEH-GRANT, LINDA;SCHNEIDER, MICHAEL F;CLAYMAN, BARBARA;MASSAD, L STEWART;ANASTOS, KATHRYN M;BURK, ROBERT D;MINKOFF, HOWARD;PALEFSKY, JOEL;LEVINE, ALEXANDRA;STRICKLER, HOWARD Serum immunoglobulin A response to human papillomavirus type 16 virus-likeparticles in human immunodeficiency virus (HIV)-positive and high-riskHIV-negative women. J Infect Dis 188 1834-44 2003

PATTON DL, TSAI CC, COSGROVE SWEENEY Y, SAIFUDDIN M, DONCEL GF. Establishing a Chlamydia + SHIV Co-infection Model in Nonhuman Primates: Preliminary Data. Microbicides 2004, London, England. March 28-31, 2004

In press publication

In press publication

In press publication

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BUCKNER, C., L. G. GINES, C. J. SAUNDERS, L. VOJTECH, I. SRIVASTAVA, A. GETTIE, R. BOHM, J. BLANCHARD, S. W. BARNETT, J. T. SAFRIT AND L. STAMATATOS. 2004. Priming of B anti-HIV envelope responses by vaccination is essential for the long lasting containment of viral replication in macaques infected with an R5-tropic SHIV isolate. Virology. 320; 167-180.

SRIVASTAVA, I, K., L. STAMATATOS, E. KAN, M. VAJDY, Y. LIAN, S. HILT, L. MARTIN, C. VITA, P. ZHU, K. H. ROUX, L. VOJTECH, D. MONTEFIORI, J. DONNELLY, J. B. ULMER AND S. W. BARNETT. 2003. Purification, characterization and immunogenicity of a soluble trimeric envelope protein containing a partial deletion of the V2 Loop derived from SF162, an R5-tropic primary HIV-1 isolate. J. Virol. 77; 11244-11259.

SRIVASTAVA, I., K. VANDORSTEN, L. VOJTECH, S. W. BARNETT AND L. STAMATATOS. 2003. Changes in the immunogenic properties of soluble gp140 HIV envelope constructs upon partial deletion of the second hypervariable region. J. Virol. 77; 2310-2320.

In press publication

In press publication

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ABEL, KRISTINA;LA FRANCO-SCHEUCH, LISA;ROURKE, TRACY;MA, ZHONG-MIN;DE SILVA, VERONIQUE;FALLERT, BETH;BECKETT, LAUREL;REINHART, TODD A;MILLER, CHRISTOPHER J* Gamma interferon-mediated inflammation is associated with lack ofprotection from intravaginal simian immunodeficiency virus SIVmac239challenge in simian-human immunodeficiency virus 89.6-immunized rhesusmacaques. J Virol 78 841-54 2004

DORIA-ROSE NA, OHLEN C, POLACINO P, PIERCE CC, HENSEL MT, KULLER L, MULVANIA T, ANDERSON D, GREENBERG PD, HU SL, HAIGWOOD NL Multigene DNA Priming-Boosting Vaccines Protect Macaques from Acute CD4(+)-T-Cell Depletion after Simian-Human Immunodeficiency Virus SHIV89.6P Mucosal Challenge. Virol. 2003 Nov;77(21):11563-77

BUSCH, MARC;LU, DING;FRITTS, LINDA;LIFSON, JEFF D;MILLER, CHRISTOPHER J Comparison of virology and immunology in SHIV 89.6 proviral DNA andvirus-inoculated rhesus macaques. J Med Primatol 32 240-6 2003

HSU, M;BUCKNER, C;HAROUSE, J;GETTIE, A;BLANCHARD, J;ROBINSON, J E*;CHENG-MAYER, C Antigenic variations in the CD4 induced sites of the CCR5-tropic,pathogenic SHIVsf162p3 gp120 variants. J Med Primatol 32 211-7 2003

SINGH, DINESH K;GRIFFIN, DARCY M;PACYNIAK, ERIK;JACKSON, MOLLIE;WERLE, MICHAEL J;WISDOM, BO;SUN, FRANCIS;HOUT, DAVID R;PINSON, DAVID M;GUNDERSON, ROBERT S;POWERS, MICHAEL F;WONG, SCOTT W;STEPHENS, EDWARD B The presence of the casein kinase II phosphorylation sites of Vpu enhancesthe CD4(+) T cell loss caused by the simian-human immunodeficiency virusSHIV(KU-1bMC33) in pig-tailed macaques. Virology 313 435-51 2003

NEUROSCIENCE DIVISION

SPID(s): 0189, 0194, 0269, 0270, 0291, 0292, 0293, 0294, 0296, 0297, 0314, 0315, 0316, 0328, 0332, 0333, 0334, 0335

A major strength of the WaNPRC is its outstanding Neuroscience Division, which pursues and supports state-of-the-art brain research using non-human primates. The Neuroscience Division has a unique "critical mass" of investigators studying the neural mechanisms underlying behavior and provides invaluable resources for colleagues both within and outside the WaNPRC. The Scientific Research Resources component consists of eight laboratories, which pursue outstanding research in the areas of primate sensory, motor and cognitive neuroscience and provide training for many students, postdoctoral fellows and visiting scientists. In addition, the Neuroscience Division includes three valuable resource Cores. The Bioengineering Core designs and constructs sophisticated custom instrumentation meeting a wide range of experimental needs, and during the last year has developed a website that will provide technical information to the neuroscience community. This past year the Bioengineering Core provided custom-designed instrumentation for several people that have worked as postdoctoral fellows in the Primate Center and are now setting up their own labs to pursue similar research. The Biostructure Technology Laboratory provides neuroanatomical research services and shared instrumentation for acquisition and quantitative analysis of neuroanatomical images. The "BSTL" has also developed the popular "BrainInfo" website, which provides neuroanatomic knowledge to scientists throughout the world, allowing investigators to download neuroanatomical maps on which to record such findings as neural activity, neurochemical locations, and gene expression for inclusion in the BrainInfo knowledge base. The website is currently being expanded into an interactive resource, allowing experimenters to upload their data. A new PET Imaging Laboratory has become operational this year, featuring a dedicated state-of-the-art PET scanner to provide high-resolution imaging capabilities to a wide range of researchers studying the physiology and pathophysiology of the brain. By imaging all of the brain regions activated during particular behaviors the PET scanner represents a valuable complement to neural recording studies. Conversely, the electrophysiological recordings will help identify the neural activity underlying the PET signal. The PET Imaging Laboratory has opened the door for numerous investigators to explore their research questions with a powerful new tool.

Much of the onsite neuroscience research in the WaNPRC involves recording the activity of single neurons in monkeys trained to perform appropriate tasks. Various Core Staff and Research Affiliates are using such "chronic recording" and related techniques to study the oculomotor system [A. Fuchs, C. Kaneko, R. Robinson], somatomotor system [E. Fetz, M. Anderson, S. Perlmutter], and cortical association areas involved in perception and decisions [B. Jagadeesh, M. Shadlen]. Other neuroscientists in the Division are developing the comprehensive interactive atlas of the primate brain [D. Bowden], or studying the anatomy and physiology of primate retina [D. Dacey, [name]]. Each of these research programs involves extensive collaborative work with students, postdoctoral fellows and international colleagues.

Publications:

E In press publication

E In press publication

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POSTUPNA N, MARTIN B, RUFFO M, MINOSHIMA S, CROSS D, ANDERSON M. Consequences of chronic administration of rotenone to a monkey. Abstract, Society for Neuroscience 2003

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In press publication

In press publication

In press publication

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SOETEDJO, R. and FUCHS, A. F. Climbing fiber dischargesin the cerebellar oculomotor vermis change during saccadic adaptation Program No. 274.11. Washington, DC: Society for Neuroscience, 2003.

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In press publication

In press publication

REPRODUCTIVE BIOLOGY PROGRAM

SPID(s): 0280, 0288

A constant barrier to the development of safe and effective human medicines is the limited application of information derived from non-primate mammalian test species to human beings. Several species of non-human primates represent valuable pre-clinical test species as a result of physiological and, more importantly, pathophysiological similarities to human beings. Despite these obvious benefits largely unknown differences in the genetic make-up of out-bred non-human primate test subjects of the same species often prevent an unambiguous understanding of the disease process under investigation and, its susceptibility to therapeutic intervention. Although studying out-bred populations more clearly reflects the human situation in large clinical efficacy trials, unknown genetic differences ensure that studies on small numbers of macaques are difficult to interpret. As a result, large numbers of test animals are needed to gain pathophysiological and therapeutic information. Therefore production of genetically identical individuals (twins) of clinically relevant non-human primate species would be expected to significantly enhance translational research in fields of biomedicine where a limitation in genetic variation is critical to an understanding of the disease process and its therapeutic sensitivity (e.g. gene therapy, tissue transplantation, vaccine development and developmental and behavioral disease/modeling). In addition, reduced numbers of identical animals will be required for a given project due to known genetic similarities in identical animal pairs, thus reducing the numbers of wild-caught out-bred macaques required each year for biomedical research.

Publications:

CURNOW E.C. AND E.S. HAYES (2004). In Vitro Fertilization of Macaca nemestrina Oocytes with Fresh and Frozen-Thawed Epididymal Sperm. Reprod. Fert. Dev. 16(1,2): 252.

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HAYES E.S., E.C. CURNOW, A.O. TROUNSON AND E.N. UNEMORI. (2004). Pharmacological Manipulation of the Endometrium During IVF/ET in Macaca fascicularis. Proceedings of the Western Pharmacology Society. January 25-29th, 2004. Honolulu Hawaii.

ADMINISTRATIVE INFORMATION

ALLOCATION OF RESOURCE ACCESS

The Center grant supports a wide variety of resources to the research community including the following nonhuman primates, tissues, cells, DNA, specialized animal housing and laboratory facilities, specialized reagents for nonhuman primate applications, surgical facilities, imaging facilities, bioengineering shops, virology and immunology services, animal model development services and applications, specialized veterinary and research support staff, pathology services, diagnostic assay services, welding and fabrication services, training at the professional and undergraduate level, information technology services, shared equipment access (Facsan/Facstar/DNA array), library services, administrative services, conferences/seminars on selected issues of concern to nonhuman primate users, pilot funding for appropriate Investigator requests, a core of faculty scientists including emphasis in the areas of AIDS-related research, developmental biology, neurobiology and behavioral sciences, cardiovascular physiology, molecular and cell biology, immunology, virology, transplantation and stem cell biology, genomics, bioinformatics, proteomics The scope and breadth of the grant-supported resource is among the most complex and expansive within the NIH extramural system

Access to these resources is most commonly gained through sponsored research awards. We allocate resources to the sponsored awards as defined within the research protocol for any combination of the above outlined resources: human, facility, service, non-human primate, financial, and intellectual. The sponsored award Principle Investigator works with the Director, or other service group provider, to establish a mutually acceptable timetable to accomplish the objectives of the sponsored programs. Although to date, no formalized enumerating and reporting system to evaluate resource access to the Center has been requested by NCRR, over the past year, no approved and funded sponsored award has been denied access to the Center resources. Access is achieved through sponsored research proposals and the intellectual infrastructure of the Center program. Allocation of resources is determined according to the needs of the research protocol. Scheduling of access to Center resources occurs after consideration of relevant competing resource demands.

DISSEMINATION

The scientific community is made aware of the Washington Primate Center resources and scientific accomplishments through a variety of mechanisms: our website, seminar series, the annual report, scientific publications, presentations/attendence at professional meetings and societies, participation on NIH committtees, and through the ongoing collaborations of our Core staff and Affiliated scientists and programs within the national and international research community.

AWARDS, HONORS, SPECIAL RECOGNITIONS

Awards, Honors, and Special Recognition

The Washington National Primate Research Center is privileged to include among its core staff and affiliates several nationally and internationally known researchers who were honored with awards and invited lecutres during the 2003 fiscal year. The honors and awards received this year including the following:

Travel award to present the progress of the testing of IL7 in monkeys at American Society of Hematology 2003 Meeting, San Diego, CA

Jan Storek, Ph.D.

Travel award to present the progress of the testing of IL7 in monkeys at the American Academy of Allergy, Asthma and Immunology 2004 Meeting, San Francisco, CA

Eric Hayes, Ph.D. was invited to present several lectures, including:

Invited Lecture, 1st National Symposium on Vascular Medicine in Jakarta, Indonesia August 23-24, 2003, ¿Stem Cells in Human Medicine: Progress and Limitations for Organ Ischaemia.¿

Invited Lecture, 30th Annual Conference of the International Embryo Transfer Society in Portland, OR USA January 10-15, 2004, ¿Pharmacological Manipulation of the Endometrium During IVF/ET in Macaca fascicularis.¿

Invited Lecture, 47th Annual Meeting of the Western Pharmacological Society in Honolulu, HI USA January 25-29, 2004, ¿Non-Human Primates: Partners in Academic Pharmacology and Drug Discovery.¿

L name 3

Russian news sources have recently announced Russian prize winners for the highest achievements in Science, Technology, and the Arts. Among the winners were Professor Boris A. Lapin, Director of the Primate Research Center of the Scientific Institute of Medical Primatology Academy of Medical Sciences, and lifetime colleagues, Violeta Agrba, Leonora V. Indzhiia, Merabi G. Chikobava, and Lelita A. Yakovleva, for their body of research in the ¿role of viruses in the production of malignant lymphomas of primates and pathology of the spread of viruses and disease.¿ A special medal, a diploma, and a monetary award are bestowed upon the winners. This prize is considered an extremely high honor in Russia, and will be presented by President Putin. Historically, in the Soviet era there were two separate prizes: the Lenin Prize and the Stalin Prize. Later in the 1950¿s, Mr. Khrushev renamed the Stalin Prize into the USSR State Prize. In the 1990¿s, the Lenin Prize was also eliminated, and the Russian State Prize remains as an honor bestowed upon citizens for meritorious achievement in science, technology and the arts.

