

ORIP

OFFICE OF RESEARCH
INFRASTRUCTURE PROGRAMS



COMPARATIVE MEDICINE RESOURCES

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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.



OVERVIEW

Comparative medicine plays an essential role in biomedical discovery by looking for similarities and differences between disease in humans and animals. Thus, animal models enable scientists to better understand, diagnose, prevent, and treat human diseases. Often serving as a bridge between basic science and human medicine, animal models¹ have enabled numerous major medical breakthroughs—among them safe and effective vaccines, including hepatitis A and hepatitis B immunizations; improved cancer treatments; blood transfusions; organ transplantation; bypass surgery; and joint replacement. Animal models are actively used to understand the causes of, and develop therapies for, almost all human conditions, including cancer; cardiovascular diseases; diabetes; obesity; and neurodegenerative and infectious diseases, such as COVID-19.

The Division of Comparative Medicine (DCM) within the Office of Research Infrastructure Programs (ORIP), Division of Program Coordination, Planning, and Strategic Initiatives, Office of the Director, National Institutes of Health (NIH), works to—

- Ensure that NIH-supported researchers have access to, and facilities for, animal models critical to research.
- Support phenotypic and genetic characterization of animal models and the development of new and improved long-term storage of animal germplasm.
- Support studies aimed at improving the welfare and husbandry of laboratory animals.
- Enable career development and translational research training for veterinary students and veterinarians and for postdoctoral investigators who use animal models.
- Increase public-private partnership opportunities with small businesses.

USING ANIMAL MODELS TO ADVANCE TRANSLATIONAL RESEARCH

DCM supports a broad range of translational research projects and resources that develop and enhance access to animal models, including rodents, aquatic models, nonhuman primates (NHPs), invertebrates, and others. Visit the [DCM webpages](#) for a complete list of resources.

Rodents



Rodents are the most frequently used species in biomedical research. Mice, for example, have much in common with people in terms of genetics, development, physiology, behavior, and disease susceptibility. To ensure that mice and other genetically altered rodents with defined mutant genes are accessible to the research community, DCM supports several rodent resource programs to sustain special animal colonies and genetic stocks.

- Mutant Mouse Resource and Research Centers (MMRRCs) maintain and distribute mutant mouse strains for use in biomedical research. The centers collect transgenic, knockout, and other kinds of induced
- mutant mouse lines and distribute them for a small fee to requesting researchers. A national network of four MMRRCs (University of California, Davis; University of Missouri; The University of North Carolina at Chapel Hill; The Jackson Laboratory) and an Informatics, Coordination, and Service Center (University of California, Davis) collectively strives to preserve, protect, and ensure quality control for these models and to provide them for the benefit of research scientists and investigators across the nation and the globe. Each center provides services on a fee-for-service basis, such as cryopreservation of mouse embryos and gametes; rederivation of living mice from cryopreserved embryos and sperm; quality-control testing for mouse pathogens; mutagenesis and embryonic stem cell isolation; and cloning, phenotyping, and genotyping services.
 - The Special Mouse Strains Resource (SMSR) provides valuable tools for genetic analysis of complex diseases at The Jackson Laboratory. The strains include panels of recombinant inbred (RI) and chromosome substitution (CS) strains. The SMSR imports, cryopreserves, and distributes RI and CS strain panels that are vital to the discovery of quantitative trait loci and, ultimately, the genes responsible for complex diseases.
 - The Rat Resource and Research Center (RRRC) distributes high-quality, well-characterized inbred, hybrid, and mutant rat strains to investigators. This center selects and imports rat strains and stocks that are

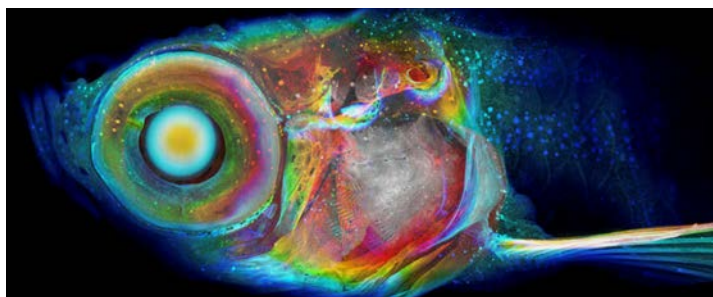
¹ NIH considers very carefully the use of animals in research. Long-standing policies require careful review of all biomedical research studies that propose the use of animals. Research projects using animals are funded only if justified by the potential impact on human health. See the latest news, policies, education and training materials, and information about animals in research at the NIH Office of Extramural Research's [Animals in NIH Research](#) webpage. All animal laboratory facilities funded by DCM are accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International.

important to biomedical research, achieves pathogen-free status, cryopreserves gametes and embryos, and performs genotyping and infectious disease monitoring to ensure the quality of the rats.

