ORIP

OFFICE OF RESEARCH
INFRASTRUCTURE PROGRAMS

Photo by Kathy West, courtesy of the California National Primate Research Center.

NONHUMAN PRIMATE RESOURCES

2021

ORIP'S MISSION

ORIP advances the NIH mission by supporting infrastructure for innovation. This support is focused on research resources, including animal models for human diseases, cutting-edge scientific instrumentation, construction and modernization of research facilities, and research training opportunities for veterinary scientists. Through continued engagement with NIH Institutes, Centers, and Offices and the biomedical research community, ORIP empowers and expands existing programs and develops new initiatives to support NIH research at the forefront of scientific progress.

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National Institutes of Health
Office of Research Infrastructure Programs

OVERVIEW

The Division of Comparative Medicine (DCM) within the Office of Research Infrastructure Programs (ORIP), Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI), Office of the Director, National Institutes of Health (NIH), advances biomedical research by supporting research resources, such as those that provide animal models for human disease.

Because of their genetic, anatomical, physiological, and behavioral similarities to humans, nonhuman primates (NHPs) are among the best models for human disease research when studies in humans are not ethical or feasible. Among other important medical advances, NHPs have played key roles in the understanding and treatment of a variety of infectious diseases, such as AIDS, tuberculosis, Zika virus disease and congenital Zika syndrome, Ebola, and, recently, COVID-19. Additionally, NHPs have been critical in advancing therapeutics for type 2 diabetes and other metabolic disorders, treatment of glioblastoma (brain cancer), deep brain stimulation to treat Parkinson's disease, neuroprosthetics (including the decoding of brain waves for brain–machine interfaces), pain management interventions, and organ transplantation. NHPs help determine the safety and efficacy of vaccines, devices, and therapies before they are used in humans. The COVID-19 pandemic demonstrated the pivotal role of NHPs in developing medical countermeasures for SARS-CoV-2, the virus that causes COVID-19; this included understanding infection progression and pathophysiology, preclinical development of vaccine candidates and therapeutics, and development of a variety of SARS-CoV-2-specific diagnostic assays.

Costs related to stringent breeding and housing requirements limit access to NHPs throughout the biomedical research community. To mitigate these issues, ORIP's DCM supports multiple NHP colonies and research-related resources that are available to the community of NIH-funded researchers. These NHP resources support biomedical research spanning scientific disciplines, with studies supported across almost all NIH Institutes, Centers, and Offices.

