ORIP

OFFICE OF RESEARCH
INFRASTRUCTURE PROGRAMS



BIOLOGICAL MATERIALS AND REAGENTS

Provided by ORIP Centers and Research Resources

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ORIP'S MISSION O

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.





OVERVIEW

Research to advance our understanding of diseases and develop new treatments may require biological materials and specialized reagents in addition to animal models. Examples of such research resources include organs, tissues, biofluids, cell lines, microbiome components, cell-depleting antibodies,

antibodies for immunoassays, virus stocks, and culture media, among others. ORIP supports Centers and Research Resources that provide investigators with donated human tissues as well as biological materials from, and specialized reagents for, nonhuman primates, rodents, and a number of other animal species. These critical resources fulfill the research needs of investigators across a wide spectrum of topics in biomedical research.

HUMAN TISSUE AND ORGAN RESEARCH RESOURCE

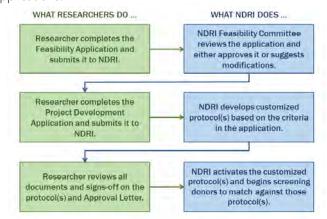


The <u>Human Tissue and Organ</u>
<u>Research Resource (HTORR)</u>
provides investigators with
fresh, frozen, or fixed human
biospecimens, such as organs
and tissues from the nervous,

pulmonary, cardiovascular, lymphoid, endocrine, renal, digestive, and reproductive systems, as well as eyes, skin, bone, cartilage, synovium, and muscle. These biospecimens facilitate human tissue research across the gamut of noninfectious and infectious diseases, including diseases that are public health priorities and rare diseases such as genetic disorders. HTORR collaborates with a nationwide network of organ procurement organizations, tissue banks, eye banks, and surgical medical centers to recover and distribute both normal and diseased tissues from post-surgery and post-mortem donors. For more than 30 years, HTORR has been managed by the National Disease Research Interchange (NDRI).

HTORR utilizes a prospective procurement model with projectspecific recovery and preservation protocols to collect human biospecimens from a diverse pool of donors. This approach provides the scientific expertise and technical support needed to tailor tissue collection procedures to investigators' requirements. As a result, HTORR offers standardized collection procedures that enhance the rigor and reproducibility of research using human biospecimens.

Investigators who are interested in requesting human tissues or organs from HTORR must initiate their requests by completing a <u>feasibility application</u>. Once approved, investigators are provided with biospecimens as tissues matching their requests become available from HTORR's large donor pool. HTORR also can support investigators with letters of support and budgetary information for NIH and other grant applications.



Interactive process for requesting human biospecimens from HTORR.

NONHUMAN PRIMATE BIOLOGICAL MATERIALS



Biospecimens Query System of the National Primate Research Centers Consortium

The Biospecimens Query System (BQS) is an informatics tool that helps investigators obtain biological resources from the National Primate Research Centers (NPRCs) and other participating nonhuman primate (NHP) facilities. This tool contains an inventory of resources that include tissues, serum, blood, DNA, and selected cells obtained from NHP species across participating facilities. The BQS allows investigators to make prospective requests or to search for existing NHP biospecimens according to species, sex, age, tissue type, and preservation method. Once an investigator identifies a

particular biospecimen of interest, the system can be used to contact the distributor of the biospecimen. Material transfer forms, shipping costs, and grant acknowledgement information then can be shared to allow transfer of the biospecimen(s) to the requesting investigator. Use of the BQS requires registration for approved access.

Primate Pathology Image Database

The NPRCs Consortium Primate Pathology Image Database (PPID) is an informatics tool that enables investigators to search for images of NHP organs and tissues based on disease name, etiology, organ, NHP genus and species, and image type. Some images are annotated, allowing the user to go directly to the anatomical region of interest. In addition to being an important research tool, the PPID is widely used as a learning tool by trainees in NHP clinical medicine and pathology. Use of the PPID requires registration for approved access.

Vervet Research Colony



The Vervet Research Colony (VRC) at Wake Forest School of Medicine maintains a multi-generational, pathogen-free, genotyped colony of Caribbean-origin, U.S.-born vervet monkeys, which also are known as African green monkeys (AGMs). This

colony consists of individuals ranging in age from newborns to geriatric animals over 27 years old. In addition to providing well-characterized AGMs, training opportunities, data on colony animals, and expertise in the care and use of NHPs, the VRC distributes biological samples from age-diverse AGMs to qualified researchers. These biospecimens have contributed to research on diabetes, metabolism, microbiome influences, reproductive biology, cardiovascular disease, aging, orthopedics, virology, pharmacology, and other topics.