Dennis M. Dacey , Ph.D., £20,000 Vivianne C. Smith, Ph.D., £10,000 Joel Pokorny, Ph.D., £10,000 and Barry B. Lee , Ph.D. £10,000 were all awarded the 2004 Rank Prize for Opto-electronics. The joint prize amount totals £50,000.

Dr. Dennis Dacey is one of four researchers to be awarded the Rank Prize for his accomplishments in the study of vision. This joint award, with Professor B. Lee, and Professor V. Smith is in recognition for their studies on new pathways in the visual system. Their prize is awarded through the category of Opto-electronics which explores the interface between the science of optics and new technologies in fields such as thermal imaging, optical fibers, liquid crystal displays, and lasers and thermography. Another major category of the Rank Prize is directed toward human and animal nutrition and crop husbandry.

The Rank Prize Award was established in 1972 through the wishes of the late Lord J. Arthur Rank to honor those who have made significant advances in specific areas that were of great interest to him. Lord and Lady Rank held a life-long commitment to charitable organizations and were interested in a broad range of activities. In the 1940¿s, Lord Rank was very dominant in the British film industry, and was still active late in his life in his father¿s flour milling business in Yorkshire. Lord Rank¿s focus lent itself toward technological advances that would be of benefit to all. Since the inception of the awards in these categories in 1972, very few have been
bestowed to researchers in vision science, and the Rank Prize is considered to be one of the most prestigious. Former winners of the Rank Prize include Japanese researcher Kenichi Iga, and US researchers Robert Burnham and Donald Scifres, inventors of the vertical cavity surface emitting laser (VCSEL). US researchers James Fujimoto, Eric Swanson and Carmen Puliafito have also been honored for their work in the development of the biological imaging technique, optical coherence tomography (OCT). A formal ceremony was held at The Institute of Physics in London in February of 2004. During this ceremony, Dr. Dacey and other award winners were honored with a commemoration and a monetary award.

Alexander W. Clowes, M.D., was the recipient of the Sheen Award for his work in cardiovascular research.

Mike Shadlen, M.D., Ph.D. was appointed to several editorial boards:

Journal of Vision
Trends in Neuroscience
Journal of NeuroscienceAppointed to ¿Faculty of 1000¿

Dr. Shadlen also gave several invited lectures and seminars:

Department seminar, Columbia University, NY, June, 2003.

Visiting Lecturer, Neurobiology of Vision, Cold Spring Harbor, NY, June, 2003.

McDonnell Summer Institute in Cognitive Neuroscience, Lake Tahoe, CA, July, 2003.

Plenary speaker, ¿Cortical Foundation of Visual Perception¿, 23rd Annual International Summer School of Brain Research. Amsterdam, The Netherlands, August, 2003.

Invited speaker, Meeting on Intra- and Intercellular Communication, Howard Hughes Medical Institute, Chevy Chase, MD, September, 2003.

Invited speaker, Laboratory of Sensorimotor 25th Anniversary Symposium Bethesda, MD, September, 2003.

Invited speaker, The McGovern Institute Symposium: Mechanisms Underlying Perception, Action, and Mind. Cambridge, MA, October, 2003.

Department seminar, UC Berkeley, October, 2003.

Department seminar, Neurobiology and behavior Colloquium Series, UC Irvine, December, 2003.

Invited workshop speaker, Neural Coding Under Uncertainty, Seventh Annual Conference on Neural Information Processing Systems Whistler, BC, December, 2003.

Invited workshop speaker, Banbury Meeting on Neural Representation and Processing of Temporal Patterns Banbury Center, Cold Spring Harbor Laboratory, NY, December, 2003.

Invited speaker, Twenty-Ninth Annual Interdisciplinary Conference, Jackson Hole, WY, February, 2004.

Eberhard Fetz, Ph.D., is the head of the neuroscience core in our center. This year Dr. Fetz was honored with several national and international invited addresses :

Invited speaker 34th Neural Prostheses Workshop at NIH, Oct. 21-23, 2003.
Invited speaker International Symposium on Multidisciplinary Approaches to Sensorimotor Integration The National Institute for Physiological Sciences (NIPS), Okazaki, Japan, March 15-18, 2004

Invited seminar presentations at:

University of Rochester, Rochester, NY, March 6, 2003

State University of New York, Syracuse, NY, March 7, 2003

University of Pittsburgh, Pittsburgh PA, August 21, 2003

University of Pennsylvania, Philadelphia PA, August 23, 2003

Murali-Krishna Kaja, Ph.D. is a Core Scientist in the center¿s Immunology division. Dr. Kaja was honored with several invited addresses this year:

Invited Seminar, Seattle Biomedical Research Institute, Seattle, WA July 28, 2003.

Invited Seminar, The Scripps Research Institute, Aug 21, 2003. LaJolla, CA.

[name] UW undergraduate student in Psychology
Psychology student, [name] has been named a recipient of the Guthrie prize this spring for his honors paper entitled, ¿Conservation Biology: The ¿Crisis Discipline¿ and its Significance to Primatology. [name] became aware of his sincere interest in primatology and conservation biology during the summer of2000, while participating in the Indonesian Field Study Program on Tinjil Island. The program is directed by Dr. Randy Kyes, Core Staff Scientist and Head of the International Programs Division of the Washington National Primate Research Center. [name] presented his honor¿s research work at the American Society of Primatologists Annual Meeting in Calgary last August. Dr. Kyes remarked that, [name] has pursued his interests and conducted a thoughtful review of the literature. He has shown exceptional ability to identify key aspects and provide a logical assessment of the evidence at hand.¿ The Guthrie prize is so named in memory of the late Edwin R. Guthrie, and the intent is to recognize undergraduates for scholarly achievement in either a conceptual or analytical work. Nominations are submitted by professors in the Department of Psychology, and winners are presented with a monetary award. [name] also a student of Dr. Kyes, was a

recipient of the Guthrie prize in 2002.

INFRASTRUCTURE

1. Physical Plant

2003 Capital Projects and Physical Plant

Award of the Regional Center for Excellence to the University of Washington, along with numerous funding applications requiring ABSL3/BSL-3 lab space prompted WaNPRC to begin space and bio-containment site analysis. A multiple user team was organized to evaluate regulatory requirements and design an efficient renovation to meet all required standards at the Western facility location As part of this analysis numerous consultants with expertise in the field of bio-containment and non-human primate housing facilities have presented the Center with information on infrastructure and equipment options. The planning phase was completed in 2003 with a C06 grant submittal for the project scheduled for February, 2004. Facility security and bio-safety/security planning have begun at the WaNPRC as a result of Federal and University regulations pertaining to usage of select and high risk agents

animal location?

A Construction grant submitted to NCRR Extramural Research Facilities Improvement Program for a Cognitive Neuroscience Research Center to be located in the Health Sciences [illegible] awarded in 2002 has progressed through schematic and design development. A thorough evaluation of the existing structure was performed to assess vibration affect on research to be conducted in the space. The total project cost is estimated at $3,100,000. Estimated timeline to award and commence construction is September 2004.

Design plans have begun in 2003 to renovate multiple small animal holding rooms for more efficient use of space in the I-wing -1 level of the WaNPRC campus facility. Demolition and replacement of an antiquated autoclave will further enhance design of this area and satisfy requirements for an adjacent P3 lab. This project will further require redesign of several surrounding rooms into one floor plan, electrical and HVAC upgrades. Another design plan in the I-wing on the -1 level has begun in order to replace and relocate an aging cage washer. The equipment needs to be replaced due to lack of available replacement parts; concern over reliability and down time for colony operations has made this project a priority. Once the design and estimation work are completed for both these projects, G20 renovation grants will be submitted for funding in June of 2004.

AAALAC site visit of WaNPRC in July of 2003 mandated renovation of two animal holding rooms due to health and safety concerns for personnel working in a narrow space between cages. Remedy required demolition of curbing, removal of automatic flush systems, and resurfacing of floors and walls. The project was completed by September, 2003 and reported to council.

The Machine shop, previously relocated in 2002 has been reorganized and added an additional staff member in 2003. This will greatly increase fabrication and repair capability of caging, trapping run equipment, Psychological well-being program requests and various equipment apparatus for research support projects.

Continued lab and office upgrades were implemented at the WaNPRC I-wing campus facility, including reorganization and library consolidation of the Primate Information Center, Psychological Well-being lab space, Neuroscience workstations, and Information Technologies offices and server locations.

The University of Washington space survey database became utilized for indirect cost negotiation beginning in June of 2003. The database provides a mechanism for the WaNPRC to access central information and update and correct data as well as monitor and report on space resource usage.

Major Equipment Purchased With Primate Center Grant Funding

- Spectrometer--linear quadruple ion trap mass
- Facscalibur 4 clr basis sensor unit; facstation calibur; facsloader; facsflow
- Freezer (4)
- Abi prism 6100 nucleic acid prep station; reagents starter kit
- Allegra 6r refrigerated centrifuge & rotor
- Computer (23)
- Centrifuge--refr, allegra
- Centrifuge & rotor; adapters; swing bucket
- Allegra bench top 6r centrifuge & rotor
- Revco ultra low temp chest freezer

- ¿ Primate transfer lift w/ transfer box
- ¿ Eppendorf conc vac w/ pump
- ¿ Centrifuge-micro r bench top; rotor (fixed-angle)
- ¿ Microplate reader w/ internal thermal printer (2)
- ¿ Power edge 2650 intel xeon 2.6ghz
- ¿ Steam autoclave sterilizer w/ mesh basket
- ¿ Biophotometer
- ¿ Balance level stand, ph/mv meter with electrode
- ¿ Easy-load peristaltic pump

2. Colony Management

Primate Resources is a core unit with responsibility for the husbandry, breeding, veterinary care, psychological well-being, pathology, SPF testing, and research support for WaNPRC nonhuman primates. It provides a safe, efficient environment for housing and research activities involving nonhuman primates, thereby facilitating efficient operations for both colony and research staffs Primate Resources is divided into a number of management divisions responsible for oversight of specific areas These include Clinical Medicine and Surgery, Husbandry, Psychological Well-Being, Animal Records, Research Support, Information Technology, Reproductive Colony Breeding and Genetics, and Combined Pathology. The Head of each management division reports directly to the Associate Director for Primate Resources, who in turn reports to the Director.

The Seattle animal census at the close of the 2003 calendar year remained approximately comparable to calendar year 2002 and reflects an emphasis on utilization of available space for appropriate research-related activities. The majority of breeding operations continue to be located at the Tulane National Primate Research Center. The trend towards increased census in the Papio cynocephalus colony has continued over the previous year. The non-SPF Macaca nemestrina breeding colony has demonstrated little increase over the previous year due to significant harvesting for research applications The SPF Macaca nemestrina has demonstrated moderate growth over the preceding year with intensive management for preservation of breeding females in this population Production of the Macaca nemestrina time-mating colony at the Washington facility has demonstrated significant growth over the previous year reflecting intensive management of breeding groups to maximize production Supply issues for the macaque populations in general remain challenging for the present and foreseeable future.

Personnel issues continue to be a major area of focus for Primate Resources. The Husbandry division has taken significant strides over the previous year to address a shortage in personnel numbers through implementing novel recruitment strategies with the assistance of the University of Washington Human Resources Department Additionally, this division has continued its commitment to provide AALAS training for the husbandry staff and a majority of personnel are currently either certified or in training Focused efforts have been developed to recruit individuals with a more rigorous academic background into the husbandry division with approximately one-half of new hires having undergraduate degrees.

The WaNPRC has also successfully met a number of programmatic requirements during the previous year These include site inspections by both the US Department of Agriculture (general inspection) and Center for Disease Control (international quarantine facilities) as well as inspections by the UW Institutional Animal Care and Use Committee No major deficiencies were noted in any inspection by any agency during the 2003 calendar year.

Clinical Medicine and Surgery

The Veterinary Medicine and Surgery unit continues to deliver excellent medical and surgical support for animals housed at the WaNPRC. This unit provides basic veterinary care as well as surgical and medical support for research animals, thus enabling investigative groups to perform complex experimental procedures requiring a high degree of animal-related support. This division has continued the trend towards a steady decline in overall numbers of clinical cases. The overall incidence of the most common clinical admissions, diarrhea and trauma, has continued to decrease over the 2002 period. Additional efforts have focused on preventive medicine for animals originating from other sources (e.g. domestic and international) to ensure the health of animals admitted to the Seattle colonies. The preceding year has shown an increase in the number of animals admitted to the Seattle and Tulane colonies from diverse outside sources. Additional emphasis has been directed towards characterization of these animals prior to admission to WaNPRC colonies with treatment as necessary to protect the health status of current animals. The number of surgical procedures performed for 2003 remained relatively unchanged from the previous year and new imaging capabilities(MRI, fluoroscopy) continue to be developed.

