



COMPARATIVE MEDICINE RESOURCES

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FACT SHEET

ORIP MISSION

The Office of Research Infrastructure Programs (ORIP) advances the NIH mission by supporting research infrastructure and research-related resources programs, and coordinating NIH's science education efforts. ORIP's programs support biomedical researchers with the infrastructure and researchrelated resources they require to advance medical research and continue improving human health.





National Institutes of Health Office of Research Infrastructure Programs

OVERVIEW

Comparative Medicine plays an essential role in biomedical discovery by enabling 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 advances—safe and effective vaccines, including Hepatitis A and B immunizations; improved cancer treatments; blood transfusions; organ transplantation; bypass surgery; and joint replacement. Animal models are actively being used to understand the causes of, and develop therapies for, almost all human conditions, including cancer, cardiovascular disease, diabetes, obesity, and neurodegenerative and infectious disease.

- The Division of Comparative Medicine (DCM), within the Office of Research Infrastructure Programs (ORIP), Division of Program Coordination, Planning, and Strategic Initiatives (DCPCSI), National Institutes of Health Office of the Director (NIH/OD), 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 germ plasm.
- Support studies aimed at improving the welfare and husbandry of laboratory animals.
- Enable career development and translational research training for veterinary students and veterinarians as well as for post-doctoral investigators who use laboratory animals.
- 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, 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 at Davis, University of Missouri, University of North Carolina at Chapel Hill, and The Jackson Laboratory) and an Informatics, Coordination, and Service Center (University of California at Davis) collectively strives to preserve, protect, ensure quality control, and provide these models 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) is a resource of special strains of mice that are valuable tools for genetic analysis of complex diseases at Jackson Laboratory. They 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 discovery of quantitative

1 The National Institutes of Health 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 website, OER Animals in Research. All animal laboratory facilities funded by DCM are accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International.



trait loci and, ultimately, the genes responsible for complex diseases. These special strains of mice are important tools for genetic analysis of such diseases as diabetes, cardiovascular disease, obesity, autoimmune disease, and cancer.

- Several resources supported by DCM are developing mouse strains for improved humanized mouse models. A humanized mouse is one that carries functioning human genes, cells, tissues, and/or organs. Such animals are commonly used as small animal models in biological and medical research for human therapeutics. The Center for Humanized Mice offers environmentally, genetically, and xenotransplantation-engineered mouse models for translational studies and drug discovery; activities focus on improved animal models to study human immunity, human-specific infections, vaccines, and human-specific drug interactions. Stem cells and regenerative medicine are the focus of a number of other DCM projects.
- 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 important to biomedical research, achieves pathogen-free status, cryopreserves gametes and embryos, and performs genotyping and infectious disease monitoring to assure the quality of rats. Germline-competent rat embryonic stem cell lines, including several on different genetic backgrounds and several containing EGFP, are also available.
- The National Gnotobiotic Rodent Resource Center provides a resource for broadly based NIHfunded investigators to examine physiologic and pathophysiologic differences in germ-free (sterile) vs. gnotobiotic (known life, selectively colonized) vs.

specific pathogen-free (SPF) mice of different genetic backgrounds, to explore the functional alterations of normal vs. dysbiotic bacterial communities in murine models and human diseases, and to define the functional relevance of bacterial genes. The microbiota can be precisely manipulated by colonizing germ-free rodents with single or multiple resident or pathogenic bacterial or viral or fungal species using isogenic wild type or genetically-engineered bacterial strains.

The Adult Mesenchymal Stem/Stromal Cell Resource provides fully characterized rodent bone marrowderived cells referred to as mesenchymal stem cells or mesenchymal stromal cells (MSCs). These cells are isolated from bone marrow, expanded, tested under standardized protocols, and made available to the scientific research community. The cells can serve as a standard against which other sources of MSCs are compared or as a source of cells for specific research applications

Aquatic Models

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

Using these model organisms, researchers can identify potential functions of specific genes; this 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 of research through funding the development and maintenance of critical genetic stocks, biological materials, and online information.



The Zebrafish International Resource is a central repository for wild-type and mutant strains of zebrafish, and it 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.

Nonhuman Primates

The close molecular, immunological, molecular, metabolic, reproductive, and neurological relationships between nonhuman primates (NHPs) and humans make NHPs valuable in biomedical studies. Such research enables discoveries that apply directly to human health and can help scientists test therapies and treatments for conditions such as obesity, diabetes, and drug addiction and infectious diseases such as AIDS, influenza, malaria, and Zika virus infections. DCM facilitates the use of NHPs in biomedical research by supporting animal colonies, facilities, materials, and technologies.

For more than five decades, a national network of National Primate Research Centers (NPRCs) has provided NHPs as models of human health and disease for basic and clinical biomedical studies. Closely affiliated with U.S. academic institutions across the nation, the NPRCs provide animals, facilities, and expertise in all aspects of NHP biology and husbandry.

DCM supports many other NHP resources, including specialized animal colonies, databases. and reagent resources. To learn more about NHP resources, visit DCM's listing of Nonhuman Primate Programs.

Other Comparative Models

Larger animal models, such as swine, share many anatomic and physiologic characteristics with humans. They have been particularly useful in studies on diabetes; heart, lung and kidney transplantation; and obesity.



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 and performs research aimed at improving swine models.

DCM also supports the development and use of invertebrate comparative models as a complement to rodent, fish, and NHP models. Simpler species, including *Drosophila* (fruit flies) and *C. elegans* (roundworms), are genetically well characterized and can be readily manipulated genetically. Additional simple models supported by DCM include in *Strongylocentrotus purpuratus* (sea urchins), *Euprymna scolopes* (squids) and *Tetrahymena* (cilia). Because these models are relatively inexpensive and easy to maintain, they can provide a highly productive and cost-effective approach for scientific investigation. Results from experiments involving these less complex models can help scientists decide whether to use higher animal species in studies aimed at therapies for humans and companion animals.

Enhancing Career Development Opportunities for Veterinarian 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 individual training grants and institutional training grants to foster the development of the next generation of veterinarian-scientists that want to pursue a scientific career. Veterinarian scientists have unique comparative medicine experience in laboratory animal medicine, pathology, and zoonotic infectious diseases that make them valuable players in biomedical research.

The following are some of the training opportunities available:

 Mentored Research Scientist Development Awards support veterinarians who want to further pursue a career in biomedical research. Institutional Research Training Grants and Individual Training Grants are designed especially for veterinary students and veterinarians that are considering a career in biomedical science. Institutional awards are made directly to universities and other research institutions to provide advanced training in biomedical/translational research. In addition, short term (summer) research experience opportunities funded by institutional training grants are also available for veterinary students interested in biomedical research. Individual training grants are available to obtain mentored research training and to enhance an individual's potential to develop into a productive, independent researcher. For information on these and other career development opportunities, visit DCM's Training Training and Career Development web pages.

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. It accomplishes this through the federal government's Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs. To learn more about these programs, visit DCM's Small Business web pages read ORIP's Fact Sheet.

CONTACT FOR MORE INFORMATION

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