ORIP

OFFICE OF RESEARCH
INFRASTRUCTURE PROGRAMS

RODENT RESOURCES

Fact Sheet 2025

ORIP'S MISSION

ORIP advances the National Institutes of Health (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

Comparative medicine plays an essential role in biomedical discovery by enabling scientists to better understand, diagnose, prevent, and treat human diseases. ORIP's Division of Comparative Medicine (DCM), within the Division of Program Coordination, Planning, and Strategic Initiatives in the Office of the NIH Director, supports an intellectual infrastructure for biomedical research through the creation of models for human disease using animals and cultured cells and management of the infrastructure required to maintain, distribute, and utilize these models.

MODELING HUMAN DISEASES USING RODENT MODELS

Mice and rats are a preferred mammalian disease model because of their high genetic homology with humans, rapid reproduction, efficient and inexpensive housing and husbandry, easily characterized phenotypes, and well-developed resources and tools for genetic manipulation. The use of rodents has enabled several noteworthy medical milestones—the discovery of penicillin and the type 2 diabetes drug metformin, as well as the first prophylactic HIV drug, Truvada®, to name a few. Using mice and rats reduces the dependence on higher-order species and allows for easier genetic engineering. The advent of precision (i.e., personalized) medicine will benefit greatly from integrative bioinformatics and innovative rodent-based research and validation studies. Over the past several years, awareness has grown of the need for rigorously designed published research studies that are transparent and reproducible. In response, NIH launched a formal initiative aimed at improving research reproducibility through an emphasis on scientific rigor and transparency. Eliminating variability in animal research is accomplished by supporting the creation and encouraging the use of animal repositories. NIH-funded rodent repositories ensure the quality and welfare of distributed animals and supply expertise to guide reliable studies.

Through ORIP's DCM grant mechanisms, scientists are equipped with the latest techniques, including CRISPR-Cas9 genomic editing, genotyping, pathogen monitoring, microbiome characterization, and strain tracking. Cryogenic preservation and freeze-dried sperm preservation are ideal methods for biobanking important rodent strains, which limits experimental variability. DCM-funded resources provide high-quality control measures and scientific knowledge to support rigorous, reliable, and reproducible research.

Repositories

DCM has developed strategies to expand access to rodent models through collaboration with university-based and regional resource centers. Following are a few examples of the resources that DCM has supported and made available to the biomedical research community.

Mutant Mouse Resource and Research Centers: The Mutant Mouse Resource and Research Centers (MMRRC) distribute and cryopreserve scientifically valuable, genetically engineered mouse strains and mouse embryonic stem cell lines. In addition, the MMRRC member facilities develop new technologies to improve the handling of mutant mice, including advances in assisted reproductive techniques, cryobiology, genetic analysis, phenotyping, and infectious disease diagnostics. The MMRRC comprises an Informatics, Coordination and Service Center and four regional distribution facilities: The Jackson Laboratory; the University of California, Davis; the University of Missouri; and The University of North Carolina at Chapel Hill.

Rat Resource and Research Center: The Rat Resource and Research Center (RRRC) at the University of Missouri provides ready access to well-characterized inbred, hybrid, and mutant rat strains; embryonic stem cells; and other related resources. Importantly, this program focuses on cryopreservation of gametes and embryos, *in vitro* fertilization, and genotyping and characterizing the gut microbiota.

Special Mouse Strains Resource: The Special Mouse Strains Resource (SMSR) at The Jackson Laboratory offers special mouse strains and associated tools important for the genetic analysis of complex human diseases. The SMSR imports, cryopreserves, and distributes recombinant inbred and chromosome substitution strains that are necessary for the discovery of quantitative trait loci and genes responsible for complex diseases.

National Gnotobiotic Rodent Resource Center: The National Gnotobiotic Rodent Resource Center (NGRRC) at The University of North Carolina at Chapel Hill School of Medicine allows researchers to evaluate physiologic and pathophysiologic differences between germ-free (sterile), gnotobiotic (i.e., selectively colonized with microbes), and specific-pathogen-free mice.

Mouse Strains for Testing Regenerative Medicine Therapies: This collaborative project of the UMass Chan Medical School and The Jackson Laboratory is improving existing immunodeficient mouse strains to support robust and efficient engraftment of varieties of human tissues. The investigative team is focusing on the early development of a human immune system in mice by expression of human factors required for elaboration of functional lymphoid architecture. Validated humanized mouse models will be an effective platform for evaluating human stem cell–derived cell function *in vivo*.