- The National Gnotobiotic Rodent Resource Center provides a resource for NIH-funded investigators to examine physiologic and pathophysiologic differences in germ-free (sterile), gnotobiotic (known life, selectively colonized), and specific-pathogen-free (SPF) mice of different genetic backgrounds; to explore the functional alterations of normal versus dysbiotic bacterial communities in murine models and human diseases; and to define the functional relevance of bacterial genes.
- Mouse Resources for Comparative Mendelian Disease Genomics from The Jackson Laboratory focuses on the discovery and validation of genomic variants that cause Mendelian disease phenotypes in mice, with an emphasis on variants that escape exome sequencing detection. The long-term goal of this project is to employ forward genetic discovery and reverse genetic validation to create genomic resources that will facilitate functionalization of naturally occurring variation.
- The Pilot Centers for Precision Disease Modeling includes three centers: The University of Alabama's Pilot Center for Precision Animal Modeling, Baylor College of Medicine's Center for Precision Medicine Models, and The Jackson Laboratory's Center for Precision Genetics. All three centers develop rodent models that more precisely mirror the genotype and phenotype of human disease processes and promote the creation of new therapeutics.

To learn more about other rodent resources, visit DCM's [Rodent Resources Fact Sheet](#).

Aquatic Resources



Aquatic animals—including zebrafish, *Xiphophorus*, salamanders, frogs, and marine slugs—can serve as models for studying human development, behavior, and disease. Because of their short reproductive cycles and transparent embryos, they offer researchers the ability to easily observe them as they develop.

Using these model organisms, researchers can identify potential functions of specific genes, which allows them to better understand the underlying basis of genetic disorders in people. Aquatic models have been important in studies

of gene function, protein interactions, and pathological processes related to humans. DCM supports aquatic models for research through funding of research resources for the development and maintenance of critical genetic stocks, biological materials, and online information.

The Zebrafish International Resource Center is a central repository for wild-type and mutant strains of zebrafish and serves as a resource for zebrafish research information and biological materials. The resource maintains healthy stocks of zebrafish and frozen sperm, as well as appropriate strains of wild-type fish for distribution to the research community.

To learn more about other aquatic model resources, visit DCM's [Aquatic Models: Centers and Research Resources Fact Sheet](#).

Nonhuman Primates



The close genetic, anatomical, physiological, and behavioral similarities of NHPs to humans make NHPs invaluable in wide-ranging biomedical studies. Such research enables discoveries that apply directly to human health and can help scientists test therapies and treatments for such conditions as obesity; aging; diabetes; Alzheimer's disease; drug addiction; and infectious diseases, including AIDS, influenza, malaria, Zika, and—more recently—COVID-19. DCM facilitates the use of NHPs in biomedical research by supporting animal populations, facilities, and technologies.

Closely affiliated with U.S. academic institutions across the nation, a network of National Primate Research Centers (NPRCs) provides NHPs as models for human health and disease for basic and clinical biomedical studies. DCM also supports many other NHP resources, including informatics tools and reagent resources, as well as specialized animal colonies, such as vervet, squirrel monkey, and SPF macaque and baboon breeding and research resources.

To learn more about NHP resources, visit DCM's [NHP Resources Fact Sheet](#).

Other Comparative Models

Larger animal models, such as swine, share many anatomic and physiologic characteristics with humans. They have been proven to be useful models for coronary artery disease, diabetes, heart and lung transplantation, xenotransplantation, hemophilia, obesity, hypertension, and other cardiovascular diseases.

Through the [National Swine Resource and Research Center](#), DCM ensures that valuable swine models are available to the biomedical research community. The repository creates new genetically modified pig lines as requested by the scientific research community and performs research aimed at improving swine models.

DCM also supports the development and use of invertebrate comparative models. Such species, including *Drosophila* (fruit flies) and *Caenorhabditis elegans* (roundworms), are genetically well characterized and can be readily manipulated genetically. Additional models supported by DCM include *Strongylocentrotus purpuratus* (sea urchins), *Aplysia californica* (sea slugs), and *Tetrahymena* (cilia). Because these models are relatively inexpensive and easy to maintain and most are highly genetically amenable, they can provide productive and cost-effective approaches for scientific investigations. Results from experiments involving these models can provide insights into mechanisms underlying human health and diseases and help develop therapies for humans.

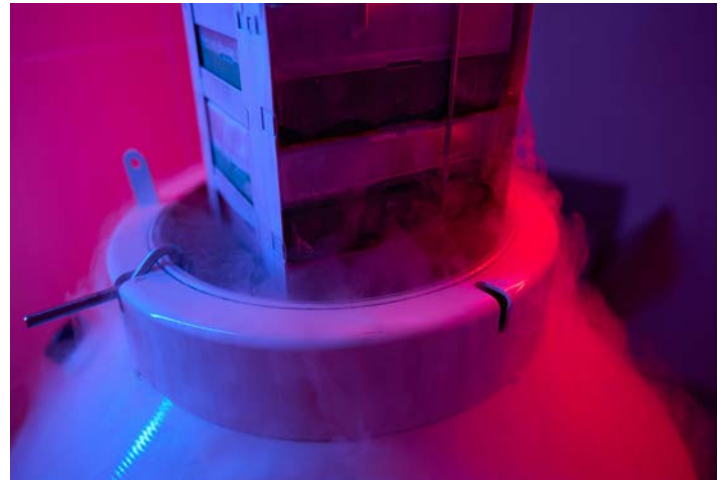
To learn more about other comparative model resources, visit DCM's [Large Animal Models: Centers and Research Resources Fact Sheet](#) and [Invertebrate Models: Centers and Research Resources Fact Sheet](#).

