

# ORIP

OFFICE OF RESEARCH  
INFRASTRUCTURE PROGRAMS



## RODENT RESOURCES

### Office of Research Infrastructure Programs

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## 2019

### ORIP'S MISSION

*The Office of Research Infrastructure Programs (ORIP) enhances biomedical research in all disease areas and across basic, translational, and clinical research through its support of research infrastructure and resource programs. ORIP grants enable biomedical researchers to purchase state-of-the-art instruments; validate and disseminate research models, materials, and genetic stocks; and establish specialized research resource centers. ORIP also supports training and career development of individuals with DVM/VMD degrees, as well as predoctoral veterinary students.*



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## 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 of 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 the discovery of several noteworthy medical milestones—the discovery of penicillin and the type 2 diabetes drug metformin, as well as the first prophylactic anti-HIV drug, Truvada®, to name a few. Using mice and rats reduces the dependence on higher ordered species and allows for easier genetic engineering. The advent of precision (personalized) medicine will benefit greatly from integrative bioinformatics and innovative rodent-based research and validation studies. Over the past several years, there has been a growing awareness of the need for rigorously designed published research studies that are both transparent and reproducible. In response to this need, the 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 that include 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 resources. Here are a few examples of the resources that are supported and made available to the biomedical research community.



#### **Mutant Mouse Resource and Research Centers (MMRRC):**

The MMRRC consortium distributes and cryopreserves 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 is comprised of an Informatics, Coordination and Service Center (ICSC, University of California, Davis) and four regional distribution facilities: the Jackson Laboratory; University of California, Davis; University of Missouri; and University of North Carolina, Chapel Hill. <https://www.mmrrc.org>

**Rat Resource and Research Center (RRRC):** The 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, as well as genotyping and characterizing the gut microbiota. <http://www.rrrc.us>

**The Center for Humanized Mice:** Located at the University of Nebraska Medical Center, the Center offers xenotransplantation-engineered mouse models for translational studies and drug discovery. Center goals include improving existing mouse models for studies of human-like adaptive immune responses, vaccines, human-specific drug interactions, and the human immunodeficiency virus (HIV)-1 and HIV-1 associated comorbidities and coinfections.





### **The Special Mouse Strains Resource (SMSR):**

The 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. <https://www.jax.org/research-and-faculty/resources/special-mouse-strains-resource>

### **The National Gnotobiotic Rodent Resource**

**Center:** This resource at the University of North Carolina allows researchers to evaluate physiologic and pathophysiologic differences between germ-free (sterile), gnotobiotic (i.e., selectively colonized with microbes), and specific pathogen-free mice. <https://www.med.unc.edu/ngrrc>

**Cre/lox Rat Models:** This project at the University of Southern California develops a panel of universal Cre/lox reporter rats, cell-specific and inducible Cre rats, and floxed rats in which specific genes of interest are flanked by loxP sites. These Cre/lox rats allow investigators to visualize specific cell types *in situ* and also can serve as the basis for the generation of conditional/inducible knockout rats.

**Cre Driver Strain Resources:** The purpose of this resource 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, congenic Cre driver strains on new genetic backgrounds, and deep functional characterization of these models to enhance their utility. <https://www.jax.org/research-and-faculty/resources/cre-repository>

**Hybrid Rat Diversity Panel:** This program 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.

### **Biorepository of iPSC Lines From Diverse**

**Rat Strains:** This repository at McLean Hospital in Massachusetts is establishing well-validated and viable rat pluripotent stem cell lines along with their biological and genomic characteristics. The final goal is to use these rat-derived cells to provide insights into the generation of cell replacement therapy for degenerative illnesses.

## **Precision Rodent Models**

DCM supports the Pilot Centers for Precision Disease Modeling. Two of the Centers develop rodent models that more precisely mirror the genotype and phenotype of human disease processes and promote the creation of new therapeutics.

### **The Jackson Laboratory Center for Precision Genetics (JCPG):**

The JCPG uses cutting-edge technologies and expertise to develop and disseminate new precise animal models of incurable and genetically complex human diseases. The JCPG is managing the interactions and use of existing resources, driving innovation, expanding the pipelines necessary to improve mouse model development, and accelerating the translation of research findings to create better therapies. <https://www.jax.org/research-and-faculty/research-centers/precision-genetics-center>

### **Memorial Sloan-Kettering Cancer Center Pilot Center for Precision Disease Modeling:**

This Center aims to translate genome-based knowledge into novel therapeutics for human diseases. The Center addresses significant and innovative basic, translational, and clinical questions relevant to the understanding and treatment of diseases, including the mechanistic basis for early bone marrow failure in premature aging syndromes, the molecular origins and dependencies of colorectal cancers, and the development of precision treatment strategies for patients with acute leukemia. <https://www.mskcc.org/research-programs/geoffrey-beene-research/pilot-center-precision-disease-modeling>

## **Education/Training**

Funded by ORIP and the National Institute on Aging, the Jackson Laboratory hosts an annual workshop on mouse model pathology. This workshop offers a week of intensive training in histopathology and pathology, as well as didactic sessions in disease areas and models. <https://www.jax.org/education-and-learning/course-and-conferences/annual-workshop-on-the-pathology-of-mouse-models>