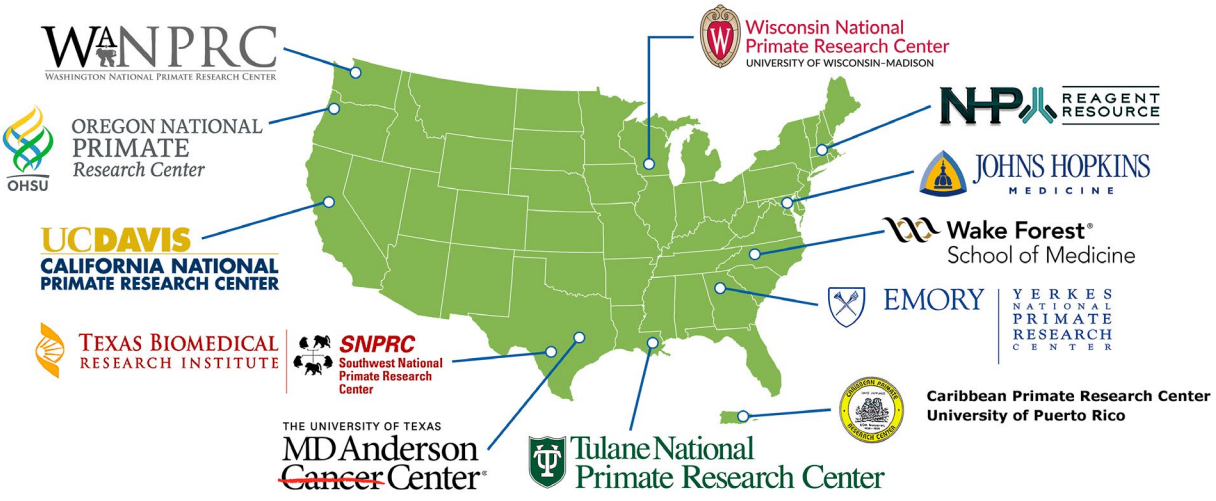
NONHUMAN PRIMATE RESOURCES

NPRC NATIONAL PRIMATE RESEARCH CENTERS
Causes | Preventions | Treatments | Cures

National Primate Research Centers

The National Primate Research Centers (NPRCs) are a national network of seven Centers that increase access to and promote sharing of valuable NHP-related resources among biomedical researchers. Additionally, the NPRCs advance the missions of NIH Institutes, Centers, and Offices by providing the animals, facilities, expertise, and resources required by investigators in disease-specific areas. ORIP's DCM funds NPRCs located in California, Georgia, Louisiana, Oregon, Texas, Washington, and Wisconsin. Collectively, the NPRCs maintain breeding colonies for rhesus, pigtail, and Japanese macaques; common marmosets; olive baboons; and titi monkeys.

Each Center provides expertise on the use of various NHP species as models for human disease to address specific research projects. Each provides a variety of services both individually and through inter-NPRC collaborations. The NPRCs provide services for research funded by NIH, other federal agencies, nonprofit foundations, and the private sector. Additionally, the program offers a Pilot Research Program for new investigators or exploratory research and a Visiting Scientist Program that offers advanced research training. The NPRCs have scientific programs addressing major research fields, such as infectious diseases, aging, cardiovascular disease, diabetes and metabolic disorders, neuroscience, pediatrics, regenerative medicine, reproductive health, and women's health. For detailed information on NPRC capabilities and programs, visit NPRCresearch.org. Recent advances by the NPRCs can be viewed at nprc.org.



Nonhuman primate research resources supported by ORIP.

NHP COVID-19 research being conducted in an Animal Biosafety Level 3 laboratory. Photo courtesy of the Southwest National Primate Research Center.

Specific-Pathogen-Free Macaque Colonies

Macaque monkeys are premier research models for HIV/AIDS. For example, macaques infected with the simian immunodeficiency virus (SIV)—the NHP analogue of HIV—are used to address basic research questions about viral infection routes, acute phases of infection, and latent viral reservoirs because these cannot be explored in humans. Likewise, SIV-infected macaques serve as models for developing HIV vaccines, infection prevention devices, new therapeutics, microbicides, and cure strategies prior to first-in-human trials.

The presence of specific viral pathogens in experimental animals can confound the results of HIV/AIDS-related investigations or pose a health risk to staff. Therefore, a consortium of colonies was developed to provide specific-pathogen-free (SPF) macaques for AIDS research that are negative for SIV, type D simian retrovirus, simian T-cell lymphotropic virus, and herpes B virus. Additionally, SPF macaques are characterized for major histocompatibility complex class I alleles, which are known to be associated with SIV viral load and rate of disease progression. ORIP supports SPF rhesus macaque colonies at the California, Oregon, Southwest, Tulane, and Yerkes NPRCs, as well as the Caribbean Primate Research Center in Puerto Rico.

ORIP also supports SPF pigtail macaque colonies at the Washington NPRC and the Johns Hopkins University School of Medicine. Visit the ORIP website for more details on these critical SPF macaque resources.