Nonhuman Primate Antibody Resources



The Nonhuman Primate Reagent Resource (NHPRR) Nonhuman Primate and the Neotropical Primate Reagent Resource are

located at Mass Biologics, a business unit of the University of Massachusetts Chan Medical School. The NHPRR develops, manufactures, and distributes immune cell-depleting antibody

reagents to optimize research using Old World NHPs (e.g., rhesus and pigtail macaques). These reagents support research on HIV and other infectious diseases, transplantation, cancer, and gene therapy. The Neotropical Primate Reagent Resource characterizes the immunoglobulin repertoire and antibody responses of New World NHPs (e.g., marmosets and squirrel monkeys) and uses this information to engineer species-matched lymphocyte-depleting and diagnostic antibodies. Investigators may request reagents from both resources via the NHPRR website.

The New World Monkey Immunoreagent Resource, located at Trinity University in San Antonio, Texas, develops mouse monoclonal antibodies to be used in novel immunoassays specific for biomarkers of inflammation and metabolic hormones in marmosets, squirrel monkeys, and owl monkeys. Immunoreagents for such biomarkers are useful in studies of aging, infectious diseases, neurodegenerative diseases, diabetes, metabolic syndrome, and obesity, all of which are being modeled in New World monkeys.

Specific-Pathogen-Free Baboon Research Resource

The Specific-Pathogen-Free Baboon Research Resource, located at The University of Texas MD Anderson Cancer Center's Michale E. Keeling Center for Comparative Medicine and Research, provides researchers with blood and bloodderived products from colony animals.

RODENT BIOLOGICAL MATERIALS



Mutant Mouse Resource and Research Centers

The Mutant Mouse Resource and Research Centers (MMRRCs) are a national network of mouse breeding and distribution facilities plus an

information coordinating center, serving together as NIH's premier repository of spontaneous and induced mutant mouse and cell lines. The MMRRCs at The Jackson Laboratory, University of California, Davis, University of Missouri-Columbia, and The University of North Carolina at Chapel Hill provide mouse embryonic stem cells to researchers, as well as a variety of mouse tissues, upon request. The MMRRC at the University of California, Davis, also provides hybridomas that produce the monoclonal antibodies targeting proteins for genes that are knocked out in mouse strains distributed by the consortium. The same facility provides plasmid vectors for the NIH Knockout Mouse Phenotyping Program (KOMP), the goal of which is to produce and characterize strains of mice in which single genes are knocked out for every protein-coding gene in the mouse genome.

National Gnotobiotic Rodent Resource Center

The National Gnotobiotic Rodent Resource Center (NGRRC) at The University of North Carolina at Chapel Hill provides researchers with gnotobiotic wild-type and mutant mouse tissues and cells, defined human microbial communities, and a library of bacterial strains. The NGRRC also derives new germ-free mouse strains and trains investigators to establish and run their own gnotobiotic animal facilities

to create mouse strains colonized with defined microbial communities. The biological materials provided by the NGRRC support investigations on a wide range of host and microbial physiological and pathophysiological processes. These investigations target such organs as the intestine, liver, brain, bones, pancreas, lungs, and heart, and they support advances on multiple disease mechanisms and treatment approaches.

Special Mouse Strains Resource

The Special Mouse Strains Resource at The Jackson Laboratory provides biomedical researchers with germlinecompetent mouse embryonic stem cells (mESCs) from a panel of the eight founder inbred strains of the Collaborative Cross and Diversity Outbred mouse populations. These mESCs are from mouse genetic backgrounds that traditionally are difficult to target. They contain Bxb1 docking sites in the Rosa26 locus for high-efficiency targeted transgenesis into this locus across genetically diverse inbred strains.

Rat Resource and Research Center



The Rat Resource and Research Center (RRRC) at the University of Missouri-Columbia provides rat embryonic stem (ES) cell lines. Pluripotent rat ES cell lines are valuable reagents for producing genetically modified rats for the study of a wide variety of human diseases and biological processes. The RRRC has several

proven germline-competent cell lines on different genetic backgrounds with and without fluorescent markers. The RRRC also provides protocols and consultations on how to properly culture and manipulate rat ES cells.

