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

5P51RR013986-08
SOUTHWEST NATIONAL PRIMATE RESEARCH CENTER

Final

SOUTHWEST NATIONAL PRIMATE RESEARCH CENTER

ANNUAL PROGRESS REPORT

Reporting From: 04/30/2005

Reporting To: 04/29/2006

25.859% AIDS Related

withheld

Patent or Copyright was not awarded this grant year.

PERSONNEL ROSTER

Core Doctoral Scientists

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withheld		SNPRC: TX, USA
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SUBPROJECT DESCRIPTIONS

NPRC MANAGEMENT SUBPROJECTS

CONSTRUCTION OF SPF RHESUS MACAQUE FACILITY (0276)

NPRC UNIT: ADMINISTRATIVE

%NPRC $: 2.297% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
withheld				, TX USA

SUBPROJECT DESCRIPTION

The proposed construction will provide a complex of six buildings to be used for SPF Indian-origin rhesus monkeys and using them in AIDS-related research. The breeding facilities will consist of four buildings each with 14 indoor-outdoor cages. Total square footage of these buildings is 14,864. The breeding cages are separated into four buildings to reduce disease transmission. A climate-controlled building (544 sq. ft.) will be constructed in close association with the breeding cage buildings to be used for treating ill animals. It will have a treatment room, an isolation room and support rooms. The remaining building in the complex will be a personnel support facility. It will include two locker rooms, an office and a break room (624 sq. ft.). The SPF breeding colony to be housed in this complex is funded by a National Institutes of Health (NIH) Cooperative Agreement (U42-RR16024). Under this cooperative agreement, the SNPRC will produce SPF rhesus monkeys for use primarily by NIH-grantees conducting AIDS-related research. The SWRPRC breeding colony, currently consisting of about 290 animals, is housed in a 40-year-old complex approximately 20 miles from the SNPRC and on a military base that is scheduled to be turned over to the City of San Antonio in 2002. In addition to the operational difficulties of maintaining such a facility from a distance, the present facility can not accommodate the approximate doubling in colony size that is expected within the next four years. The SNPRC combines experienced professional staff, proven methods, and excellent facilities for the virological and immunological evaluation of SPF rhesus macaques used in simian immunodeficiency virus (SIV)/AIDS research. These resources, combined with the recently acquired SPF rhesus colony and staff skilled in state-of-the-art genetic and demographic management, position the SWRPRC to play a pivotal role in meeting the national need for SPF rhesus in AIDS-related research. The proposed construction will provide the animal housing facilities necessary for the SNPRC to fully realize its potential to meet this national research need.

IMPROVEMENT OF PRIMATE CLINICAL CARE FACILITY (0278)

NPRC UNIT: ADMINISTRATIVE

%NPRC $: 0.189% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
withheld				, TX USA

SUBPROJECT DESCRIPTION

Research on chronic diseases has been and will continue to be an important and well-funded component of the National Institutes of Health (NIH)-supported research program at the SNPRC. The ongoing success of chronic disease research is dependent upon the continued provision of high-quality clinical care; however, growth in investigator research support and animal utilization has taxed ability to provide necessary clinical care and support for NHPs. This application requests funding to improve existing animal care facilities to fulfill the following long-term objectives: 1) to modernize and expand the Institution's capacity for providing clinical care for treating NHPs, especially baboons, that are active participants in or are being held for future research protocols; 2) to equip the renovated treatment rooms with additional examination tables, gurneys, carts, and procedure lights which are needed to provide high-quality animal care; 3) to upgrade the Institution's radiographic capabilities by acquisition of digital x-ray equipment; and 4) to bring the facilities into compliance with current National Research Council (NRC) ventilation recommendations for animal care areas. The proposed alteration and renovation will remediate current inefficiencies of space utilization and traffic movement and will utilize the space gained to create a larger treatment area. Clinical procedure capabilities will be expanded and modernized with needed equipment, and a critical care area will be established adjacent to the clinic area. An office space currently adjacent to the clinic will be relocated away from animal care areas. Finally, the heating, ventilation, and air-conditioning (HVAC) system will be replaced with a system that supplies 100 percent fresh air. The net result of the proposed renovations is to modernize aged facilities and to increase institutional capacity for provision of high-quality animal care.