During the 2003 period, this unit has developed closer interactions with several investigative groups using challenging animal model

systems to answer research questions. They have provided extensive input regarding protocol development and monitoring These efforts have continued to result in improved experimental protocols with reduced impact to the nonhuman primates over the course of the study. The Institutional Animal Care and Use Committee continue to assignee projects to a monitoring protocol administered by the Medicine and Surgery unit to monitor progress on challenging research protocols.

Another area of emphasis has been to provide a more integrated, comprehensive training opportunity for postdoctoral fellows in the Laboratory Animal Training Program, based in the Department of Comparative Medicine, University of Washington The Clinical Medicine and Surgery unit has significantly re-organized the training program provided by the WaNPRC resulting in more interest and satisfaction on the part of the trainees. The duration of the training period has been extended and the trainees are afforded greater responsibility under the current program, providing a more challenging experience.

Breeding Program

WaNPRC Animals at Tulane. The majority of breeding operations for the WaNPRC are located at the Tulane NPRC in outdoor group housing configurations. This arrangement allows for natural social interactions between breeding animals, thereby maximizing psychological enrichment of the nonhuman primates. The pigtailed macaques are housed primarily in quarter-acre, outdoor field-cages, while the baboons are housed primarily in two outdoor corrals, each nearly one acre in size. Smaller groups of pigtailed macaques, 3-10 per group, are occasionally housed in outdoor ¿corn-crib¿ housing enclosures with circumstances or management considerations during the year dictating occupancy in these units. These outdoor housing facilities provide excellent environmental enrichment with access to both complete family social groups as well as the outdoor environment. Additionally, the outdoor facilities are much more cost-effective, allowing a conservation of resources devoted towards standard breeding operations.

The growth of the baboon colony continues to be very strong, reflecting the excellent distribution of breeding animals within the groups. The growth of the standard pigtail colony has been limited due to the extensive research demands by the Seattle facility for research animals. In particular, the demand for mature females for AIDS-related and therapeutic agent research studies has proven to be a significant impediment to growth of this colony. The growth of the SPF pigtail colony has continued over the 2003 period, however current housing resources are limited and continued growth of this colony at the TNPRC will not be possible without additional housing capabilities.

The WaNPRC operations at Tulane also have access to limited indoor housing facilities, currently utilized for staging of animals prior to transfer to Seattle. These facilities allow conditioning of small numbers of animals prior to shipment, thereby diminishing the conditioning and treatment process required upon arrival at either of the Seattle facilities.

A collaborative effort with laboratories at the Southwest Foundation for Biomedical Research utilizes micro satellite identification procedures to provide genetic information regarding each animal in the SPF breeding colony, including paternity identification for animals in outdoor breeding groups.

Seattle Breeding Colony. The Seattle Breeding Colony is maintained to provide fetal and/or neonatal nonhuman primates to investigative groups requiring this resource for accomplishment of experimental aims. The physical distance to the Tulane facility and the outdoor, large group housing configurations preclude transport of very young animals to the Seattle facility. Therefore, the WaNPRC maintains a dedicated group of breeding animals onsite to furnish this resource for specific research protocols. Most animals are maintained in small harem groups consisting of a single adult male and variable numbers of adult females forming a relatively stable social group. This structure allows maximal social interaction between animals within the same harem, thereby establishing an optimally-enriching environment for breeding animals. Animals are checked for pregnancy via ultrasound examination on a monthly basis and once identified as pregnant are followed as necessary to monitor the course of the pregnancy prior to delivery.

Additional, smaller numbers of females are maintained in cages without routine access to males for investigative groups requiring precise determination of gestational age. The menstrual cycle of these females is followed on a daily basis to determine optimal timing for exposure to males, at which time the male and female are co-housed for a two-hour period on a single day of the cycle. Females are then followed via observation and ultrasound examination to confirm pregnancy. This allows precise identification of gestational age (to within hours) for investigative groups as needed for specific research projects.

Psychological Well-Being

The Psychological Well being (PWB) Program oversees the implementation of the Environmental Enhancement Plan for nonhuman primates at the WaNPRC. The purpose of the Environmental Enhancement Plan is to provide a psychologically enriching environment for laboratory primates housed at the WaNPRC to address their psychological needs while also meeting or exceeding regulatory

requirements. The PWB Program utilizes a multi faceted approach to provide enrichment opportunities for nonhuman primates compatible with housing requirements and research objectives. PWB Program staff evaluates new enrichment options before widespread adoption. The diagnosis and treatment of behavioral problems of WaNPRC primates is in the domain of the Program. Behavioral assessments and interventions are conducted by the PWB Program Coordinator and Enrichment/Research Technologists. Enrichment and behavioral issues relating to the physical health and medical conditions of the animals are reviewed by veterinary staff. Husbandry staff, under the supervision of the Colony Manager, implements certain aspects of Environmental Enhancement Plan. To achieve the goal of maximizing the mental health of laboratory primates, PWB Staff develop protocols and forms for monitoring and documenting enrichment, social compatibility, behavioral assessment and intervention strategies. Communication among PWB staff, husbandry staff, and veterinary staff is facilitated by frequent meetings of the Environmental Enhancement Committee, which serves as a forum for ideas, implementation, and communication with respect to environmental enrichment and behavioral health issues of the WaNPRC's laboratory primates. PWB staff also present training seminars for WaNPRC personnel to provide extensive information regarding nonhuman primate behavior and the PWB Program.

Infant Primate Research Laboratory (IPRL)

The Infant Primate Research Laboratory (IPRL) is supported as a core facility of both the Center on Human Development and Disability (CHDD) and the Washington National Primate Research Center. For over 30 years, the overall objective of this Core has been to provide a range of services, equipment and supplies to CHDD Research Affiliates using nonhuman primates in research related to developmental disabilities. The following broad range of services is provided to individual investigators.

(1) Consultation services regarding appropriate research designs, methods and data analysis techniques are provided to assist investigators who are unfamiliar with the unique characteristics of nonhuman primate research. This helps to ensure that affiliate investigators are provided the critical assistance they need to develop and implement studies with state-of-the-art methods.
(2) Routine and specialized housing and care for animals are provided twenty-four hours a day, seven days a week for studies conducted by affiliates to optimize animal survival and minimize morbidity. This reduces the financial costs to investigators and increases the number of healthy animals available to the overall primate colony.

(3) Specialized equipment, protocols and databases are provided to affiliates for assessing the development of physical growth as well as sensory, motor, social and cognitive development in nonhuman primates. Many of the assessments are based on studies of human infants and have been successfully adapted for use with infant monkeys. A large normative database is available for many of the assessments. The databases provide investigators with normative data for pilot studies as well as information regarding normal variability in responses for estimating the numbers of animals required for studies. The databases have also been the source for several publications regarding the natural growth and development of laboratory reared macaques.

(4) Experienced laboratory personnel provide assistance, training and on-site supervision to the staff of Research Affiliates conducting research in the IPRL. The IPRL personnel are trained using modified Good Laboratory Practice procedures and provide continuity in testing to ensure reliable data collection over time. They also provide training for undergraduate, graduate and post-doctoral students. This includes training in the various developmental assessments as well as the safe handling of animals.

Accomplishments

During the past year, Drs. Burbacher and Grant have consulted with a team of investigators from the Children's Hospital and Regional Medical Center and Department of Otolaryngology at the University of Washington to develop new test procedures for use at the IPRL. [Name] [illegible] [illegible] [illegible] are providing the test equipment and expertise to study the longitudinal development of oculomotor function in infant primates. [Name] is assisting with the design and implementation of test procedures to examine fovea development in young monkeys. These new test methodologies will parallel those given to human infants in both clinical and experimental settings and will enhance the biobehavioral assessment battery used at the IPRL.

An internal advisory committee continues to help develop plans for expanding IPRL services to CHDD Affiliates. The members of the advisory committee are Dr. Gene Sackett (Emeritus Professor in Psychology), Dr. Julie Worlein (Affiliate Assistant Professor, Psychology) and Dr. Eric Hayes (Research Scientist, Washington National Primate Research Center (WaNPRC). These individuals, along with Dr. Burbacher, are members of the Division of Reproductive and Developmental Sciences within the Primate Center. As such, they are all involved in helping provide services to investigators using the IPRL.

We are also continuing the process of recruiting for a new faculty position that would be supported by the WaNPRC and an appropriate academic department at the University of Washington. Due to budget constraints, the search for a new core staff member was postponed until 2004. We continue to work with [Name], head of the Pediatric Neurology program in the Department of Neurology, and have agreed to confine the search to a pediatric neurologist with a focus in the area of genetic models for developmental disabilities.

Thirteen research projects used the services of the IPRL during the past year. Most of the projects utilized the full range of services available in the lab. The names of investigators and projects and the IPRL facilities that were used are listed below.

Burbacher, Thomas M.
Primate Developmental Effects of Methylmercury
Primate Developmental Effects of Methanol
Thimerosal in Vaccines Safety Study
Crockett, Carolyn
Prospective Studies of Self Injurious Behavior in Captive Primates
[illegible]
Perinatal Transmission of Pathogenic SHIV
Ho, Rodney J. Y
CNS Drug Delivery Targeting the HIV Sanctuary
Juul, Sandra
Safety and efficacy of Recombinant Epo (rEpo) as a Rescue
Agent for Asphyxia
[illegible]
Development of Visual Function
Sackett, Gene P.
Phenotypic Similarity of Pigtail Macaque Identical Twins
Produced by Embryo Splitting
Antiepileptic Drug Exposure
[illegible]
Allogeneic In Utero Stem Cell Transplantation in Primates.
Worlein, Julie
Behavioral & Physiological Consequences of Loss

These 13 projects accounted for approximately 150 of the animals that were housed in the laboratory during the past year. Four of the research projects were successfully completed in 2003. The remaining projects will continue during the next year.

To accommodate the research requirements for these projects, we continued our review and standardization of protocols. New Standard Operating Procedures were developed for the nonhuman primate version of the Brazelton Neonatal Behavioral Assessment Scale, temperament, visual recognition memory, object permanence, color discrimination and reversal, Hamilton Search and learning set. The technical staff continued to work with the Instrument Development Laboratory Core to upgrade several of the tests in the IPRL. Upgrades of the equipment for the Visual Recognition Memory test have been completed. Dr. Grant is currently working with the Instrument Development Laboratory Core to revamp the visual acuity apparatus and new test equipment will be delivered in 2004.

Upgrades of our data collection and management programs also continued. New programs were developed to collect and process activity data using a hand-held device and programs were updated for routine electronic data collection and the processing of temperament, weight and object permanence data. All data from the learning and memory tasks administered in the WGTA are now entered into laptop computers for automatic processing. We have also successfully implemented the use of wireless technology in the lab to study sleep patterns in young Macaca nemestrina. New input programs for formula intakes and backlogged data sets have been developed and are now routinely used in the laboratory. An improved data processing system has also been implemented which includes automatic error checking for all data sets. Data collection and processing procedures for the BSL2/3 laboratory were also updated, with the assistance of Dr. Julie Worlein. Three investigators used this facility during the past year [illegible] Ho, and Worlein).

Laboratory personnel are continuing to offer services to affiliate investigators in conjunction with the Reproductive Biology program, headed by Dr. Eric Hayes. Staff from the IPRL provides assistance with daily observations for menses, training animals for blood draws, ultrasound imaging and embryo transfers.

After discussions with Dr. Satoshi Minoshima, Director of the new positron emission tomography (PET) imaging service core at the Primate Center, we have begun training procedures for functional PET imaging with complex reaction time in adult animals. The

protocol requires that the animals perform the task while both of the legs are restrained for radioactive infusion. The IPRL is now certified for the use of radiation and Dr. Burbacher, as well as two support staff, have completed training and received certification in the safe handling of radioactive materials. Dr. Julie Worlein continues to utilize PET imaging to help characterize the development of her lentivirus infected infants.

Finally, the studies conducted in the laboratory during the past year provided opportunities for training 15 undergraduate students. These students were enrolled in our Undergraduate Research Program and received academic credit for their work in the lab. Students are expected to write a review of their experience in the laboratory during their initial quarter. Students typically come from the departments of Psychology, Anthropology, Zoology, and Environmental Health This program has been highly successful in meeting one of the major goals of the University, providing quality undergraduate training in research. In addition, two graduate students are currently engaged in doctoral level research at the IPRL and will continue their studies through 2004.

Future Plans

During the next year, we will continue to update the neurobehavioral test battery used at the IPRL. This will include the new test procedures being developed to study oculomotor and foveal maturation as well as visual contrast sensitivity. As noted, the new apparatus to collect visual acuity data is currently under construction and will be delivered in 2004. Upgrades of our data collection and management programs will also continue.

