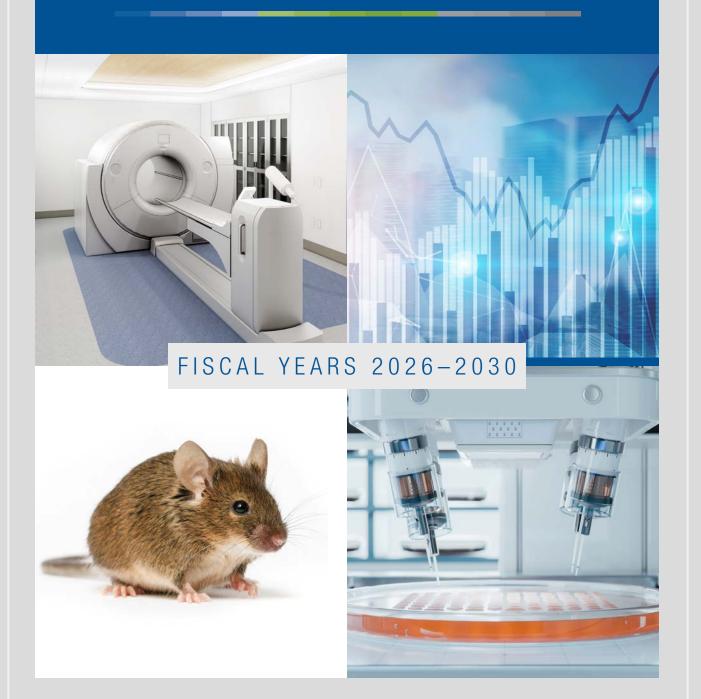


# STRATEGIC PLAN

INFRASTRUCTURE for INNOVATION





# Director's Message

Research infrastructure provides an essential foundation for groundbreaking biomedical discoveries. The Office of Research Infrastructure Programs (ORIP) helps enable research across nearly all National Institutes of Health (NIH) institutes, centers, and offices (ICOs). ORIP collaborates with NIH ICOs, as well as other federal partners, to develop and maintain infrastructure that strengthens existing programs, advances areas of emerging science, and facilitates new research initiatives. In the ORIP 2026–2030 Strategic Plan, ORIP outlines its vision to create and maintain resources to advance biomedical research.

As our office worked on its previous strategic plan in mid-2020, the world was experiencing a pandemic of global scope and scale. Thus, our strategic plan was focused on emergency response, resilience, and immediate public health needs. In the current landscape, however, investigators are identifying new, complex needs in the biomedical research ecosystem. These include fostering reproducibility and rigor in science, promoting the integration of new approach methodologies (NAMs), upgrading aging and obsolete research infrastructure, maintaining a well-trained core of young scientists, and addressing new challenges and opportunities in data science.

In recent years, NIH has shifted from crisis response to rebuilding and strengthening infrastructure. Now, the community's focus must move toward deliberate strategic planning for adaptable infrastructure that supports a wide range of future research needs. In support of the NIH mission, this strategic plan provides a framework for strengthening research infrastructure that is robust and flexible. Our nation's research infrastructure must remain agile and future-ready—with laboratories engineered for modularity, redundancy, scalability, and synergistic collaboration—to accommodate rapid shifts in research priorities.

ORIP's new strategic plan is aligned with NIH's key strategic themes: (1) focus on human health, (2) emphasis on replicability and generalizability of research, and (3) promotion of innovation and academic freedom. ORIP plays a key role in advancing these priorities by investing in foundational infrastructure that supports research outcomes, as well as enabling progress across the research continuum—from basic discovery to real-world implementation.

Research infrastructure functions as a pillar of public health advancement by supporting major scientific objectives. All levels of science depend on the quality and availability of these essential resources. Consequently, research infrastructure and model systems are critical enablers of human health and translational outcomes. Ultimately, these investments help advance the development of therapeutics that lead to improved clinical outcomes for patients.

ORIP is part of the NIH Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI), which identifies scientific research gaps and emerging opportunities, as well as arising public health challenges. ORIP is uniquely positioned to provide a crosscutting vantage point within NIH by identifying emerging critical infrastructure for research that is relevant to emerging public health needs. In this role, ORIP supports NIH ICOs and engages with broad scientific communities.

As a core guiding principle, ORIP's mission is centered on "Infrastructure for Innovation." In alignment with this principle, our office provides investments for research that would be unachievable without such support. ORIP's strategic investments enable a broad range of critical areas, including shared instrumentation for investigators or institutional programs with limited resources; advancement and integration of NAMs; and well-characterized, pathogen-free, and genetically modified animal models for studying human diseases. Validated NAMs can complement traditional research models and contribute to a more complete understanding of disease mechanisms—ultimately accelerating the development of targeted diagnostics and therapeutics.