RHESUS BREEDING COLONY IN NEPAL AND IMPORTATION TO USA (0399)

NPRC UNIT: ADMINISTRATIVE

%NPRC $: 0.714% **AIDS RELATED RESEARCH**

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
withheld				, TX USA

SUBPROJECT DESCRIPTION

There is a severe shortage of rhesus monkeys (Macaca mulatta) required to fulfill critical needs in research on AIDS, on development of vaccines against infectious agents that could be used as biological weapons, and on a wide variety of other topics in biomedical research. Rhesus macaques derived from monkeys of Indian origin have unique characteristics that are particularly valuable in research on the development of AIDS vaccines. Despite the recent expansion of breeding colonies in the United States, the shortage of these important research animals is actually increasing in severity, accentuating the need for new sources of Indian-type rhesus. Indian-type rhesus macaques exist in large numbers throughout many regions of Nepal. The production and exportation of captive born rhesus macaques is approved under Nepalese law. The objective of this proposal is to address the urgent need for a new source of Indian-type rhesus macaques for use in biomedical research by developing a captive breeding colony in Nepal. We are developing a self-sustaining colony capable of supplying 75 animals per year to the US to meet critical biomedical research needs.

SUBPROJECT PROGRESS

The current year has been devoted to constructing relocatable buildings at the site selected for establishment of the breeding colony in Nepal. The first set of buildings is 80% complete. A senior veterinarian has received advanced training in the management of macaques at the Southwest National Primate Research Center and Personal Info The first wild-caught founders of the breeding colony are expected to enter the facilities during 2006.

RESEARCH SUBPROJECTS

DIET-INDUCED OBESITY IN MARMOSETS (0428)

NPRC UNIT: ADMINISTRATIVE

%NPRC $: 0.210%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
withheld				SNPRC, TX USA

SUBPROJECT DESCRIPTION

The purpose of this project was to develop a diet-induced obesity model, using the common marmoset. Animals were to be characterized relative to body composition, baseline metabolic parameters (such as insulin and glucose), and response to an oral glucose tolerance test, then placed on a high fat diet to induce obesity.

SUBPROJECT PROGRESS

The study was completed in May 2006. Results are proprietary.

MARMOSET OBESITY STUDY, PHASE I (0429)

NPRC UNIT: ADMINISTRATIVE

%NPRC $: 0.500%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
withheld				SNPRC, TX USA

SUBPROJECT DESCRIPTION

The objective of this work is to define obesity and external markers of obesity in marmosets. The animals will ultimately be sued to screen compounds for efficacy in treatment of obesity and/or Type II diabetes.

SUBPROJECT PROGRESS

Animals have been assigned to this project and habituation processes associated with physiological data collection have begun.

TB VACCINE DEVELOPMENT IN NONHUMAN PRIMATE MODEL (0400)

NPRC UNIT: ADMINISTRATIVE

%NPRC $: 0.714%

INVESTIGATOR	DEGREES	STAFF	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
withheld				, TX USA
				Proprietary Info
				Proprietary Info

SUBPROJECT DESCRIPTION

More than 2 billion people, one-third of the world's population, are infected with Mycobacterium tuberculosis. Three million people die each year of TB. The public health problem is intensifying as the heavy use of antibiotics is leading to antibiotic resistant strains of M. tuberculosis. Existing vaccines have serious limitations. This project is determining the immunological responses of rhesus monkeys to M. tuberculosis infection, and the pathological development of disease, in more detail than has been done previously. When the immune correlates of TB have been well defined, a formulation of heat shock protein 65 (hsp65) and a plasmid containing the hsp65 DNA sequence will be encapsulated together with an immunostimulatory protein in microspheres, and tested as a vaccine. The rationale is that the plasmid will quickly exit the microspheres, integrate into host DNA, and produce hsp65, which will serve as an immunogen. Later, the hsp65 protein will be slowly released for up to 60 days, serving as antigen for a booster immunization. Based on prior experiments with mice, the vaccine is expected to have prophylactic activity and also to be capable of stimulating a more effective immune response than is normal in people who already are infected with M. tuberculosis.