Technical assistance for the Reproductive Biology program will be maintained. We anticipate the arrival of our first set of twins in the next year. Dr. Hayes will be involved in the search for a pediatric neurologist given the relevance of research to the development of genetic models such as fragile X.

Adult animals will be retrained to work on the complex reaction time procedure with leg restraint by the summer of2004. With the guidance of Dr. Satoshi Minoshima, we will begin PET studies with these animals to pilot the procedure for use with younger subjects.

Finally, we have restarted the process of searching for a new core staff member for the division We will develop the qualifications for the position and advertise the position by this summer. Hopefully, interviews of the candidates will begin by the end of the year.

Reproductive Biology Group

To date efforts in the RBG have been focused on 1) developing the infrastructure for a full-scale twinning program, 2) using the tissue program to initiate as many of the first years preliminary experiments as possible3) acquiring undergraduate and post graduate level research personnel and 4) producing preliminary data for use in RO1 type and other grant applications and, seeking out substantial collaborative research programs based on the infrastructure available to the group.

The RBG now has a fully functional embryology laboratory located at the Western facility. This facility is now capable of supporting funded affiliate and collaborative research programs in most areas of non-human primate reproductive biology. Animals were acquired in late 2002 and preliminary embryo production runs were completed to test existing animal biometry and surgical procedures required for successful application of assisted reproductive techniques. Preliminary results using four donor females were as follows: 75.7% of oocytes were mature at collection, 96.4% of mature oocytes were successfully fertilized in vitro and 96.3% of fertilized oocytes developed in vitro. Eight sets of twin embryos were produced from this limited exercise. Significant changes were made to both animal biometry and surgical procedures. Revised procedures will be used from March 17, 2003 onwards for full-scale twin embryo production.

The Tissue Redistribution Program has been of critical importance to the RBG. Male reproductive tissues have been used to store sperm from M. nemestrina, M. fascicularis, M. mulatta and P. anubis (615 0.5 ml straws of sperm; 5-220 x 106 sperm/ml) some of which has been used for in vitro fertilization (IVF) procedures (23 straws). Molecular and pharmacological studies of novel and known ion channels in immature and mature spermatids have been initiated. Female reproductive tissues have been used to develop in vitro maturation protocols for immature oocytes, cryostorage protocols for immature and mature oocytes, in vitro culture protocols for embryos produced by IVF and pharmacological characterization of intracellular signaling mechanisms during oocyte maturation in vitro. Maturation protocols developed during these studies promote in vitro maturation of immature oocytes at a rate of41%. Those oocytes fertilize (80%) and develop during in vitro culture (80%) and represent a significant source of embryonic material for in-house and collaborative research programs. To date 24 embryos have been cryostored. A total of 91 oocytes have been subjected to slow and rapid cooling (n = 91 total) and survive warming at a rate of 69%. The majority of oocytes that survive (64.3%) exhibit normal spindle and chromosome configurations. Interspecies (bovine versus macaque) comparisons of protein kinase C (PKC) signaling

during oocyte maturation in vitro indicate that very subtle concentration- and support cell¿dependent differences exist for the effects of PKC activators.

The RBG has been host to 1 overseas undergraduate research student (BSc. Honors program) and will take on two post-graduate level research scientists (1 MD, 1 DVM) in July and September 2003, respectively. The data produced by the undergraduate research student was sufficient to satisfy her program requirements and the MD and DVM will join the group with salaries provided from external funding sources.

C

Pending support

Personnel in the RBG were responsible for 11 publications in 2002-2003 (6 published, 3 accepted or in press, 2 submitted). The PI has been invited to speak at international symposia in Singapore (November, 2002) and Indonesia (April, 2003) and has been asked to organize and speak at a symposium on reproductive pharmacology (Western Pharmacological Society, Hawaii, 2004).

Developmental Psychology

Research in the Developmental Psychology program addresses processes of growth and behavioral development in nonhuman primates. The long-term goal is to understand how parental characteristics and other intergenerational influences, prenatal and perinatal factors, and postnatal experience interact in affecting developmental systems. Specific aims include (1) identifying mechanisms producing poor pregnancy outcomes and studying how these mechanisms affect prenatal and postnatal offspring development; (2) studying if, when, and how prenatal processes affect risk for deviant postnatal development; (3) identifying primate models of reproductive and developmental failure using computerized colony records and at-risk newborns such as premature, low birth weight, abused, diseased, and genetically abnormal individuals; and (4) studying the developmental consequences of experimental treatments designed as models of human diseases or therapeutic agents for human diseases. This research program operates at two levels: basic developmental mechanisms and breeding and husbandry of captive primates.

Comparative Pathology Unit

The Comparative Pathology Unit (CPU) has provided diagnostic and research pathology support to the WaNPRC and the Department of Comparative Medicine (DCM). The unit was established so that the combined expertise of comparative pathologists and support staff previously assigned to individual deartments could be integrated into a more efficient, productive group. The overall goal of the CPU is to provide a technologically broad, responsive and interactive pathology program.

The program is driven by four specific aims:

(1) To provide research and diagnostic pathology and histology support to all projects based within the WaNPRC. In pursuit of this aim, the CPU supports AIDS-related and neuroscience-related projects and other research projects requiring histology and pathology expertise. Support is provided for experimental as well as diagnostic needs related to animals assigned to individual studies. A wide variety of services are provided by CPU personnel: basic tissue processing and sectioning, immunohistochemical assays, in situ hybridization assays, polymerase chain reaction techniques, electron microscopy, and consultation on various histologic techniques tailored to individual projects. The lab also facilitates provision of tissues and slides for routine diagnostic purposes. Accessions to the laboratory have increased somewhat from the previous year. The vast majority of accessions (~90%) are research-related. The search for a new pathologist begun in 2000 was ultimately successful with addition of a primate pathologist late in the 2001 period. This pathologist has research interest in viral diseases and will devote a significant portion of her activities towards interactions with the AIDS research groups located at the Western facility.

(2) To participate in the investigation of spontaneous disease outbreaks affecting colony animals. This aim directs efforts toward investigation of persistent and sporadic disease outbreaks that cause morbidity and mortality in the colony or threaten to adversely influence data obtained from these animals. In addition to routine diagnostic cases, attention during the past year was spent in supporting continued investigation of an Epstein-Barr-like virus infection in association with cutaneous T-cell lymphoma. Additional cases of lymphoma were diagnosed at necropsy in animals infected with specific lentiviruses and investigations concerning development of neoplasia within this group are proceeding.

(3) To continue to operate the Tissue Distribution Program (TDP) as an efficient resource to provide valuable nonhuman primate tissues to investigators within and outside the WaNPRC. The TDP has, as additional goals, increases in the use of tissues from project-specific animals, the dissemination of information via electronic media, and the ability to provide specialty services During the last year, the TDP has increased the number of tissues procured from each animal, reflecting a steady increase in efforts to maximize the effective use of the resource. To maximize utilization of research-assigned animals, the program is working with individual researchers to schedule terminal procedures so that tissue samples can be provided to secondary researchers. The TDP has established an internal web page and is continuing work on developing an external web presence.

(4) To establish an environment where critical expertise in comparative primate pathology can be encouraged and utilized to promote training and scientific enterprise. To facilitate the establishment of an excellent nonhuman primate pathology core, it is essential to generate an intellectual environment where a critical mass of expertise in this area can thrive. Since 1996 the CPU has sponsored well-attended quarterly conferences on nonhuman primate-oriented histopathology, supported pathology rotations for comparative medicine trainees (who are funded by an NIH training grant), and offered support for core and pilot projects.

Hematologic Resources

The Hematologic Resources Division consists of three resources projects and two cores. During the last year Progress has been made in these projects as follows:

Dendritic Cell Resources (E.A. Clark): Four papers supported by RR00166 have been published during the last year or are in press. The first (1) describes the role that cyclic nucleotides play in regulating the differentiation of human dendritic cells (DCs). The second describes the regulation of DCs by estrogen (2), an important hormone that has not been examined carefully for its effects on DCs. beta-estradiol was found to regulate both cytokine and chemokine expression in DCs and to profoundly enhance migration of DCs to the MIP-3beta chemokine. Another study (3) showed that DCs could regulate the proliferation of human B cells that have been activated via their B cell antigen receptors. This work is pertinent for understanding how humans and nonhuman primates develop protective immunity to encapsulated bacteria. The fourth paper (4) describes the role that caspases play in regulating the entry of B cells into cell cycle. Several studies are submitted or about to be submitted describing the function of human and nonhuman primate associated C type lectins DCAL-1 and DCAL-2.

Stem Cell Resources [illegible] A comparison was made between hematopoietic repopulation in NOD/SCID mice with autologous reconstitution in the baboon, a well-established preclinical large animal model for stem cell transplantation (5). Distinct hematopoietic stem/progenitor cells were found to be responsible for hematopoietic reconstitution in NOD/SCID mice compared with nonhuman primates. In utero transplantation of stem cells was examined in baboons and pigtailed macaques (6). Chimerism was noted in seven of eight live-born animals and the level of chimerism in the progenitor population was related to the fetal T-cell dose. Some animals achieved levels of chimerism in the marrow hematopoietic progenitor cell population that would likely have clinical relevance However, the levels of chimerism in peripheral blood were too low for therapeutic benefit. In other studies, it was found that IL-7 improves reconstitution of stem cells in autologous baboons (7) and that no abnormal hematopoiesis or leukemia developed in 42 rhesus macaques and 23 baboons with significant levels of gene transfer for a median of 3.5 years after infusion of CD34+ cells transduced with retroviral vectors expressing marker or drug-resistance genes (8).

Immunologic Resources (Murali-Krishna Kaja): Progress has been made in establishing a new laboratory and obtaining additional funding. An R01 grant to define the role of type I interferons (IFNs) in anti-viral CD8 T cell responses was obtained and as well as Project on a program grant to design effective vaccines for HIV using the prime boost approach. A key paper is about to be submitted describing the role of IFNs in generating and maintaining adaptive immune responses to viruses.

The Flow Cytometry Core [illegible] and MHC Tissue Typing Core (L. Gaur) continue to provide services to a number of investigators and are operating efficiently and effectively. The MHC Core assisted in the In utero hematopoietic stem cell transplantation [illegible] et al., 2003) and in typing for many other projects.

SRV Diagnostic Laboratory

The SRV Laboratory provides diagnostic support for the Primate Center with the goal of creating an SIV-, SRV-, herpes B-, STLV-free macaque colony. Working closely with the veterinary staff, the SRV Diagnostic Laboratory has played an important role in eliminating SRV infections from the colony and supporting establishment of a core of breeding M. nemestrina that are also uninfected by herpes B and STLV. The SRV Laboratory has provided serologic assays on all animals housed at both the Tulane and Seattle facilities and Colony management personnel rely heavily on testing results to determine management activities. The SRV Diagnostic Laboratory has significantly refined the reporting mechanisms used to communicate test results to Colony management and Veterinary

personnel. Automatic downloading of assay results to the Animal Records System has been instituted to speed the transmission process and positive results are communicated immediately via email and telephone. These modifications have significantly reduced the lag time between sampling and results, thereby increasing the overall efficiency of operations

The prevalence of gamma herpes viruses and spumivirus in the colony is being studied in order to determine whether it would be reasonable to develop small colonies negative for these viruses. Additionally, the SRV laboratory provides critical resources for testing of animals prior to entry into WaNPRC facilities. The shortage of nonhuman primate resources makes acquisition of animals from outside sources an important capability. The SRV Laboratory provides the ability to characterize the pathogen status of animals before entry to the general population, thereby protecting both animals and research integrity.

Animal Records System

The WaNPRC's Information Technologies Division supports the Animal Records System(ARS). The system is based on Oracle¿s Enterprise relational database server. During this year the ARS servers were replaced with two new Dell servers running Windows Server 2003. The Oracle Enterprise database server software was upgraded from version 7.3.4 (no longer supported) to 9.2.0.4.0 (the current release) and all of the ARS tables, services, reports and interfaces were ported to the new systems. Windows-based PCs are used to input and update data and to run predefined queries. In addition, Microsoft Access database software with Oracle¿s ODBC database connectivity drivers can be used to formulate ad hoc queries. A web based interface is also available for a limited number of the ARS reports. The system is currently made up of over 186 forms, 267 tables and 120 code packages which together provide ¿point and click¿ ease of use. The system architecture provides automatic updates of forms and system software so that once the system has been installed on a client machine it keeps itself updated with any changes and improvements. Currently over 160 users have access to the system.

New capabilities and improvements continue to be implemented. An advisory committee meets monthly to discuss requirements and improvements to the system and to set priorities for that work. The ARS staff continued to refine a number of forms and reports utilized in daily operations of the Center.

The ARS development staff has continuously acted on user input and requests to improve the functionality and ease of use of the system. All normal system maintenance, backups and offsite backup rotations were performed. The staff has continued to work diligently to create upgrades that make the systems as useful and efficient as possible.