As the field of biomedical research continues to progress, infrastructure must evolve to match scientific needs across disciplines. Through its programs, ORIP is empowering the biomedical workforce and enabling progress within research facilities. ORIP supports the career development of veterinary scientists, who offer unique contributions to human health research by leveraging their expertise in comparative medicine and public health. ORIP also invests in state-of-the-art shared biomedical research facilities that foster collaborations and scientific progress across the nation.

As we look toward the future, ORIP will remain committed to supporting NIH and the scientific community. Our office will continue to drive transformative innovation through strategic infrastructure and resource investments. This strategic plan emphasizes ORIP's commitment to adapting and leading across the biomedical research landscape. ORIP remains responsive and anticipatory to national and global health challenges, and we maintain our commitment to promoting scientific excellence, collaboration, and flexibility across NIH.



Franziska B. Grieder, D.V.M., Ph.D. ORIP Director

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# Strategic Plan Framework

# ORIP's Strategic Plan Framework Infrastructure for Innovation

#### **Mission**

ORIP advances the NIH mission by supporting resources and infrastructure for innovation. Through continued engagement with NIH institutes, centers, offices and the biomedical research community, ORIP empowers and expands existing programs and develops new initiatives to support NIH at the forefront of the scientific progress.

# **Organization**

Division of Comparative Medicine

Division of Construction and Instruments

Small Business Programs

# **Strategic Priorities**



Priority 1: Model Resources to Advance the Study of Human Diseases

Priority 1.1: Develop research models, biomaterials, and technologies to address emerging human health needs, prevent disease, promote health, and advance foundational science.

Priority 1.2: Expand access to a broad range of research models, resources, and services—with high transparency standards and comprehensive data—to strengthen rigor and reproducibility in biomedical research.



Priority 2: Modern Physical Infrastructure to Accelerate Research Discoveries in Human Health and Diseases

Priority 2.1: Support the acquisition of state-of-the-art scientific instrumentation.

Priority 2.2: Support the acquisition of equipment for the modernization of laboratories and other shared research-supporting facilities.

Priority 2.3: Construct or modernize biomedical research facilities.



Priority 3: Innovative Cross-Disciplinary Research Training in Model Systems for Human Health and Diseases

Priority 3.1: Promote innovative approaches for integrated career development of biomedical researchers involving interdisciplinary teams.

Priority 3.2: Advance the career development of scientists to align with the management and use of comparative medicine resources.



Priority 4: Expanding Outreach and Awareness of ORIP Resources and Programs

Priority 4.1: Strengthen outreach to the biomedical research community.

Priority 4.2: Expand collaborations with NIH ICOs and other federal agencies.

Priority 4.3: Promote ORIP's impact to the public and strategic partners.

# **Crosscutting Themes**

Conducting Responsible Stewardship to Maximize Research Efficiency Enhancing Scientific Transparency, Rigor, and Reproducibility Investing in Resources and Infrastructure for Translational Research

Promoting Research and Training Opportunities

# Overview of the Office of Research Infrastructure Programs

#### **Mission Statement**

**ORIP advances the NIH mission** to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability.

**ORIP contributes to this mission** by working to support innovative research ultimately aimed at promoting human health; train biomedical scientists and develop scientific infrastructure; contribute to the country's economic growth by expanding the biomedical knowledge base; and promote integrity, public accountability, and societal responsibility in scientific research.

Specifically—



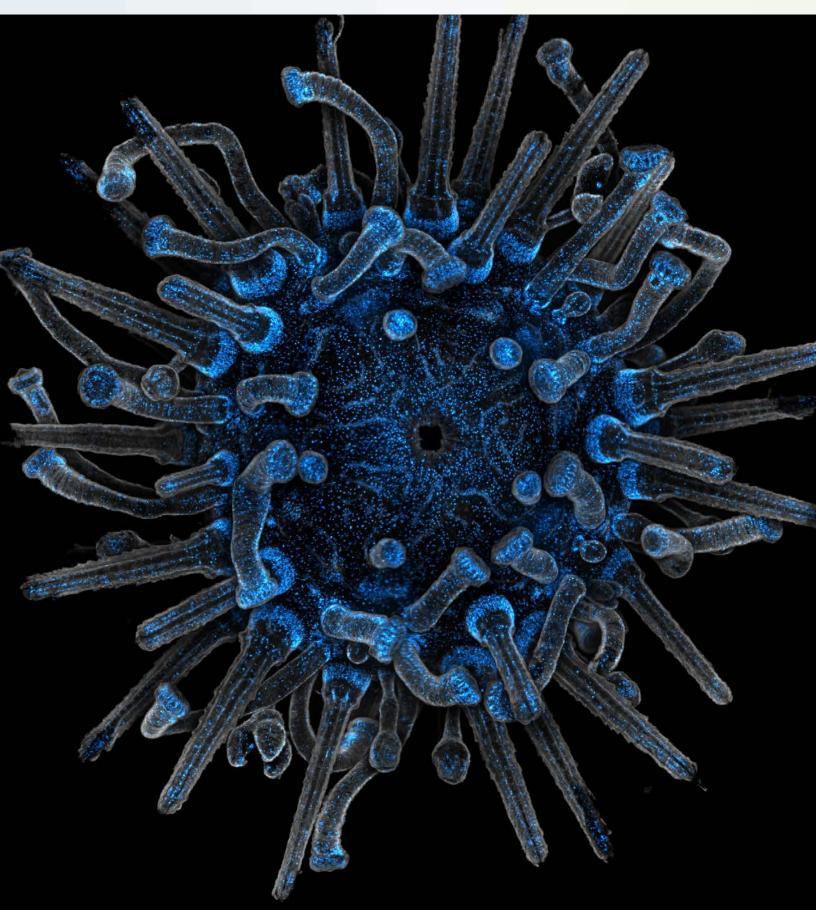
**ORIP** awards grants to support research resources, such as models for human disease and cutting-edge biomedical instrumentation.