SUBPROJECT PROGRESS

During the current year, we developed and refined immunological techniques to measure in rhesus macaques, lymphocyte proliferation, cytokine levels, and numbers of cells that produce genome interferon when their T-cell receptors recognize the proper combination of a peptide and the major histocompatibility type. These techniques will enable us to monitor the immune responses of rhesus macaques to infection with M. tuberculosis and to immunization with the vaccine preparations. The vaccine, if successful, will have a major advantage in that only a single injection will include antigen for a primary response and for a secondary response. This capability would enhance the success of a vaccination program in developing countries, where it is often logistically difficult to obtain access to subjects for the purpose of booster vaccinations.

FUNGIFORM PAPILLAE AND THE EVOLUATION OF TASTE PERCEPTION IN PRIMATES (0418)

NPRC UNIT: COMPARATIVE MEDICINE

%NPRC $: 0.210%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
withheld				

SUBPROJECT DESCRIPTION

The purpose of this study is to gain a better understanding of the evolution of taste perception by gathering data on the tongue anatomy of various non-human primates. In order to better understand differences in taste ability and anatomy, data on the number of fungiform papillae will be gathered on a variety of primate species across the primate order. Fungiform papillae are one type of papillae on the tongue that are involved in the perception of taste and their density has been correlated with taste ability, or sensitivity, in humans. To count these papillae, animals must first be anesthetized. In order to avoid additional anesthetizations, data collection at SFBR will be done in conjunction with the annual physicals performed on the chimpanzees. After anesthetization the mouth is propped open with a plastic tube placed between the upper and lower canines and a blue stain is applied to the tongue. This stain is mostly comprised of ethanol and has been used on humans and non-human primates without adverse effects. While most of the tongue will be temporarily dyed blue by the stain, fungiform papillae do not stain and are therefore easily identifiable. A digital camera is used to take photographs of the tongue and later the papillae are counted on an enlarged image using Proprietary Info Photographs are localized to the mouth, nose, and chin only. This process takes no longer than 10 minutes per animal.

Data on the anatomy of a large number of chimpanzees is particularly important to this project. Research on humans has shown that there is a significant difference in fungifrom papillae density (and thus taste sensitivity) between males and females, but no data are available for non-human primates. Accordingly, testing to see if this pattern exists in Homo sapiens' closest relative is of great interest. In addition, determining whether or not there are significant sex differences in chimpanzees will only be possible with a large sample size. Although taste physiology and human taste abilities are well researched, little is known of taste evolution or comparative anatomy. This project will add a great deal to what we know about primate behavioral ecology because taste perception is integral to making food choices, and dietary decisions affect an individual's nutritional state and reproductive success.

SUBPROJECT PROGRESS

Approximately 50 chimpanzees have undergone this phenotypic characterization procedure. The results will be used for the Principal Investigator's Ph.D. dissertation.

INVESTIGATION OF BITTER TASTE SENSITIVITY IN CHIMPANZEE (PAN TROGLODYTES) (0420)

NPRC UNIT: COMPARATIVE MEDICINE

%NPRC $: 0.210%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
withheld				UNIVERSITY OF WASHINGTON, WA USA
				UNIVERSITY OF UTAH, UT USA

SUBPROJECT DESCRIPTION

Humans vary in their ability to taste the synthetic compound, phenylthiocarbamide (PTC). While some people find PTC to be nearly tasteless, others find it to be intolerably bitter. Recent efforts have identified a gene that accounts for the ability of humans to taste PTC. Chimpanzees have, like humans, been reported to vary in their ability to taste PTC; however results of tests performed to date are ambiguous. In this experiment, we will test the ability of individual chimpanzees to taste PTC by giving them apple slices soaked in a low-concentration (1mM) PTC solution or a control (1mM vitamin C) solution. We will then observe whether or not the individual rejects the apple slice. Finally, we will compare these behavioral data with genetic data obtained from the same individuals. This test will reveal whether chimpanzees vary in their ability to taste PTC and whether the same gene as in humans accounts for this ability.

SUBPROJECT PROGRESS

Approximately 50 chimpanzees have been tested. Additional animals will be tested in the future.