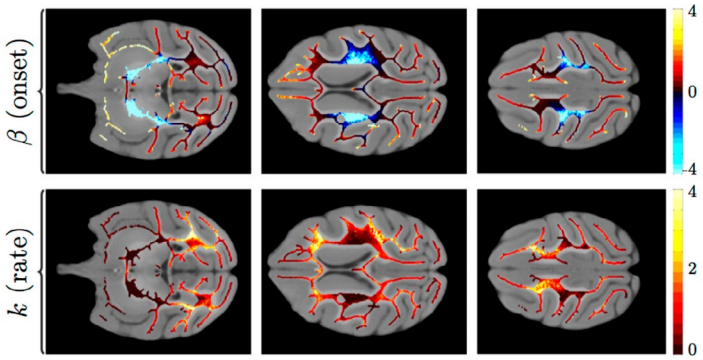
Other Nonhuman Primate Research Resources

Baboon Research Resources: Relative to most other NHP models, baboons share the greatest similarity to humans in terms of their larger size, year-round breeding, and placental biology. Because of similarities between the baboon and human immune systems, baboons are critical for vaccine development, xenotransplantation, and studies of infectious disease and bacterial sepsis. The baboon colony at MD Anderson Cancer Center's Michale E. Keeling Center for Comparative Medicine and Research (KCCMR) is maintained free of infection from an extensive list of at least 18 viruses, bacteria, and parasites and is a valuable research resource for studies requiring the unique similarities of baboons to humans without the complicating influences of coinfections.

Squirrel Monkey Breeding and Research Resource: Housed at KCCMR, this is the only national squirrel monkey breeding and research resource available for biomedical research and one of the few NIH-supported national research resources that specialize in a New World (neotropical) primate species. Squirrel monkeys are valuable for neuroscience research because of their small size and similarities to humans in brain structure, which makes them superior neuroscience models compared to small nonprimate mammals, such as rodents. Squirrel monkeys are used widely in neuroscience, vision, and hearing research; in studies of infectious diseases (malaria vaccine, polyoma virus disease, Zika virus); as a model of sporadic cerebral amyloid angiopathy; and in research on drug addiction and its behavioral and physiological consequences.

Caribbean Primate Research Center Program: The Caribbean Primate Research Center (CPRC) Program maintains conventional and SPF macaque colonies. Additionally, the CPRC maintains a free-ranging colony of rhesus macaques of purely Indian origin that was established over 80 years ago from a substantial founder population. This colony exhibits the lowest levels of genetic admixture with non-Indian-origin rhesus macaques among all rhesus monkey colonies surveyed in the United States,

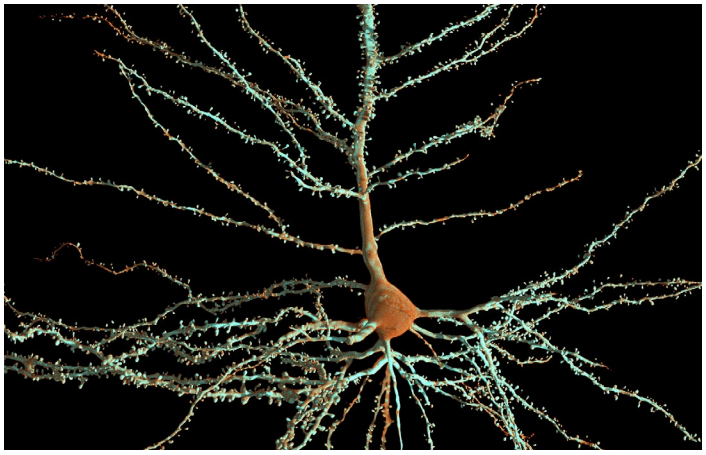
Data on gait parameters as a common marmoset in the Wisconsin National Primate Research Center's Preclinical Parkinson's Research Program walks through a Noldus CatWalk XT10.6 (apparatus not shown).



Postnatal brain structural maturation in infant rhesus macaques during the first 18 months of age. Top: White matter onset intensity at birth (β). Bottom: Median rate (k) of normalized white matter intensity change per day. Image courtesy of the Yerkes National Primate Research Center and collaborators, Drs. M. Styner and M. Niethammer.