Hybrid Rat Diversity Program

The <u>Hybrid Rat Diversity Program (HRDP)</u> at the Medical College of Wisconsin provides researchers with tissues of interest from a panel of 96 inbred rat strains. The HRDP banks and distributes tissues collected from adult male and female rats, including heart, kidney, liver, spleen, brain, lung, and retroperitoneal fat pad. Requests also are considered for the collection and distribution of additional tissues, tissues from rats of different ages, and tissues collected using specialized protocols. When paired with genome sequences, HRDP tissues are ideal for systems genetics studies.

OTHER BIOLOGICAL MATERIALS AND REAGENTS

Drosophila Genomics Resource Center



The <u>Drosophila Genomics Resource</u> <u>Center (DGRC)</u> at Indiana University Bloomington collects, curates, archives, and distributes <u>Drosophila</u> cDNA clones, plasmid vectors, and cell lines for biomedical research using fruit flies. The DGRC has more than 1

million unique cDNA clones and transformation vectors and more than 100 unique, tissue-specific and developmental stage–specific cell lines for genetic, genomic, and proteomic research. As a central repository and distribution center, the DGRC distributes more than 3,000 products annually. The Center also provides cell culture media, transgenic cell and cell authentication services, and genomic protocols for improving rigor and reproducibility in research using *Drosophila*. These resources and services facilitate the investigation of fundamental developmental pathways and the understanding of a broad range of human disease mechanisms.

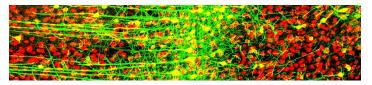
National Natural Toxins Research Center

The National Natural Toxins Research Center (NNTRC) at Texas A&M University-Kingsville provides native and nonnative venoms and purified venom components, recombinant venom proteins, and specialized venom research services to support NIH-funded investigators. Snake venoms have helped to decipher complex physiological and pathophysiological processes and have served as the starting point for the development of novel drugs. Snake venoms possess a rich repertoire of highly evolved, bioactive molecules (enzymes, proteins and peptides, amines, lipids, nucleosides, and carbohydrates), some of which target functional cell surface receptors with high specificity. For example, the main targets of snake neurotoxins are acetylcholine receptors, both nicotinic and muscarinic. The NNTRC maintains a collection of venomous snakes primarily from North America with a growing collection of non-native species consisting of 32 species and 20 subspecies, as well as an extensive library of single-snake venoms. The Center constructs cell-based assays for conventional and high-throughput testing of antivenoms and toxin inhibitory molecules, and it develops and helps develop next-generation antivenoms and

inhibitory molecules that can replace or supplement existing antivenoms. The NNTRC also provides training in toxinology and state-of-the-art research technologies as part of a minority-serving institution.

Center for Neuroanatomy with Neurotropic Viruses

The <u>Center for Neuroanatomy with Neurotropic Viruses</u> (<u>CNNV</u>) at the University of Pittsburgh serves as an international repository for viral transneuronal tracers that are used for studying the functional organization of the nervous system. The CNNV has a specialized biosafety level 2 facility, distributes herpesvirus and rabies virus recombinants as transneuronal tracers, and provides training for neuroanatomical studies in rodents and NHPs. Resources and services provided by the CNNV have enabled pivotal studies of the synaptic organization of neurons, which is fundamental to our understanding of normal brain function, as well as of brain diseases.



Neurons of rat cortex infected with rabies virus (green) by transneuronal transport from a forearm muscle. Red cells are labeled with NeuN antibody. Image courtesy of Dr. Marcel Oberlaender (Max Planck Institute for Neurobiology of Behavior) and Dr. Peter L. Strick (University of Pittsburgh Brain Institute).

Referral Center for Animal Models of Human Genetic Disease

Located at the School of Veterinary Medicine at the University of Pennsylvania, the Referral Center for Animal Models of Human Genetic Disease (RCAM) identifies naturally occurring animal models for studying human genetic diseases and acquires breeding animals or semen from an international network of veterinary specialists. The Center phenotypes and genotypes deposited models, provides veterinary expertise for preclinical trials, and disseminates the disease models to investigators. The RCAM also distributes primary cell cultures, tissues, and biofluids from canine and feline models of human diseases. These resources have supported investigations to better understand lysosomal storage disorders, protein-losing nephropathy, epilepsy, and other diseases.

Zebrafish International Resource Center

The <u>Zebrafish International Resource Center</u> at the University of Oregon offers a variety of antibody reagents to support research using the zebrafish model.

CONTACT FOR MORE INFORMATION

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