EVALUATING THE IMMUNOGENICITY OF HBV-C295 ISS CONJUGATE IN COMBINATION WITH HBV (0405)

NPRC UNIT: COMPARATIVE MEDICINE

%NPRC $: 0.210%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
withheld				

SUBPROJECT DESCRIPTION

The objective of this experiment is to assess the dose response of a new conjugate Proprietary Info vaccine in baboons. This experiment will help determine if the addition of Proprietary conjugate to free Propri can enhance the immune response t Propr surface antigen, and the optimal dose of conjugate for enhanced immune response in baboons. This new Pro vaccine Proprietary may be beneficial to society since it could improve responses to Prop surface antigen.

SUBPROJECT PROGRESS

Study is still open. As of 12/05 all animals with the exception of 5 were released from the study. An amendment was approved January 2006 to collect 30mL of uncoagulated blood from the 5 remaining animals on the study. The purpose is to determine if baboon cells isolated from whole blood samples can generate immune responses in vitro. These samples will assist in the development of a new hepatitis B vaccine in humans. protocols from withheld lab.

HBV + C295 ISS-PMXB VACCINE IN BABOONS (0406)

NPRC UNIT: COMPARATIVE MEDICINE

%NPRC $: 0.210%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
withheld				

SUBPROJECT DESCRIPTION

The objective of this exneriment is to assess the dose response of a new formulation consisting of Proprietar in combination wit Propr urface antigen. This experiment will help determine the optimal dose of y Info for increased immunogenicity of Propr ntigen in adult baboons. This study will consist of 4 groups of 5 animals per group. This experiment will help determine if Proprietary an enhance the immune response to Prop urface antigen, and the optimal dose of Proprietary for enhanced immune response in baboons. This new Propriet vaccine Proprietary Info may be beneficial to society, since it could improve responses to Prop urface antigen, especially in poor responders to currently approved hepatitis B vaccines. Proprietary formulation Proprietary has been previously tested in baboons in combination with Prevnar vaccine (ongoing study 952-PC-0). However, the Proprietary formulation in combination with HBV vaccine antigen has never been tested in baboons.

SUBPROJECT PROGRESS

This Study is now closed.

PREVNAR + C295 ISS VACCINE FORMULATION IN INFANT BABOONS (0407)

NPRC UNIT: COMPARATIVE MEDICINE

%NPRC $: 0.210%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
withheld				

SUBPROJECT DESCRIPTION

The objective of this experiment is to test for the first time in infant baboons the immunogenicity of a commercial pneumococcal 7-valent vaccine formulation (PREVNAR®) alone, or in combination immunostimulatory DNA sequences Proprietary Info PREVNAR® vaccine in combination with Proprietary Info was tested in adult baboons (952-PC-0) and was shown to be safe. This study will help decide if PREVNAR® combined with Proprietary Info vaccine formulation can elicit improved antibody responses in infant baboons to pneumococcal polysaccharide antigens, which will assist in the development of a new pneumococcal vaccine for human infants.

SUBPROJECT PROGRESS

Study is going according to protocol. There are no unforeseen problems.

BABOON OPSONOKINE VACCINE STUDY (0411)

NPRC UNIT: COMPARATIVE MEDICINE

%NPRC $: 0.210%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
withheld				

SUBPROJECT DESCRIPTION

A new immune system stimulator, Proprietar has shown great promise in inducing strong immune cell responses (killer cell responses) against both cancer targets and infectious disease targets (Hepatitis B Virus , HBV) in mouse models. The Proprietar consists of a protein normally involved in the body to activate and recruit cells involved in presenting targets to the immune system (so called Antigen Presenting Cells, APC). This protein, human Proprietary Info is linked to the influenza molecule Proprietary Proprietary binds to sialic acid, which is present on virtually all mammalian cells and allows the now "sticky" molecule to bind and stay at the injection site which prevents it from diffusing away. We will evaluate an HBV vaccine, using the HBV target protein HBsAg (Hepatitis B surface antigen) mixed with two different concentrations of the Proprietar We will study the induction in the baboon of both an anti-HBsAg cytotoxic (killer) T-cell response and B-cell antibody response. This will be done by first immunizing the animals at 0 and 28 days and for the next 14 weeks collect blood samples to determine the immune response. The existing vaccines for HBV are limited to protecting individuals from infection but do not work as therapy in already infected patients. The goal here is to determine if we can generate a proper immune response that ultimately results in a therapy for individuals already infected with a infectious disease virus.