**ORIP plans, organizes, and conducts workshops,** both independently and in collaboration with NIH ICOs, to identify and pursue scientific opportunities.



**ORIP supports research training opportunities for biomedical scientists** to capitalize on their distinct perspectives and expertise resulting from their deep understanding of comparative medicine and insight into biomedical models for human diseases.



A transgenic sea urchin (*Lytechinus pictus*). Nuclei are labeled with blue fluorescent protein. Image courtesy of Dr. Yoon Lee, University of California, San Diego.

# **Strategic Plan Framework**

To achieve our mission—

ORIP developed a research framework that capitalizes on the unique capabilities of the office by supporting resources, infrastructure, collaboration, and training programs to advance research in a variety of health topics. The framework promotes biomedical and biobehavioral research that advances our knowledge base on living systems to aid human health. It builds on the strengths of models and related resources to better understand and treat complex diseases, address newly emerging health issues, and minimize long-term illness and disability.

#### **Capacity Priorities**

#### Priority 1: Model Resources to Advance the Study of Human Diseases

Scientists can find new biomedical discoveries because of models and related resources used in their research; this allows a better understanding of the mechanisms underlying human disease and development of potential prevention or treatment methods. Using a broad array of models, in conjunction with integrating different data types through emerging technologies, allows researchers to mimic the pathobiology of disease and enhance human health. Models and related resources are developed and maintained through ORIP-supported repositories and centers, which provide the necessary infrastructure to understand and mitigate common diseases, chronic disorders, and future public health crises.

# Priority 2: Modern Physical Infrastructure to Accelerate Research Discoveries in Human Health and Diseases

Sustainable, cost-effective, modern physical infrastructure—including instruments, equipment, and shared-use research facilities—is vital to facilitate progress and new scientific discoveries. ORIP-supported physical infrastructure programs allow investigators to use emerging technologies and novel instrumentation in their research, promote new collaborations, and enhance the accessibility of infrastructure to a wider audience in the local and regional community. Partnerships with NIH ICOs provide the opportunity to have a broader impact on the biomedical community by providing infrastructure resources that address shared research interests.

# Priority 3: Innovative Cross-Disciplinary Research Training in Model Systems for Human Health and Diseases

To sustain the biomedical research venture, current and future trainees must be prepared to fulfill roles as principal investigators, mentors, program leaders, and comparative medicine resource directors. ORIP-funded research training programs provide biomedical scientists with hands-on experience in emerging areas critical to human health, as well as cross-training to develop an extensive skillset needed to be successful in these roles. Biomedical scientists in research-driven careers can leverage their expertise to efficiently develop different models and related resources and assess their value. Their unique insights will advance the translational impact of research conducted by interdisciplinary teams.

#### **Operational Priority**

#### Priority 4: Expanding Outreach and Awareness of ORIP Resources and Programs

Raising awareness of ORIP-supported resources is fundamental to having a far-reaching impact on the research community. A wide range of outreach techniques and communication platforms are used to distribute relevant information to the biomedical community, NIH ICOs and federal partners, and the lay public. Transparent communication of research results, new scientific discoveries, and resource successes with the public are necessary to demonstrate responsible stewardship and ensure continued funding support.

#### Crosscutting Themes That Guide ORIP-Supported Research

ORIP's research framework includes crosscutting themes to promote rigorous, reproducible, and transparent research results that will contribute substantially to the office's mission over the next 5 years. ORIP-funded investigators emphasize these crosscutting themes in their research and training programs to ensure that their efforts effectively contribute to the office's mission.