Cre Driver Strain Resources: The purpose of the Cre Repository at The Jackson Laboratory is to create, distribute, and extend characterization of mouse Cre driver lines. The program supports generation and enhancement of Cre driver strain models that include embryonic stem cell resources and congenic Cre driver strains on new genetic backgrounds, as well as the functional characterization of these models to enhance their utility.

Hybrid Rat Diversity Panel: The Hybrid Rat Diversity Panel (HRDP) at the Medical College of Wisconsin offers animal models and baseline molecular and physiological phenotypes under the National Rat Genetics Resource Program. This resource provides phenotypic characterization, genomic sequencing, data analysis, and distribution of hybrid rat models.

Enabling Artificial Intelligence–Based Mouse Genetic Discovery: This project from Stanford University uses a recently developed artificial intelligence (AI)–based computational pipeline to analyze millions of published papers and assess candidate gene–phenotype relationships. Information obtained from assessment of protein–protein interaction networks and protein sequence features of candidate genes is being incorporated into a graph neural network–based analysis.

Mouse Resources for Comparative Mendelian Disease Genomics: The goal of this project at The Jackson Laboratory (JAX) is to create genomic resources that facilitate functionalization of naturally occurring variation by employing forward genetic discovery and reverse genetic validation. This resource focuses specifically on robust discovery and functional validation of variants that cause Mendelian disease phenotypes in mice, with an emphasis on those variants that escape detection by exome sequencing. Investigators are using newly affordable, third-generation, long-read sequencing technologies to discover structural variants and are further developing pipelines integrating these new data types into a data-driven framework for mouse variant interpretation and candidate gene prioritization for use by the research community. The lab also uses CRISPR-based engineering and phenotyping to prove disease causation from a subset of the most relevant candidate genes.

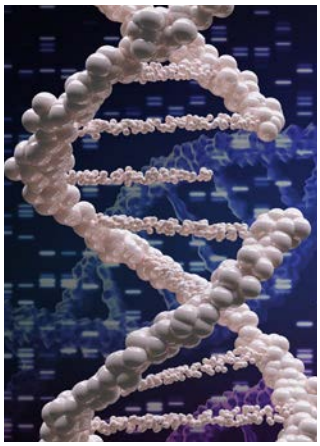
Precision Rodent Models

DCM supports three Pilot Centers for Precision Disease Modeling: The University of Alabama at Birmingham's Center for Precision Animal Modeling, Baylor College of Medicine's Center for Precision Medicine Models, and the JAX Center for Precision Genetics. All three U54 centers develop rodent models that more precisely mirror the genotype and phenotype of human disease processes and promote the creation of new therapeutics.

This program is creating pipelines for research of community-nominated unique human genomic variants linked to diseases for cost-effective, high-throughput testing in a variety of animal model species, including rodents. Diseases modeled include ciliopathy; RASopathy; cohesinopathy; Marfan syndrome and Ehlers-Danlos syndrome; macular degeneration; and musculoskeletal, cardiovascular, and neurodevelopmental defects. After validation of the expected gene editing, the centers are establishing assays to conduct comprehensive functional and phenotypic analysis to evaluate disease-causing variants. Additionally, the centers ascertain the relevance of these animal models to the molecular,

cellular, pathophysiological, and phenotypic characteristics observed in patients to improve the biological understanding of disease mechanisms, develop diagnostic tools, and test targeted or repurposed therapeutics. Creating and distributing precision animal model resources and related services are core functions of the centers.

Baylor College of Medicine–Rice University Genome Editing Testing Center



The Baylor/Rice Genome Editing Testing Center offers high-quality mouse resources and robust somatic genome editing testing pipelines to support researchers developing new genome editing technologies and conducting preclinical tests with these novel tools. The Center uses wild-type, genome editing reporter, and human disease model mouse lines to evaluate (1) the efficacy, tissue specificity, and safety of genome editing technologies and delivery systems and (2) disease gene-editing approaches and genome editing thresholds required to ameliorate specific diseases.

Mouse Peroxisome Research Resource

The Mouse Peroxisome Research Resource (MPRR) at The Jackson Laboratory is a community-driven effort that produces novel high-priority mouse models with defined genotypes on standardized genetic backgrounds, cryopreserves them, and distributes them to the public. Moreover, the MPRR assists in targeted phenotyping of these models, including measurement of relevant peroxisomal metabolite levels.