SUBPROJECT PROGRESS

This project is half completed.

IN VITRO NEUTRALIZATION OF HCV WITH MONOCLONAL ANTIBODIES BEFORE ADMINISTRATION (0419)

NPRC UNIT: COMPARATIVE MEDICINE

%NPRC $: 0.210%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
withheld				

SUBPROJECT DESCRIPTION

Hepatitis C virus infections in man become chronic in approximately 85% percent of individuals exposed. At present there are an estimated 2.7 million chronically infected people in the United States and an estimated 200 million worldwide. There is no vaccine and therapy for chronic HCV infections is limited a combination of interferon and ribavirin, but treatment is successful in less than half the patients. For these reasons, vaccination and/or immuno-therapy may be an important alternative. The envelope proteins of HCV are an obvious target for any HCV vaccine. Unfortunately, due to poor cell culture systems for the virus, classic in vitro neutralization tests using antibodies cannot be performed using infectious virus. An alternative method to test the neutralization potential of an antibody is to combine HCV and antibody in vitro overnight and then test the inactivation of the virus by inoculation into chimpanzees. Recently, HIV-HCV pseudotype particles were developed that can be potentially used to test the neutralizing capabilities of antibodies in vitro without the use of an animal model. However, it needs to be established that the pseudotype particles do represent authentic HCV particles and that antibodies that neutralize these pseudotype particles also neutralize HCV using an in vivo system. The only way to establish this is through a comparison of monoclonal antibodies shown to neutralize pseudotypes in vitro with an in vitro neutralization test using the chimpanzee as a read-out. This study aims to make this comparison. If a firm correlation is established the need for chimpanzees to determine neutralizing antibodies will be greatly reduced.

100 chimpanzee infectious doses of monoclonal HCV will be combined with each of 4 monoclonal antibodies in vitro overnight. Following incubation the combined mixtures will be inoculated i.v. into chimpanzees. (Total volume approx 5ml). Animals will be bled weekly and monitored for HCV viremia. If no infection is indicated after 8 weeks the animals will be challenged with un-neutralized HCV to demonstrate infectivity.

SUBPROJECT PROGRESS

One animal is currently active on this study.

TESTING INFECTIVITY OF HCV ISOLATED FROM CELL CULTURE IN CHIMPANZEES (0421)

NPRC UNIT: COMPARATIVE MEDICINE

%NPRC $: 0.210%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
withheld				

SUBPROJECT DESCRIPTION

Hepatitis C virus infections in man become chronic in approximately 85% percent of individuals exposed. At present there are an estimated 2.7 million chronically infected people in the United States and an estimated 200 million worldwide. There is no vaccine and therapy for chronic HCV infections is limited a combination of interferon and ribavirin, but treatment is successful in less than half the patients. There currently exist poor cell culture systems for the virus which have not proved to be reproducible between labs and the only animal model for the virus is the chimpanzee. Recently we succeeded in producing infectious hepatitis C virus in cell culture (termed HCVcc). The goal of this chimpanzee experiment is to test the infectivity of these particles in vivo. For most HCV isolates, adaptive mutations are required for efficient RNA replication in cell culture. Although only a limited number of these adaptive changes have been tested in vivo, they appear to be deleterious for replication in chimpanzees and have only rarely been detected in sequences of natural HCV isolates. Testing this isolate or cell culture infectious chimeras in chimpanzees is potentially of great importance to the HCV field. Until this point, HCV produced in vivo (from chimpanzees or humans) is non-infectious or poorly infectious in cell culture. Conversely, HCV RNAs adapted to replicate in cell culture are compromised in their ability to replicate in vivo. Having an isolate that can replicate both in cell culture and in vivo would be a very powerful tool for characterizing HCV replication, entry and pathogenesis. This will enable us to compare the behavior of true HCV particles produced in the liver to HCVcc produced in cell culture. The will be particularly important for studies of virus entry and neutralization and also reduce the need for future chimpanzee experiments.