During this period a senior programmer for the ARS took retirement. Another programmer has been assigned to the ARS and is learning the system and is gradually taking on more responsibility however our backlog or tasks continues to grow. We hope to replace the retiree during the coming budget year so that we can better manage the growing backlog of tasks

Please see appendix for remainder of Infrastructure section

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ANDERSON, DAVID M
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COMPARATIVE MEDICINE

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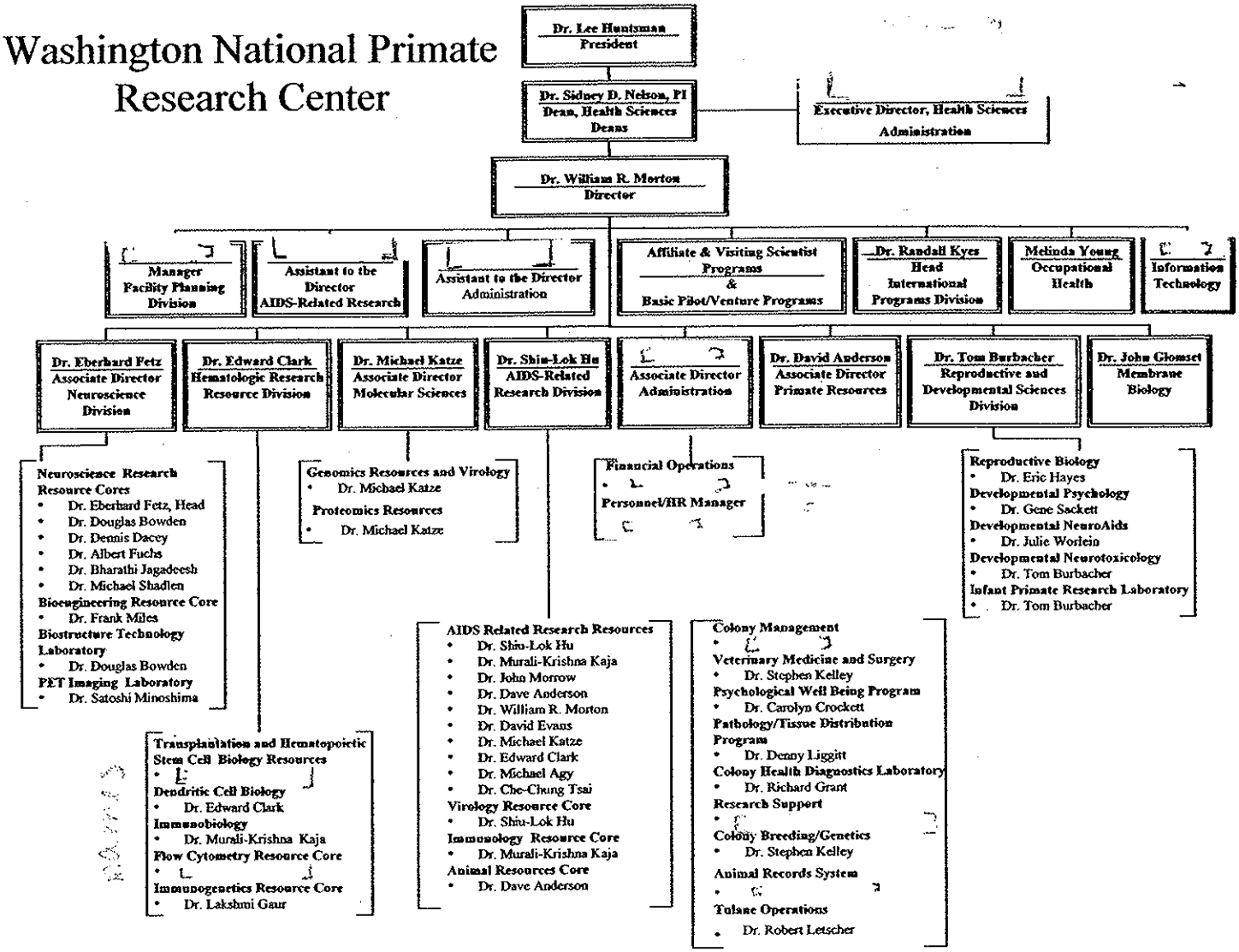

Appendix

C. **Infrastructure** (continued from page 195)

Immunology Typing Core

The Immunology Typing Core (ITC) routinely harvests peripheral blood mononuclear cells and DNA from colony animals. These PMBC and DNA are used for phenotyping and genotyping the nonhuman primates as necessary. Animals are screened from major histocompatibility alleles (MHC class I and class II). The ITC depends on the MHC typing methods developed by Dr. Lakshmi Gaur. The goal is provide accurate MHC typing for all animals in the colony. To that end this core continuously works on improving the typing techniques and identifying novel allelic variants. Since not much emphasis was placed on M. nemestrina in other centers the sequence data are hard to come by. As a first step Dr. Gaur has moved her laboratory to the Primate Center Western facility from Puget Sound Blood Center to concentrate completely on nonhuman primate typing. To expedite the process of improving the typing grant proposals were submitted to obtain funding for nucleotide sequencing.

Though both class I and class II loci are polymorphic, the polymorphisms are localized to second exons for class II loci, but were scattered between exons 2 and 3 for class I loci. This entails sequence analysis of multiple exons for class I alleles. Further, dissimilarities in some exons between human and macaques complicate the class I sequence analysis using HLA class I specific primers. Currently, we have identified over allelic variants for class I and over 100 for class II loci. New probes will be synthesized. New allelic designations will be determined once we complete family analysis for the allelic variants identified. For this we would use cryopreserved PBLs and stored DNA.

The MHC class II (for DQA, DQB and DRB loci) typing was accomplished using oligoblots that were evolved from human (HLA) class II allele-specific probes and nonhuman primate sequencing information obtained over time. Nearly 150 nonhuman primate sequence-specific probes were synthesized; following rigorous testing, selected probes are now in use. This vastly improved the quality of typing by identifying and accounting for sequence variations naturally existing within species populations. There are over 10 DRB loci, not all of which are functional. We are currently working with One Lambda Inc that specializes in HLA typing reagents and supplies all over the world for transplant labs, for a high throughput typing method. This will be achieved by using primer probe combinations developed in our laboratory applied to their luminex technology. We hope to test various combinations and select a panel to type high throughput typing for DQA/DQB by the end of this year and extend that to other class II loci and finally to class I when adequate number of sequences become available. The key to this method is not to limit typing to M. nemestrina, but to have it for all old world monkeys in one tube.

Virology/Immunology Service Core

The overall mission of the Virology/Immunology Core is to provide virologic and immunologic resources and expertise to enable efficient and productive use of nonhuman primates for AIDS-related research. Currently, the Core provides the following services:
(1) Sample processing, including isolation of plasma, serum, and PBMC, and processing of various tissues, e.g., lymph node, vaginal wash, etc.
(2) Lymphocyte subset analysis and hematology
(3) Virus isolation by co-culture
(4) Viral load determination by various PCR methods
(5) Serology, including ELISA and immunoblots in multiple formats
(6) Virus stocks and viral antigens

To achieve its mission, the core also performs the following functions:
(1) Develop, characterize and produce reagents such as chimeric viruses, recombinant antigens, and antibodies necessary to support Core services
(2) Maintain, equip, and oversee the operation of BSL-2 and BSL-2 laboratories at the Western Facilities
(3) Develop and adopt state-of-the-art assays and technologies necessary for AIDS-related research at WaNPRC

During the last year we updated and expanded our capability in the following areas:

(1) HIV/SIV serology: we expanded our ELISA capability to measure antibodies against whole virus (SIV, HIV-1 and HIV-2) and envelope-specific (gp120) antibodies. In addition, we adapted a neutralizing antibody assay using TZM-bl cells. This cell line stably expresses high levels of CD4 and CCR5 receptors and uses luciferase and/or beta-galactosidase as reporters for HIV infection. This cell line is highly sensitive to diverse isolates of HIV-1 and, to a lesser degree, to HIV-2 and SIV. We adapted this assay in a 96-well plate format in conjunction with a luminescence assay using a Perkin-Elmer MicroBeta system. We anticipate providing this assay as a routine service in the coming year.

(2) Production and purification of recombinant proteins: we are currently producing recombinant envelope gp160 or gp140 (SIVmne, HIV-1 89.6, and HIV-1 Clade C), as well as Gag/Pol particles of SIVmne and SIVmac239. These procedures have been upgraded with the acquisition of an AKTA prime system (Amersham-Pharmacia) for purification of proteins.

(3) Upgrade of flow cytometry capabilities: we transitioned our flow cytometry capabilities from a three-color Becton Dickinson (BD) FACScan to a four-color BD FACSCalibur. In addition to the extra fluorescence detector, which detects fluorochromes that emit light above 660nm, the FACSCalibur has an automated FACSflow supply system allowing for extended "hands-off" use of the machine without recourse to frequent replenishment of the FACSflow supply or emptying of accumulated waste. The new machine allows us to expand the range of immunophenotyping services offered, specifically allowing finely detailed analysis relating to the immunologic status of lymphocyte subsets.

Dr. Shiu-Lok Hu serves as the Director of the Core, and Dr. Patricia Firpo is the Manager overseeing day-to-day operations. Dr. Nadeem Sheikh, Immunologist, supervises the hematology and lymphocyte subset analyses. There are currently seven (7) employees in the Virology/Immunology Core, of which only is paid from the Core Grant; the rest are supported by income generated by services provided and from other grants and contracts.

Neuroscience Core

A major strength of the WaNPRC is its outstanding Neuroscience Division, which pursues and supports state-of-the-art brain research using non-human primates. The Neuroscience Division has a unique "critical mass" of investigators studying the neural mechanisms underlying behavior and provides invaluable resources for colleagues both within and outside the WaNPRC. The Scientific Research Resources component consists of eight laboratories, which pursue outstanding research in the areas of primate sensory, motor and cognitive neuroscience and provide training for many students, postdoctoral fellows and visiting scientists. In addition, the Neuroscience Division includes three valuable resource Cores. The Bioengineering Core designs and constructs sophisticated custom instrumentation meeting a wide range of experimental needs, and during the last year has developed a website that will provide technical information to the neuroscience community. This past year the Bioengineering Core provided custom-designed instrumentation for several people that have worked as postdoctoral fellows in the Primate Center and are now setting up their own labs to pursue similar research. The Biostructure Technology Laboratory provides neuroanatomical research services and shared instrumentation for acquisition and quantitative analysis of neuroanatomical images. The "BSTL" has also developed the popular "BrainInfo" website, which provides neuroanatomic knowledge to scientists throughout the world, allowing investigators to download neuroanatomical maps on which to record such findings as neural activity, neurochemical locations, and gene expression for inclusion in the BrainInfo knowledge base. The website is currently being expanded into an interactive resource, allowing experimenters to upload their data. A new PET Imaging Laboratory has become operational this year, featuring a dedicated state-of-the-art PET scanner to provide high-resolution imaging capabilities to a wide range of researchers studying the physiology and pathophysiology of the brain. By imaging all of the brain regions activated during particular behaviors the PET scanner represents a valuable complement to neural recording studies. Conversely, the electrophysiological recordings will help identify the neural activity underlying the PET signal. The PET Imaging Laboratory has opened the door for numerous investigators to explore their research questions with a powerful new tool.

Much of the onsite neuroscience research in the WaNPRC involves recording the activity of single neurons in monkeys trained to perform appropriate tasks. Various Core Staff and Research Affiliates are using such "chronic recording" and related techniques to study the oculomotor system [A. Fuchs, C. Kaneko, R. Robinson],

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somatomotor system [E. Fetz, M. Anderson, S. Perlmutter], and cortical association areas involved in perception and decisions [B. Jagadeesh, M. Shadlen]. Other neuroscientists in the Division are developing the comprehensive interactive atlas of the primate brain [D. Bowden], or studying the anatomy and physiology of primate retina [D. Dacey, [illegible]]. Each of these research programs involves extensive collaborative work with students, postdoctoral fellows and international colleagues.

Dr. Albert Fuchs and colleagues have been investigating the neural mechanisms that control coordinated head and eye movements during shifts in gaze. A remarkable finding was that interneurons mediating the pure vestibular-ocular reflex are actually suppressed when eye and head movements occur together. Recording the activity of neurons in the vicinity of the vestibular nuclei during gaze shifts, they found groups of cells phasically related to either the eye movement component or to the head movement, not both. These data support the notion that eye and head movement components of gaze shift are under separate neural control.

Dr. Fuchs and colleagues also elucidated the contrasting roles of neurons in the cerebral cortex (frontal eye fields) cerebellum (fastigial nucleus) and superior colliculus in relation to control of saccadic eye movement. These studies in behaving monkeys have significantly advanced our understanding of the neural circuits underlying oculomotor function in primates.