Biological Materials and Reagents

ORIP supports research-related research projects to generate and provide 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. Some of these resources represent alternatives for animal model testing, which contributes to reduction of animal use for the biomedical research. In addition, ORIP supports Centers and Research Resources that provide investigators donated human tissues, such as the Human Tissue and Organ Research Resource, as well as biological materials from, and specialized reagents for, NHPs (NPRCs, NHP Reagent Resource, New World Monkey Immunoreagent Resource, Vervet Research Colony, SPF Baboon Research Resource), rodents (MMRRCs, National Gnotobiotic Rodent Resource Center, SMSR, Hybrid Rat Diversity Program, RRRC), and a number of other animal species (Zebrafish International Resource Center, *Drosophila* Genomics Resource Center, National Natural Toxins Research Center).

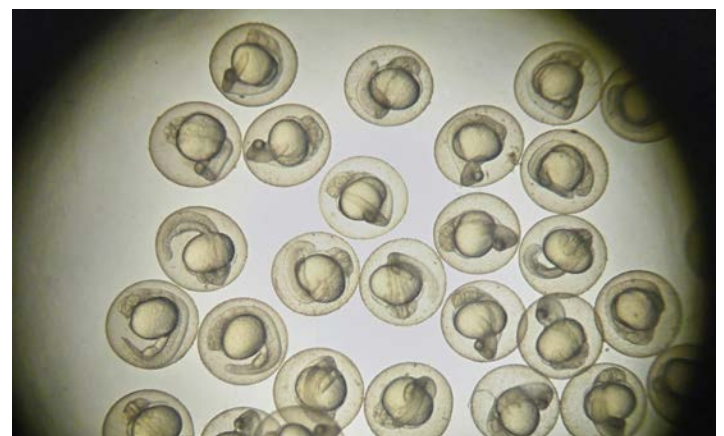
To learn more about these and other biological materials and reagent resources, visit DCM's [Biological Materials and Reagents Fact Sheet](#).

Cryopreservation Research and Resources



As long-term preservation has not been developed or well established in many research organisms, ORIP supports the development of new technologies, devices, and methods to improve cryopreservation, other long-term preservation, and revival of genetic stocks, such as the development of embryo cryopreservation in flies, aquatic species, and NHPs. ORIP also supports efforts to preserve model organisms, including invertebrate, aquatic, mouse, rat, pig, and NHP models, using established practices. To safeguard genetic resources from potential loss due to accidents, natural or man-made disasters, and other incidents, ORIP partners with the U.S. Department of Agriculture's National Laboratory for Genetic Resources Preservation in Fort Collins, Colorado, to store backup collections of *Caenorhabditis elegans*, zebrafish, other aquatic species, and rodents. ORIP-supported genetic stock repositories for zebrafish, mouse, and rat models cryopreserve their genetic strains using various established methods. For example, the Zebrafish International Resource Center cryopreserves sperm. Mouse lines deposited by research scientists into the MMRRCs are cryopreserved in one or more formats, such as sperm, embryos, or embryonic stem cells. The RRRC and the Hybrid Rat Diversity Panel typically preserve rat models by freezing embryos.

To learn more about these and other efforts, visit DCM's [Cryopreservation: Research and Resources Fact Sheet](#).



Career Development and Other Opportunities for Veterinary Scientists

DCM supports biomedical research through several programs that relate to the use, characterization, and care of animal models for human diseases. Laboratory animals are essential for biomedical research to understand the mechanisms of development and progression of the pathology of a variety of human diseases. As part of this effort, DCM funds both individual and institutional training grants to foster the development of the next generation of veterinary scientists who want to pursue a scientific career. Veterinary scientists have unique comparative medicine experience in laboratory animal medicine, pathology, and zoonotic infectious diseases that makes them valuable contributors to biomedical research.

The following are some of the training opportunities available:

- Mentored Research Scientist Development Awards support veterinary scientists who want to further pursue a career in biomedical research.
- Institutional Research Training Grants are designed especially for veterinarians who are considering a career in biomedical science. Institutional awards are made directly to universities and other research institutions to provide advanced training in biomedical or translational research. In addition, short-term (summer) research experience opportunities funded by institutional training grants also are available for veterinary students interested in biomedical research.

For information on these and other career development opportunities, visit DCM's [Training and Career Development webpages](#) and [fact sheet](#).

Small Business Program

DCM is committed to increasing small business participation in federally supported research and development by encouraging the private sector to commercialize technology developed with federal support that may benefit ORIP resources. DCM accomplishes this through the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs.

To learn more about these programs, visit [ORIP's Small Business webpages](#), read the [program fact sheet](#), or visit the [NIH Small Business website](#).



FOR MORE INFORMATION

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