10^6 cell culture infectious units of two different cell culture adapted viruses will be inoculated i.v. into two different animals. (Total volume ~1-2mL). The inoculum will consist of concentrated cell culture supernatant. Animals will be bled weekly and monitored for HCV viremia. If no infection is indicated after 8 weeks the animals will be challenged with a known infectious isolate (HCVH77 monoclonal virus) to demonstrate infectivity.

SUBPROJECT PROGRESS

The in-life portion of this experimant has been completed. The results are proprietary.

PHARMACOKINETIC, PHARMACODYNAMIC, SAFETY AND TOXICOLOGICAL COMPARABILITY STUDY (0423)

NPRC UNIT: COMPARATIVE MEDICINE

%NPRC $: 0.210%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
withheld				

SUBPROJECT DESCRIPTION

The purpose of this study is to evaluate the in vivo comparability of two monoclonal antibody (MAB) variants, Proprietary Info are identical except for one amino acid substitution in the Fc region of the antibody. Both MABs bind to the CD4 molecule found on white blood cells (lymphocytes) and are being evaluated as a potential treatment of autoimmune diseases (Chronic cutaneous lupus erythematosus), organ transplantation (kidney) and the extension of the effective use of currently available therapeutic agents (Factor VIII). In these conditions, the human body is rejecting its own protein (causing tissue damage) or a given treatment (rendering it inactive). Proprietary Info are both believed to prevent or delay this response and therefore may have an enormous benefit to patients with these diseases or medical needs. Extensive investigation into safety and efficacy has occurred with Proprietary in baboons at SFBR Proprietary single dose, multiple dose and dose ranging studies have been completed in baboons with no MAB related adverse events. Proprietary has been selected for continued clinical development as it is more representative of a naturally occurring antibody and is believed to elicit less of an immune response in vivo. A successful comparison of these two MABs may alleviate the need to repeat an extensive preclinical program in baboons to assess many biological parameters already investigated with regards to Proprietary In addition to limiting the use of baboons by streamlining the transition from Proprietary Info in the clinic, this study may enable the sponsor to accelerate the pace of moving this beneficial treatment to the populations in need of medical assistance.

The animals will be sedated and given seven 1 hour intravenous infusions of either Proprietary Info or saline every other day over a two-week period. Blood samples will be collected at various time points before and after infusions in order to evaluate a number of parameters including drug concentrations, immune response, serum chemistries, cell counts and cell typing. At the end of the seven infusions, 10 treated animals will be sacrificed and a complete necropsy performed. Tissues will be collected to examine possible effects on specific tissues due to drug administration. Prior to sacrifice, four animals, two treated with Proprietary and two treated with saline, will be monitored during a six week recovery phase to assess any prolonged effect of MAB treatment.

SUBPROJECT PROGRESS

The in-life portion of this study has been completed. A GLP-compliant report is in progress.

IMMUNOGENETHERAPY OF CHRONIC HCV CARRIER CHIMPANZEES (0427)

NPRC UNIT: COMPARATIVE MEDICINE

%NPRC $: 0.210%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
withheld				

SUBPROJECT DESCRIPTION

Vigorous HCV-specific T cell responses are typically observed in patients who recover spontaneously from acute, self-limited hepatitis C. In contrast, T cell responses are weak and narrowly focused in persistently infected patients. It has been proposed that enhancement and/or de novo induction of HCV-specific cellular immune responses in chronically infected individuals will induce HCV clearance and recovery. This hypothesis can only be tested in chimpanzees, the only animals susceptible to HCV infection.

We propose to vaccinate 2 HCV carrier chimpanzees with recombinant vectors expressing Proprietary Info to induce HCV-specific T cell responses and to evaluate whether these HCV-specific T cells can impact on HCV carrier state, by reducing or eliminating viremia and/or by controlling HCV antigen expression. The vaccine has 2 components, a recombinant Proprietary Info and a recombinant Proprietary Info and will be applied in a prime-boost regimen. The vaccine expresses 3 HCV antigens, namely Proprietary Info Both Proprietary and MVA are known to be strong inducers of T-cell immunity. One HCV carrier chimpanzee will be mock vaccinated with vectors that do not express the HCV antigens.

SUBPROJECT PROGRESS

The 3 chimpanzees are currently on protocol. Results are proprietary.