The role of spinal cord interneurons in generating voluntary movements is being investigated in awake monkeys in the laboratory of Dr. Eberhard Fetz and Dr. Steve Perlmutter. These unique studies are the first to document the normal activity of spinal interneurons in preparation and execution of normal voluntary hand movements. Like cortical neurons, many spinal cells change their activity during an instructed delay period, the time between an instruction cue and a go signal to generate movement. This delay period activity reflects information processing in the absence of any stimulus or movement, and in some cases may depend on the modality of the cue; these observations are the first indication that cognitive processes could involve spinal networks. In monkeys performing multidirectional wrist movements many spinal interneurons have been found to have broader tuning properties than cortical neurons or muscles, and are preferentially activated in relation to particular muscle synergies. Unlike cortical neurons, the target muscles of premotor interneurons are being identified by correlation techniques, and their tuning properties compared. Other spinal studies have provided direct evidence that cutaneous sensory input is preferentially blocked during active movements by presynaptic inhibition. This discovery means that mechanisms of motor control operate by blocking re-afferent cutaneous feedback before it even enters the nervous system rather than incorporating it, and helps to explain the increase in sensory thresholds during movement.

Dr. Marjorie Anderson is continuing to investigate the neural mechanism of movement control in basal ganglia and thalamus, with a view to understanding the abnormalities associated with Parkinson's Disease (PD). Using MPTP to produce a model of PD, Dr. Anderson is finding telling changes in neural activity patterns, such as increased bursting in thalamic cells. Particularly important is the discovery that deep brain stimulation in the internal glubus pallidus [which alleviates symptoms of PD] produces a decrease, rather than the expected increase, in the discharge of thalamic neurons. These findings will contribute significantly to the understanding and treatment of this devastating motor disorder.

Dr. Michael Shadlen and Dr. Bharathi Jagadeesh are investigating the cortical mechanisms mediating higher cognitive functions of visual perception. They are recording activity of neurons in association cortex that transform visual information into the decision to generate appropriate movements. Dr. Shadlen's group has found that reaching a decision on the basis of subtle visual cues involves temporal integration of sensory information over time to reach a threshold for triggering the appropriate response. This model has been investigated by manipulating the odds of the behavioral outcome by microstimulating relevant cortical areas. Another important parameter affecting the monkeys' behavior is response bias, which can be manipulated by changing expectation and rewards. Studying neurons in inferotemporal association areas, which are crucial for object recognition, Dr. Jagadeesh is investigating the neural basis of visual perception of behaviorally relevant cues. She has trained monkeys on a match-to-sample task and is using various distortions of the sample stimuli to investigate the correlations between behavior and the activity of neurons in inferotemporal cortex. These studies represent exciting and innovative probes into the neural mechanisms that mediate higher cognitive functions.

Dr. Dennis Dacey has continued to investigate the functional organization of the primate retina, using state-of-the-art in vitro intracellular recording to test the responses of retinal cells to controlled visual stimuli. Dr. Dacey and

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numerous international collaborators are identifying new types of retinal neurons and documenting the connections that transduce visual signals, from the photoreceptors to the ganglion cells that transmit information to the central nervous system. A new femtosecond 2-photon scanning laser microscope is being used in conjunction with whole cell intracellular recording to document with unprecedented precision the light-evoked calcium signals in dendrites of retinal ganglion cells. These exciting studies are providing fundamental information needed to understand the mechanisms of primate color vision and to treat associated disorders.

Dr. Douglas Bowden and colleagues have been creating a valuable "Brain Information Management System" designed to allow investigators to integrate new information about the brain with existing knowledge. Accessible on the Web, a Template Atlas indexed with 7,000 terms illustrates known brain structures in the non-human primate. The ability to display many different kinds of neural data in a single standard format [e.g., results from studies of anatomical structures, gene expression, electrical or chemical stimulation, lesions, etc.] represents a major advance in synthesizing past and future information from diverse experimental paradigms. Substantial progress was made in transferring the Template Atlas from a fixed Web format into a format suitable for interactive display using Geographical Information Systems (GIS) software. The usefulness of this resource is attested by the fact that in 2001 more than 12,000 separate users were downloading thousands of pages per day.

These selected studies exemplify only part of the wider range of research advances from the Neuroscience group, which are further described in the individual progress reports. Over the last year the efforts of the Neuroscience Division have also emphasized more its many resource functions to the neuroscience community, in keeping with the Primate Centers' mission.

Division of International Programs

The Division of International Programs at the Washington National Primate Research Center (WaNPRC) is a formal administrative division that oversees the Center's international programs. Dr. Randall Kyes, a Research Associate Professor and Core Staff Scientist, has been involved in the Center's international activities for 13 years and heads the division. The objectives of the Division of International Programs include the following: 1) to support foreign breeding operations so as to ensure the availability of nonhuman primate resources; 2) to facilitate joint research projects with collaborating institutions; 3) to provide educational and training opportunities in Primatology for faculty, students and staff from collaborating institutions; and 4) to assist in efforts to manage and conserve naturally occurring primate populations in habitat countries. The Center currently supports two long-standing, international programs in Indonesia (established in 1991 with the Primate Research Center at Bogor Agricultural University) and Russia (established in 1992 with the National Institution: Research Institute of Medical Primatology-Russian Academy of Medical Sciences). A third program was established in Nepal in July 2001 in collaboration with the Nepal Biodiversity Research Society. Recent program additions include: the China Program (established October, 2002 with Anhui University), the Bangladesh Program (established October, 2002 with Jahangirnagar University), the Thailand Program (established January, 2003 with Chiang Mai University), and the Democratic Republic of Congo Program (established in July 2003 with the Tayna Center for Conservation Biology). Ongoing collaborative research also continued with the Singapore General Hospital and the Singapore Eye Research Institute. The Division's expanding research focus includes genetic characterization of primate populations, conservation biology, and primate/human pathogen transmission and emerging infectious disease.

Indonesia Program

The Indonesia Program is a multifaceted international program that was formally established in 1991 in collaboration with the Bogor Agricultural University (IPB) and their Primate Research Center (PSSP), Indonesia. In May 2003, [name] founding Director of PSSP-IPB, stepped down from his post as Director to assume a new appointment as Director of the Veterinary Hospital at IPB. [name] a senior researcher who has been with PSSP from the outset, was appointed as the new Director of PSSP-IPB. He now serves as the responsible collaborator. Program objectives include 1) supporting breeding colonies of specific pathogen free (SPF) macaques for use in biomedical research at the WaNPRC, PSSP-IPB and collaborating institutions, 2) facilitating collaborative research with IPB and collaborating institutions, 3) providing educational and training opportunities for faculty, students and staff from IPB, collaborating institutions, and UW, and 4) assisting with primate conservation efforts throughout Indonesia. The program supports two Indonesian-based breeding facilities (the Natural Habitat Breeding

Facility on Tinjil Island and the Colony Breeding Facility in Darmaga) and a virology laboratory. The Tinjil island facility supports approximately 2300 Macaca fascicularis and the Darmaga facility approximately 110 M. nemestrina. A third WaNPRC supported breeding colony is being established at the PSSP-IPB facilities in Bogor. This colony currently consists of approximately 65 adult SPF M. nemestrina and is under the direction of Dr. David Anderson, Associate Director for Primate and Research Resources, WaNPRC.

Program supervision is provided by Dr. Kyes (Head of the WaNPRC Division of International Programs) who spends about 4 months of the year (~3 trips/yr) in Indonesia. In addition to his UW faculty appointments in the Departments of Psychology and Anthropology, Dr. Kyes holds visiting faculty appointments in the Depts. of Biology, Forestry, and Veterinary Medicine and is a core faculty member in the Graduate Program in Primatology at IPB. He also has a visiting faculty appointment in the Dept. of Animal Science at Sam Ratulangi Univ. (UNSRAT) in Manado, North Sulawesi, and a Visiting Research Scientist appointment in the Primate Research Center at the University of Udayana (UNUD), Denpasar, and Bali. Both universities have maintained long-term collaborative ties with PSSP-IPB and the WaNPRC (including three-party MOUs with PSSP-IPB and the WaNPRC as of Aug. and Sept. 2002 respectively). A third, three-party collaborative agreement was signed with the University of Dumoga Kotamobagu in May 2003. During 2003-04, Dr. Kyes continued his annual survey of the M. fascicularis population on Tinjil Island and a survey of the M. nigra population at the Tangkoko Nature Reserve in North Sulawesi. He also conducted his annual 3-week Field Courses in Primate Behavior & Ecology and Conservation Biology at the following locations: 1) the Tangkoko Nature Reserve (during May) for 12 students and staff from UNSRAT, and 2) on Tinjil island (during July) for 11 students from IPB and one staff of the Indonesian Forestry Dept. Dr. Kyes served as faculty advisor for several Indonesian undergraduate students from IPB and UNSRAT who were conducting their senior research projects. He also served as a committee member for three graduate students (two Masters and one PhD) in the Graduate Program in Primatology at IPB. Dr. Kyes also continued to serve as a member on the Scientific Advisory Board of the Balikpapan Orangutan Survival Foundation that provides consultation for Orangutan Reintroduction Project in East Kalimantan (Indonesia's official orangutan rehabilitation and reintroduction program that has collaborative ties with IPB). Dr. Richard Grant, Head of the Virology and Diagnostic Test Lab at WaNPRC, continued to serve as member of the doctoral committee for [name] from PSSP-IPB. Her dissertation research addresses the prevalence of SRV in M. fascicularis. [name] (Post-doctoral Fellow in the Div. of Intl. Programs, WaNPRC), along with [name] (Research Scientist, also in the Div. of Intl. Programs) and colleagues from UNUD and PSSP-IPB, continued to expand her collaborative research program in primate/human pathogen transmission by sampling macaques and humans at selected monkey forests in Bali. Two Indonesian scientists participated in the Visiting Scientist program at the WaNPRC during 2003-04. [name] from PSSP-IPB, worked in Dr. Kyes' Behavioral Biology Assessment Lab at the Infant Primate Research Laboratory collecting data for his doctoral research focusing on behavioral reactivity and social perception. [name] from PSSP-IPB, joined Dr. Grant's laboratory for a 6-month project to study type D simian retroviruses (SRV) and simian T-cell lymphotropic virus (STLV).

Russia Program

The Russia Program was formally established in 1992 in collaboration with the National Institution: Research Institute of Medical Primatology-Russian Academy of Medical Sciences (NI RIMP-RAMS, formerly, Institute of Medical Primatology-Russian Academy of Medical Sciences), located in Sochi-Adler. The program, however, is based on a long history of collaborative research with our Russian colleagues dating back to the early 1970s. [name] Director of the NI RIMP-RAMS, has headed the Russian center since its inception and serves as the responsible collaborator. The program objectives are now focused primarily on primate resources and joint research. Currently, the WaNPRC helps support a small SPF breeding colony of Indian-origin rhesus monkeys (Macaca mulatta) housed at the NI RIMP-RAMS. Progeny from the colony will be sent to the WaNPRC as needed to support research activities in virology and neurobiology. One visiting scientist from NI RIMP-RAMS, [name] has been at the WaNPRC participating in an extended collaborative research program in virology.

Nepal Program

The Nepal Program was formally established in July 2001 in collaboration with the Nepal Biodiversity Research Society (NEBORS, and originally with the Natural History Society of Nepal) located in Katmandu, Nepal. [name] President of NEBORS and Associate Professor at Tribhuvan University, serves as the responsible collaborator. Modeled after our Indonesia Program, the Nepal Program objectives include 1) supporting a breeding colony of SPF rhesus macaques (Macaca mulatta) for use in biomedical research in Nepal and at the WaNPRC; 2)

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facilitating joint research projects with NEBORS and collaborating institutions, 3) providing educational and training opportunities for faculty, staff and students from NEBORS, collaborating institutions, and UW, and 4) assisting with primate conservation efforts throughout Nepal. During 2003-04, the Nepali government issued formal approval of our/NEBORS proposal requesting permission to establish a collaborative primate breeding program (originally submitted 3 Dec. 2001). This represents a significant milestone for the Nepal Program. In October 2003, the Nepali government passed the Wildlife Farming Policy thus permitting the captive breeding, use, and export of certain wildlife species (including rhesus monkeys). The policy specifies that only captive-bred progeny can be used for research purposes. Passage of this policy was essential to obtaining government approval for our proposed collaborative breeding program. Finally, in December 2003, the Dept. of National Parks and Wildlife Conservation issued an official letter to NEBORS granting approval for the use of rhesus monkeys in breeding and research and with permission to send the captive-bred progeny abroad for research purposes. Plans are now underway to establish the "Nepal Primate Research Center" facilities, including colony caging and necessary support facilities, in the Kathamandu valley. In other program activities, during May 2003, [name] [name] from the Univ. of New Mexico) and Randy Kyes, along with colleagues from NEBORS conducted health assessments and collected biological samples from macaques and humans at Swoyambu Temple in Katmandu. This project helped address the temple committee concerns regarding the health status of the population and provided important data for an expanding research project addressing primate/human pathogen transmission in Nepal. During February 2004, Dr. Kyes and his colleagues from NEBORS conducted their third annual Training Program in Conservation Biology. The first week of the course (lectures) was held in Katmandu followed by a two-week field period in Langtang National Park. The program included a survey of endangered species in the park (e.g., Assamese macaque) and outreach education for local school children. Program participants included 13 students from Tribhuvan Univ. in Katmandu, four environmental journalists, and one staff member from the Dept. of National Parks and Wildlife Conservation.