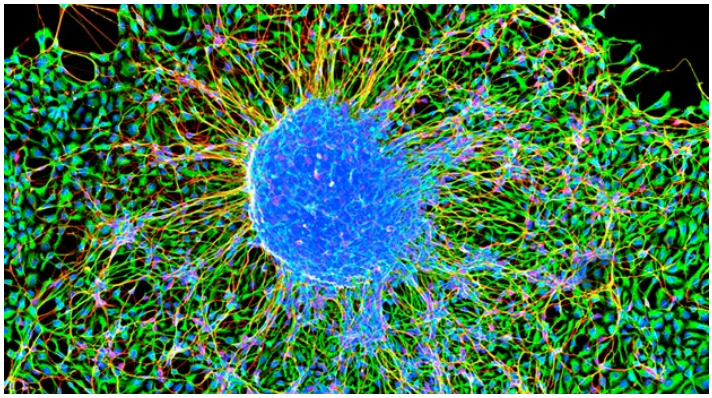
providing a unique resource for research in a naturalistic setting. The CPRC supports researchers at other U.S. institutions, as well as collaborations onsite, and it has active programs in virology (especially SIV and West Nile, dengue, and Zika viruses), genetics, diabetes, parasitology, behavior, cognition, and anatomy.

Vervet Research Colony: Vervets, or African green monkeys (AGMs), are critical research models owing to their similarities to humans in reproductive biology, development of cardiovascular disease and type 2 diabetes on a Western diet, and growth of amyloid plaques with age. The Vervet Research Colony (VRC) at Wake Forest School of Medicine maintains a multi-generational, pathogen-free, genotyped colony of Caribbean-origin AGMs. The colony consists of individuals ranging in age from newborns to geriatric animals over 27 years old. VRC animals, biospecimens, and data have contributed to research on diabetes, obesity, cardiovascular diseases, Alzheimer's disease, microbiome influences, metabolomics, and neuroscience. Additionally, VRC animals have supported vaccine research for SIV, neonatal influenza, respiratory syncytial virus, dengue virus, and SARS-CoV-2.



Pyramidal cell from the prefrontal cortex of a rhesus macaque. The NPRCs offer a wide variety of resources for research with nonhuman primates, including advanced microscopy. Photo courtesy of John Morrison of the University of California, Davis.

NHP Reagent Resource: The NHP Reagent Resource (NHPRR) program at the University of Massachusetts Medical School develops, manufactures, and distributes primate-specific immune cell–depleting antibody reagents to optimize the usefulness of NHPs in biomedical research. These reagents are critical to translational research that advances treatments and vaccines for a wide variety of infectious diseases, such as AIDS, COVID-19, tuberculosis, and Zika virus disease. Cell-depleting reagents produced by the NHPRR also facilitate transplantation, cancer, and gene therapy research involving NHPs. The NHPRR program has grown steadily since its inception in 2000; its cell-depleting antibodies now support more than 40 investigators and 50 research grants with reagents each year.



Common marmoset–derived embryonic stem cells differentiating into neurons in Marina Emborg's laboratory at the Wisconsin National Primate Research Center. A neurosphere was stained to visualize nuclei (blue) and immature neural progenitors (green) transitioning to neurons (red). Image by Scott Vermilyea, Ph.D.

NHP Centers of the Somatic Cell Genome Editing Program: The NIH Common Fund's Somatic Cell Genome Editing (SCGE) Program includes approaches for development and testing in NHPs to improve the efficacy and specificity of gene-editing approaches, with the ultimate aim of reducing the burden of common and rare genetic diseases in humans. Regulatory authorities currently require in-animal studies of safety, efficacy, and gene target specificity for nearly all genome-editing therapeutics under development for clinical use. With program management support from ORIP, Oregon Health & Science University and Massachusetts Institute of Technology are generating genetically modified rhesus macaques and marmosets, respectively, to serve as reporter models to evaluate the efficiency of delivery and editing of CRISPR-based tools *in vivo*. These modified NHP models, as well as unmodified rhesus macaques and marmosets, will be used at the University of California, Davis, Nonhuman Primate Testing Center established through the SCGE Program. After validation, all new reporter animals created by the SCGE Program will be available for distribution to the wider biomedical community.

Visit the ORIP website for more details on other supported NHP research resources.