BABOON MODEL FOR STUDY OF PRIMATE MATERNAL BEHAVIOR (0011)

NPRC UNIT: COMPARATIVE MEDICINE

%NPRC $: 1.451%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
withheld				Proprietary Info UNIVERSITY OF NEBRASKA, NE USA

SUBPROJECT DESCRIPTION

Maternal behavior in primates is a complex process, involving a number of physiological and life history variables. This study is the first to include behavioral, life history, endocrine, and genetic data from a large number of nonhuman primate subjects in the determination of factors related to maternal behavior. The project will increase our knowledge of the heritable nature of variation in maternal behavior, will characterize mothers with poor maternal qualities, and will provide information useful for selecting females used in breeding programs. This project generates behavioral and hormonal profiles to be used in the development of the baboon as a model of maternal behavior by quantifying mother-infant interactions, determining infant outcome, and measuring hormone levels in a large sample of captive baboons. It will then examine the causes of variation in maternal behavior, including hormonal, experiential, and genetic factors. It is expected that the information resulting from this study will lead to new avenues of research on the mechanisms involved in the regulation of maternal behavior, as will as providing a model for related studies in reproductive endocrinology, colony management and behavioral research.

SUBPROJECT PROGRESS

This project is ongoing and is in year 7 of the grant. Data on maternal behavior have been collected on 300 subjects. Hormonal data, collected noninvasively through urine, have been obtained from 185 females.

LOCOMOTOR ONTOGENY OF PRIMATE QUADRAPEDALISM AND THE EVOLUTION OF PRIMATE GAIT (0177)

NPRC UNIT: COMPARATIVE MEDICINE

%NPRC $: 0.020%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
withheld				

SUBPROJECT DESCRIPTION

Changes in body weight and shape may influence the biomechanics of change in four leg walking behavior during the first 6 months of baboon life. Infants change from a "lateral sequence" (arm touches down after ipsilateral leg) gait to a "diagonal sequence" (arm touches down after contralateral leg) gait, in terms of body gait and motion. This is an important transition because the diagonal sequence gait in adult primates is unique among mammals, and there is no consensus on why it evolved. This project will address that question. Biomechanics of walking will be assessed in infant baboons between 4 and 26 weeks old age. Reflective markers will be placed on limbs and motion will be recorded with a 3D motion analysis system in conjunction with a video camera. Small weights will be placed on body segments to test for changes in gait with changes in body weight distribution. We supported initial work at the Foundation to demonstrate feasibility and gather pilot date. Funding was obtained from the Private Source and a laboratory was established in Austin to continue the work. We lease infant/juvenile baboons to the research program. This project is underway. The conclusion of this study will shed light on the evolution of walking motion in primates and will help identify the changes in body structure that might have led to the evolution of diagonal sequence gait in primates.

SUBPROJECT PROGRESS

No progress this summary period.

NONHUMAN PRIMATE MODEL OF MYCOPLASMA PNEUMONIAE PNEUMONIA (0412)

NPRC UNIT: COMPARATIVE MEDICINE

%NPRC $: 0.210%

INVESTIGATOR	DEGREES	STAFF CODE	DEPARTMENT	NON-HOST INSTITUTION: STATE, COUNTRY
withheld				

SUBPROJECT DESCRIPTION

The goal of this project is to establish a non-human primate model of Mycoplasma pneumoniae pneumonia. The first step is to administer pure toxin to the lung of a cull baboon (a second cull will receive the carrier plus heat inactivated toxin and serve as the control). We will characterize the inflammatory response mechanism by defining the role of cytokines known to be markers of inflammation in bronchoalveolar lavage (BAL), their influence on histopathologic lesions, and the distribution of toxin in selected tissues. If the toxin elicits a marked cytokine response compared to the control (heat inactivated toxin) we will apply to administer live organism to additional baboons.

SUBPROJECT PROGRESS

A total of 5 baboons have been used on this project. One pilot animal was used to demonstrate the effectiveness of the apparatus utilized during the delivery procedure. The procedures on the two cull animals were completed as described above. An additional pair of baboons received the toxin in the same manner, thereby increasing the sample size. Blood and lavage samples were collected from all 4 study animals for analysis.