China Program

The China Program represents a new international program established in October, 2002 in collaboration with the School of Life Science at Anhui University (AU) in Hefie, China. [name], Professor and Dean of the School of Life Sciences at AU, serves as the responsible collaborator. The primary objectives of the China Program include 1) facilitating joint research projects with AU and collaborating institutions, 2) providing educational and training opportunities for faculty, students and staff from AU, collaborating institutions, and UW, and 3) assisting with primate conservation efforts throughout China. [name] visited the WaNPRC in March 04 and gave a talk on the behavioral ecology of the Tibetan macaques (M. tibetana) at Huangshan, China. Plans are currently underway to begin a joint research and training project addressing population status and genetic assessment of the Tibetan macaques at Huangshan.

Bangladesh Program

The Bangladesh Program represents a new international program established in October, 2002 in collaboration with the Wildlife Branch of the Dept. of Zoology at Jahangirnagar University (JU) near Dhaka, Bangladesh. Dr. [name], Associate Professor in the Dept. of Zoology at JU, serves as the responsible collaborator. The primary objectives of the Bangladesh Program include 1) facilitating joint research projects with JU and collaborating institutions, 2) providing educational and training opportunities for faculty, students and staff from JU, collaborating institutions, and UW, and 3) assisting with primate conservation efforts throughout Bangladesh. Plans are currently underway to begin joint research projects that will address both primate population status and primate/human pathogen transmission in urban areas of Bangladesh.

Thailand Program

The Thailand Program represents a new international program established in January, 2003 in collaboration with the Faculty of Science and Faculty of Veterinary Medicine at Chiang Mai University (CMU) in Chiang Mai, Thailand. [name], Senior Lecturer in the Dept. of Biology at CMU, serves as the responsible collaborator. The primary objectives of the Thailand Program include 1) facilitating joint research projects with CMU and collaborating institutions, 2) providing educational and training opportunities for faculty, students and staff from CMU, collaborating institutions, and UW, and 3) assisting with primate conservation efforts throughout

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Thailand. During May 2003, [names] along with colleagues from CMU conducted sample collection on primates and humans at Chiang Mai Zoo as part of an expanding research project addressing primate/human pathogen transmission in Thailand.

Democratic Republic of Congo (DRC) Program

The DRC Program represents the newest international program established in July, 2003 in collaboration with the Tayna Center for Conservation Biology (TCCB). [name] President of the TCCB Board of Directors, and Head of the Tayna Gorilla Reserve, serves as the responsible collaborator. The primary objectives of the DRC Program include 1) facilitating joint research projects with TCCB and collaborating institutions, 2) providing educational and training opportunities for faculty, students and staff from TCCB, collaborating institutions, and UW, and 3) assisting with primate conservation efforts throughout the DRC. In Dec 2003, Dr. Kyes helped secure a small grant award to support the educational and training mission of the TCCB.

Other International Collaboration

During 2003-04, [name], in collaboration with colleagues from Singapore General Hospital (SGH) and the Singapore Eye Research Institute (SERI), continued work on a project examining primate/human pathogen transmission in Singapore.

Animal Resource Core

The Animal Resource Core is designed to perform the necessary in vivo infectivity and pathogenicity studies to characterize prospective viral stocks for AIDS-related studies. Working closely with the Virology Core, the Animal Resource Core will develop the animal-related information required for investigative groups to utilize new, innovative virus stocks in AIDS related nonhuman primate studies. This Core structure provides the staff expertise to perform in vivo infectivity and titration studies in conjunction with the Virology Core. The preceding year the Core has performed a titration study of a SHIV virus for the Virology Core.

Biostructure Technology Laboratory

The primary focus of Dr. Bowden's research is development of neuroanatomic techniques necessary to produce a high-resolution, three-dimensional stereotaxic atlas of the macaque brain. In 2003-04 he together with [name] (UCLA) and [name] at the Functional Magnetic Resonance Imaging Laboratory at the University of California at San Diego perfected a high resolution MRI method that provides digital images of the brain in three-dimensions. This will supplement conventional methods of identifying landmark brain structures by allowing much of the tedious work to be performed automatically.

Once completed the 3-D atlas will replace the 2-D macaque brain atlas that is currently a core component of the BrainInfo website. Functionality added to BrainInfo in 2003-04 included addition of a 'Percent Overlap Tool' that allows one to select a cortical area, obtain a list of structures that overlap it and view their percents overlap; addition of NeuroMaps of 38 cytoarchitectonic areas of macaque cortex by [names] (1947) and photomicrographs of the internal structure of 150 cortical areas; interoperability established with the Brain Architecture Management System (BAMS, USC, Los Angeles) to display connectivity among brain structures based on some 10,000 reports from studies in the rat; links established to more than 700 high resolution photomicrographs of the macaque brain in three planes of section at Brain Atlas Project (Center for Neuroscience, UC Davis), 50 illustrations of cortical areas in flat maps, inflated maps and surface views at [name]Lab (Washington University, St. Louis) and 120 illustrations of human brainstem and spinal cord structures at Medical Neuroscience website (Loyola University, Chicago). Average use of BrainInfo doubled again to 250 visitors/day viewing 10,000 pages/day.

Information Technologies

The mission of the Information Technologies Division (ITD) is defined by a number of related specific aims:

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- Provide support for the development, operations and maintenance of the Animal Records System (ARS)
- Support the WaNPRC Local Area Network (LAN) and Wide Area Network (WAN) and their interconnections
- Support the Client PC Systems within the WaNPRC
- Provide "Help Desk" and hands-on, on-site support for WaNPRC computer users

The Division is comprised of a manager, one programmer, a network administrator, and a network PC client support specialist. The manager's effort is split between development and maintenance of the ARS, management tasks, and general network support; the majority of effort goes to the ongoing development and maintenance of the ARS. The programmer is heavily involved in the operations and maintenance of the ARS and in the development of extensions and enhancements for the system. Both the programmer and manager also aid researchers with customized retrievals and analysis of ARS data as required. The network administrator keeps the networks running and provides general computing support to the user community. This involves working with numerous software vendors to resolve incompatibilities and problems that arise in the network's operating system environment. The client support specialist helps to keep individual Center computers operational and working on the network. There is a strong collaborative effort among the various staff members in this division. The network administrator and PC support specialist interact and support each other's efforts on a continual basis. The manager works with and supports all other positions. Each of these persons may be called upon at any time to provide solutions for a wide variety and ever-changing assortment of computer-related tasks. ITD staff can claim over 100 years of experience with computers, software development and networking. The depth of their experience is apparent in the quality of the service they provide and in their ability to adjust to new technology as it is evolving.

percentage of effort

In the year 2003 about [ ] of the staff efforts were directed at development and maintenance of the ARS. Traffic on our networks continued to escalate throughout this period. During this period the network connection from our downtown Western Avenue facility was upgraded to a high speed fiber optic broadband connection to the U.W. campus backbone. ITD personnel continued to provide support for network services within the Primate Center, at the new Western Facility and at a growing number of remote sites both on and off campus. A senior ARS programmer retired and will be replaced in the coming year.

Typical services provided by the network included:

- File sharing
- Network printers and printing support
- Local e-mail host services
- Internet and World Wide Web (WWW) access
- WWW publishing and Primate Center Internet and private Intranet home pages
- Server backup systems

These are the services that let the Center's computers talk together, exchange data, and access worldwide information services. The ITD also provided 100% backup of all server data and software. The growing user base now includes well over 250 PCs and workstations. During a typical workday the ITD supports more than 100 simultaneous connections to the local area network which is based on Novell Netware. Staff continued to provide more than 99% uptime during weekday working hours for all ITD-supported network services. This has been achieved through the efforts of the dedicated network administrator, who spends weekend, evening and early morning hours doing required network maintenance and trouble shooting in order to be able to keep the network up during the daytime hours.
ITD personnel also continued to perform the tasks necessary to get client computers connected and working in the network environment. These tasks include:

- Client PC configuration and maintenance support
- Troubleshooting of hardware and software problems
- Resolution of compatibility issues
- Management of warranty and repair service
- "Help Desk" activities

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ITD personnel work with computer users, starting with determination of hardware requirements and preparation of purchase orders and continuing through system setup and configuration of system software so that each system can connect to and operate with other network services. Making systems work seamlessly within the Center's network infrastructure is a task that ITD personnel accomplish with a high rate of success. The "Help Desk" function has continued to be very heavily used. It provides an in-house source of help with computing problems, be they hardware, software, network or "user error." Since the ITD is an in-house organization, staff can respond with an office visit when telephone support is not adequate to solve the user's problem and get him or her working again. ITD records show that the Primate Center's owned and supported base of PCs continues to increase at a rate of at least 20 systems per year. The ITD has continued to support all Center users with the existing personnel despite continually growing demand for service and the increased number of geographic sites where service is being provided.

An advisory committee helps guide the efforts of the division with regard to the effort expended on the ARS and on general computer support issues. Committee members represent all major areas of concern: primate resources, veterinary interests, colony management and IACUC issues, research interests, colony records, and computer services. The committee meets monthly to discuss progress and problems and to define and set priorities for future efforts. This committee helps to ensure that development and operations of the ARS are not being done in a vacuum and that the system will continue to evolve to meet ever-changing requirements.

Transplantation & Stem Cell Biology and Flow Cytometry Cores

The transplantation and stem cell biology core has continued to provide ongoing support for post-natal and pre-natal (fetal) stem cell transplantation models using both baboons (P. cynocephalus sp.) and pig-tail macaques (M. nemestrina) at the WNPRC. The core has assisted in animal acquisition, training, management and procedures. In the past year fifteen animals (baboons and M. nemestrina) have undergone total body irradiation followed by transplantation with growth factor mobilized, autologous marrow or peripheral blood CD34 enriched cells that have been modified by gene transfer using viral vectors (onco-retroviral or lentiviral). Three animals (M. nemestrina) that were transplanted in utero with haploidentical CD34 enriched marrow cells were born. The activities have been broken down into specific groups based on the types of transplant activity and the investigators responsible for the experiments.

Fetal, In Utero, Allogeneic Hematopoietic Stem Cell Transplantation

The Core provided support and animals for studies of allogeneic hematopoietic stem cell transplantation into fetal Macaca nemestrina (Mn). To date all experimental transplants have been performed using stem cells from male (MHC haploidentical) donors that are transplanted into female fetuses. Three transplanted animals were born in the past year. All remain alive and healthy and have evidence of chimerism.

We have determined that we can now use plasma DNA from pregnant females early in gestation to identify if the fetus is male using quantitative PCR techniques. A similar approach can now be applied to MHC typing. As part of our work to collect DNA from maternal plasma we will also collect DNA from maternal and paternal leukocytes. The dams and sires will then be MHC typed by Dr. Lakshmi Gaur. Based on maternal and paternal MHC typing, allele specific primer and probe combinations will be generated that will allow us to use quantitative PCR (Taqman) to analyze fetal MHC alleles (see below). Using quantitative PCR on DNA from maternal plasma we will determine if fetal MHC typing can be consistently determined. This would allow identifying MHC male fetuses that are MHC mis-matched with their sire. These mis-matched animals can be used for transplantation studies as well. This would provide investigators with more options and would not limit studies to only female fetal recipients.

We have generated quantitative PCR primers and probes specific for the Mane DQA1*05d, DQA1*05b, DQA1*03f, DQA1*03a, DQA1*01b, DQB1*03a, DQB1*06a, and DQB1*03c alleles. These allow detection of cells carrying the genes for these alleles when present between 1% and 0.0001%. Dr Gaur has typed sires and dams from the M. nemestrina breeding population.

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Flow cytometry assays to assess cell mediated cytotoxicity have been developed. These assays have been used to study the function of natural killer (NK) cells from baboons (Pc) and Mn. Membrane staining dyes DIOC18 or CFSE are used to label target cells and then killing can be assessed based on expression of Annexin-V binding to target cells and labeling of target cell nuclei with 7-AAD or PI. The NK cells from these species are characterized by expression of the low affinity Fc receptor, FcRIII (CD16), NCAM/NKH-1 (CD56), CD8-alpha, NKp30, NKp46, and NKG2-D; and absent expression of CD2, CD3, CD4, and CD8-beta.

Culture system for the expansion of Mn and Pc NK cells has been developed. Sorted CD16+, CD3- blood cells or blood cells depleted of CD2, CD3, CD4, HLA-DR expressing cells are cultured in limiting dilution in the presence of irradiated allogeneic feeder (peripheral blood) cells and an irradiated HPV-transformed baboon B-cell line with recombinant IL-2 (100 – 1,000 IU/ml) in Yssel's medium. Cells expressing NKp30, NKp46, CD16 and CD56 and lacking expression of CD3 can be expanded for up to 6 weeks. Preliminary experiments infusing cultured donor NK cells into infant animals that are chimeric as a result of in utero transplantation has demonstrated no toxicity and possible increase in levels of chimerism observed in marrow and blood.

Gene Transfer into Autologous Hematopoietic Stem Cells Used For Post-Natal Transplantation

The transplantation core supports ongoing studies of gene transfer into marrow repopulating hematopoietic stem cells in non-human primates. In the last year there have been 15 animals transplanted. All animals have survived the transplant procedure and engrafted. Of these, three animals were M. nemestrina and all have done well clinically. One of the experiments involved studies to expand cells in vivo by transducing repopulating stem cells with chimeric growth factor receptors for chemical inducers of dimerization. Another experiment examined gene transfer of globin constructs into stem cells as a pre-clinical model for therapy of thalassemias and other hemoglobin defects. Other experiments have directly compared different types of viral vectors for gene transfer into hematopoietic stem cells.

Immune Reconstitution in Baboons Following Autologous Stem Cell Transplantation – The Role of Il-7

In the past year the transplantation core has supported work by Dr. Storek to study immune reconstitution in baboons after autologous stem cell transplantation. Fludarabine pharmacokinetics have been studied as a pre-transplant treatment to increase the chance of successful transplantation, demonstrating rapid clearance of fludaribine. In the past year work has demonstrated generation of CMV specific CD4 lymphocytes from genetically modified stem cells after transplantation.

Other Program Support

The transplantation core has supported activity through the national and local cores for the Programs in Excellence for Gene Therapy.

As part of the Transplantation Core's function, large animals that can serve as blood donors are housed within the primate center. Both baboon and pigtail macaque blood donors used in the past year are listed below. These donors serve not only to provide transfusions for transplanted animals but also to provide blood and marrow samples to laboratories for routine in vitro studies.

Allogeneic Stem Cell Transplantation

Three recipients of sex-mismatched allogeneic stem cell transplants continue to be followed for maintenance of chimerism. This is necessary to demonstrate that the isolated stem cells have maintained lymphohematopoiesis for the life time of an animal. With the availability of MHC typing in a controlled breeding colony it will in the future be possible to identify MHC matched siblings that will be useful for allogeneic transplant studies.

Flow Cytometry

In the past year the flow cytometry core has established a working arrangement with the local representative for [ ] to test monoclonal antibodies to human CD antigens for cross reactivity with hematopoietic cells from baboons and pigtail macaques. As part of this work this section of the core is beginning to systematically test

private source

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monoclonal antibodies to human NK cell antigens and receptors. As part of this work a flow cytometry based cellular cytotoxicity assay has been developed that can be used for measuring killing by both NK and CTL. This assay uses DIOC18 labeled target cells in a 4 hour incubation with varying ratios of effector cells. Cytotoxicity is determined by analysis of cell surface expression of Annexin-V and DNA staining with 7AAD on cells that are DIOC18-labeled.

4. Operations and Committees

Executive Advisory Committee. This Committee is composed of the WaNPRC Director, the Principal Investigator on the Center's core grant, the Chair of the Department of Comparative Medicine, and the Chair of the Department of Physiology and Biophysics, a Core Staff Faculty representative, an Industry representative, an AIDS research scientist representative, and the Associate Directors for Administration and Primate Resources. The Committee meets twice a year to discuss the administrative and programmatic direction of the Center and any other related significant personnel issues. No changes in committee members has occurred since the last reporting year.

Scientific Advisory Committee. This Committee is made up of nationally recognized scientists in various disciplines to cover the scientific research scope of the Center. It usually meets once per year, or as required, to provide critical review and recommendations for scientific research. The Committee provides direct input to the University of Washington Health Sciences Administration and the University of Washington President on the progress and relevance of the scientific programs of the Center. The Committee also conducts exit interviews with the Director and Staff and submits a written report to the Core Grant PI. No changes in committee members has occurred since the last reporting year.

Research Review Committee (RRC). This Committee is composed of the WaNPRC Director, two Core Staff scientists, two non-Primate Center, University of Washington (UW) faculty members, and the Associate Director for Primate Resources. The RRC reviews all animal-related research proposals for the WaNPRC, evaluating them for scientific merit and applicability regarding research to be carried out at a primate research center. If any proposal has not been peer-reviewed by a major granting agency and the members feel it necessary, the Committee may seek external review by one or two ad hoc reviewer(s) who have expertise in the field. New proposals are distributed to RRC members and are discussed/ reviewed via monthly scheduled meetings and/or e-mail communication, including interchanges with the investigator and NPRC colony veterinary personnel, as necessary. The Committee Coordinator [name] Assistant to the Director) coordinates RRC activities; communicates with new investigators, committee members and NPRC staff, as required; and maintains records of the decisions of all Committee members and all approved NPRC research projects. The RRC reviewed and evaluated proposed venture/ pilot and colony health-related projects included in the NPRC renewal grant application (for first year funding), and will continue to review and consider any future venture/ pilot proposals submitted to the NPRC during the ensuing years of this 5-year grant. No changes in committee members has occurred since the last reporting year.

Safety Advisory Committee. This committee meets on a monthly basis to discuss policy related to occupational health and safety in the care and use of research animals. No changes in committee members has occurred since the last reporting year

Health and Safety Committee. The aim of this committee is to assist in providing a safe working environment for employees and to address general occupational health and safety concerns. The committee reviews the Center's written Health and Safety Plan, addresses emergency planning issues as required by the University of Washington administration and advises on health and safety training programs. Melinda Young appoints the committee members from a variety of the Center's Divisions. No changes in committee members has occurred since the last reporting year

Psychological Well-Being and Environmental Enrichment Committee. This committee is an informal body that meets regularly to discuss environmental enrichment issues. The Committee serves in an advisory capacity to the Attending Veterinarian. Changes in membership include the addition of Kathy Bentson, Ph.D., [name] One member, [name] no longer works at the NPRC and is thus no longer on the committee. In addition to the appointed members, any interested members of the WaNPRC husbandry, veterinary,

and research staff, Infant Primate Research Laboratory representatives, and student researchers participating in Psychological Well-Being Program projects are invited to attend meetings and submit comments or ideas.

5. Education and Training

Education and training of WaNPRC personnel remains one of the highest operational priorities. Training exists in a number of different areas with both general and specific programs matched to the needs and occupational requirements of each employee. Extensive individual employee training programs have been developed at the WaNPRC under the office of the WaNPRC Occupational Health and Safety Coordinator with support from Primate Resources' staff. Training programs required for all new WaNPRC employees are based on risk assessments and tailored to work performance requirements. As an example, all staff working directly with animals must complete courses in biohazard safety including personal protective equipment, basic animal husbandry, zoonotic disease potential, and appropriate responses to potential exposure incidents. The Institutional Animal Care and Use Committee also requires certified training for all University of Washington personnel involved in animal studies, including nonhuman primates. Beyond these courses the UW offers an extensive program of courses through other UW departments such as the Department of Environmental Health & Safety. Employees are encouraged (and frequently required) to take courses on animal use, hazardous materials, first aid and CPR, fire safety, clean-up of chemical spills, radiation safety, use of respiratory protection equipment, shipping of biohazardous materials, supervisory procedures, and other relevant topics. Security awareness, emergency preparedness and biosecurity training are growing training programs within the WaNPRC.

The potential for exposure to zoonotic agents mandates a high level of training for all personnel in close proximity to nonhuman primates. The Occupational Health and Safety Coordinator frequently provides outreach awareness and safety orientation for non technical staff who maintain our facilities.

WaNPRC clinical veterinarians have significant leadership roles in educational efforts at the WaNPRC and affiliated programs. The Supervisory Veterinarian for Medicine and Surgery is also an Association for the Assessment and Accreditation of Laboratory Animal Care International (AAALAC) Council on Accreditation member, bringing extensive educational and training experience to the WaNPRC. He has also assumed leadership for nonhuman primate training of postdoctoral fellows enrolled in the Department of Comparative Medicine's NIH-sponsored Laboratory Animal Training Program. Postdoctoral fellows spend two to three months at the WaNPRC performing a broad array of clinical veterinary and research procedures providing extensive nonhuman primate training for developing laboratory animal veterinarians.

Several members of the WaNPRC present training, clinical, and research seminars jointly sponsored with the Department of Comparative Medicine. Primate Resources' staff is dedicated to providing training and instruction in nonhuman primate medicine, surgery and husbandry, programs in biosafety training, and other educational programs in-house for staff and affiliates. WaNPRC Primate Resources' staff annually provides an 18 week course of instruction for all new animal care employees that prepares them to take the exam for certification as an Assistant Laboratory Animal Technician (ALAT) by the Association for Laboratory Animal Science (AALAS) WaNPRC veterinarians are also members of the Public Speakers Resource of the Northwest Association for Biomedical Research and lecture at local schools on the benefits of animal-related biomedical research in our community.

A remarkable opportunity for in-depth training and education is afforded by the Infant Primate Research Laboratory (IPRL). This unique facility provides 24-hour care, is equipped with a nursery for the care of premature and clinically ill infants, and supports a number of research protocols involving nonhuman primates ranging from neonates to mature adults. Students are involved in experimental design and studies in Primatology, psychological development, physiology, teratology, pathology, virology, neurology, and growth and development. This arrangement provides students with a unique opportunity to interact with WaNPRC preventive health care programs and veterinary medical care programs, as well as the opportunity to participate in the husbandry of neonatal and developing infants. After receiving initial training in the nature of research, the students collect data relating to the growth and development of infant primates and then learn how to analyze and interpret the data. The IPRL also benefits from this arrangement, for the data are added to the Laboratory's longitudinal database, which is one of the most extensive in existence. Alumni of this program have gone on to pursue graduate and professional work in a

number of leading academic institutions and several have become full-time employees of the WaNPRC following completion of their academic studies.

Another exceptional opportunity exists with the Indonesian Field Study Program, in interdisciplinary program for students in the animal sciences and related areas of study. In collaboration with the WaNPRC, students may participate in educational, training, and research activities at the Tinjil Island Natural Habitat Breeding Facility or the Darmaga captive breeding facility. The program head, Randy Kyes, is both Core Staff at the WaNPRC and a Research Associate Professor in the UW's Department of Psychology.

Because of his frequent interactions with the facility in Indonesia, he has been able to develop a training program that exposes students to field research at a period critical to their research development but at an age when they typically are not offered field work. A didactic spring seminar at the University of Washington is followed by a field course of independent study in a natural setting in Indonesia tailored to meet the student's area of interest.

All WaNPRC faculty and staff have access to a broad base of UW education and training opportunities by virtue of location and employee benefit structure. Employees may take academic courses free of charge at the UW and a range of other state-supported institutions. The UW Training and Development Department offers a variety of courses on topics such as job skills development, management development, and UW policies and procedures training. Employees can receive certificate training in supervision, UW fiscal management, and written and oral communications. Each year staff members enroll in a job-enrichment training class or complete academic course work. These classes enhance the skill level of existing staff and improve the Center's ability to recruit and retain employees. Additionally, a highly trained staff provides more efficient technical support for animal- and laboratory-related activities, thereby The WaNPRC, with its network of local, remote and international laboratories and animal resources, offers employees and students an invaluable opportunity for training and education not easily obtained by any other means. This network of resources in Seattle, Tulane, and Indonesia represents an ideal combination of laboratory work and practical experience with nonhuman primates.

Visiting Scientists. Finally, the education and training capabilities of the WaNPRC extends to several visiting scientists from international organizations. During 2003-04, the following individuals trained at the NPRC in a variety of programs:

- Ph.D., Institute of Basic Medical Science, Tsukuba, Japan
- Ph.D., Sheffield University, England
- , M.S. , PSSP, Bogor Agricultural University, Bogor, Indonesia
- , MD, University of Washington, Seattle, WA
- , Monash University, Sydney, Australia
- S.Si (Bachelor of Science), Primate Research Center, Bogor Agricultural University, Bogor, Indonesia
- M. V. Sc. (Microbiology), College of Veterinary Science, AP Agricultural University Rajendranagar Hyderabad, India
- Ph.D. Harbin Veterinary Research Institute, Chinese Academy of Agricultural Sciences, Harbin, People's Republic of China.
- Ph.D., Post Doctoral Fellow, Moscow, Russia
- Nadeem Sheikh, Ph.D., Post-doctoral Fellow, London, England
- Ph.D., National Institution: Research Institute of Medical Primatology RAMS, Sochi-Adler, Russia
- PhD, Visual Sciences Lab, University of Chicago, Chicago, Illinois
- PhD, Visual Sciences Lab, University of Chicago, Chicago, Illinois
- PhD, Optometry, State University of New York, New York, NY
- , PhD, Visual Science Research Center, U of Alabama, Birmingham, Alabama
- , Institute of Basic Medical Science, Department of Physiology University of Tsukuba, Tsukuba Japan.
- Institute of Basic Medical Science, Department of Physiology University of Tsukuba, Tsukuba Japan.
- PhD, Stanford University, Stanford, CA

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- Laboratorium voor Neuro- en Psychofysiologie, Leuven, Belgium
- Brandeis University, Waltham, MA
- Cold Spring Harbor Laboratories, Cold Spring Harbor, NY
- University of Melbourne, Melbourne, Australia
- Stanford University, Stanford, CA
- Medical University, IPM, Niavaran, Tehran, Iran
- California Institute of Technology, Pasadena, CA
- Fujisawa Pharmacy Research Science, Tsukuba, Japan
- Asahikawa Med Instructor, Asahikawa, Japan