ORIP's priorities and goals will be achieved by—

- Conducting Responsible Stewardship to Maximize Research Efficiency
- Enhancing Scientific Transparency, Rigor, and Reproducibility
- Investing in Resources and Infrastructure for Translational Research
- Promoting Research and Training Opportunities

# **Statutory Authority and Organization**

As a result of the Fiscal Year 2012 Omnibus Appropriations Act, parts of the National Center for Research Resources were transferred to ORIP, part of DPCPSI, within NIH's Office of the Director. ORIP manages the following programs:

#### **Division of Comparative Medicine (DCM) Programs**

- Vertebrate and Invertebrate Animal Resources
- Complementary Models and New Approach Methodologies
- Genetic, Biological, and Other Resources
- Training and Career Development

#### Division of Construction and Instruments (DCI) Programs

- Extramural Construction
- Research and Resource Facilities Improvement
- Shared Instrumentation
- Modern Equipment

ORIP also participates in the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs by providing grants to support innovation and entrepreneurship in the areas of technology development and commercialization related to improvements in biomedical models for human disease and the use and management of biomedical model resources.

# **ORIP's Approach to Priority Setting**

ORIP will regularly use the best available metrics to review and evaluate its research projects and resource programs to ensure efficient management and transparent stewardship. ORIP will measure, manage, and report on the impact of projects and programs in a rigorous, robust, and data-driven manner to continually improve its resource centers and projects and to support new, innovative research resources. ORIP will assess the contribution of its resources to improving scientific rigor and reproducibility and will make strategic investments in methods and infrastructure tools to enhance the reproducibility of biomedical models and related biomaterials.

As part of its ongoing priority-setting, stewardship, and management activities, ORIP will promote scientific innovation by assessing, identifying, and supporting novel and creative research resources and approaches, particularly those aligned with NIH priority areas (e.g., NAMs). In addition to supporting NIH-wide efforts to foster innovation, ORIP will continue to support targeted initiatives to encourage paradigm-shifting research in its mission areas. ORIP also will monitor biomedical science and technology innovations and obtain regular input from the research community to identify gaps and opportunities related to biomedical resources, as well as instrumentation, equipment, and facility support required to conduct cutting-edge research.

Although innovation is an important priority, ORIP also recognizes the importance of balancing programs that support novel research topics with programs necessary to preserve established research areas. ORIP will carefully consider the support required for ongoing work in established but important research areas while providing the infrastructure necessary for scientists to take advantage of emerging opportunities and innovative approaches. Program officers and senior staff will periodically conduct portfolio analyses to assess program alignment with emerging and continuing high-priority research needs, as well as with new NIH initiatives.

Finally, ORIP will promote scientific innovation and ensure the enduring success of its programs through the development of a strong biomedical research workforce. Investment in training is an important component of ORIP's stewardship activities because training supports the success of NIH research programs and contributes to NIH's mission. ORIP will continue to support career development and training to increase the number of biomedical scientists with expertise in comparative medicine. ORIP also will seek to enhance the skillset of the biomedical research workforce by supporting training in the management and use of disease models and related resources. To assess the effectiveness of its training and career development programs, ORIP will collect the data required for long-term tracking and analysis of trainee career paths and will use these data to adjust training programs to improve outcomes and meet the needs of biomedical science. ORIP also will examine the evolving training needs of researchers involved in the management of biomedical resources to enable rigorous research resulting in improved human health.

# **ORIP's Strategic Planning Process**

The ORIP 2026–2030 Strategic Plan evolved from a comprehensive 3-year consultation process that entailed extensive discussions with and input from a broad spectrum of individuals, including biomedical scientists, members of professional organizations, and NIH senior program staff.

The development of the ORIP 2026–2030 Strategic Plan involved the following steps:

- In summer 2023, ORIP staff were tasked with organizing ORIP's next strategic planning process to seek feedback and ideas on ORIP's scientific focus areas, as well as with assessing potential research priorities, training and partnership opportunities, and opportunities related to emerging technologies.
- In summer and fall 2024, ORIP convened focus and advisory group meetings with NIH ICOs and extramural investigators to obtain input on physical infrastructure needs (e.g., instruments, equipment, construction) and opportunities for improving and increasing access to ORIP resources.
- In summer 2024, ORIP met with directors of its comparative medicine resource programs to discuss strategic planning for these resources in the future. Discussion topics included biomedical models, physical infrastructure, training, and outreach.
- In spring 2025, ORIP convened two focus group meetings to discuss ORIP's strategic planning for biomedical scientist training programs. Current and former trainees, as well as training program directors and mentors, identified current gaps in this space and crosscutting themes within the field.
- In August 2025, the draft strategic plan was sent to members of the NIH Council of Councils (ORIP's advisory council) for review and comment prior to the September 2025 Council of Councils Meeting. In September 2025, the ORIP Director presented an outline of the strategic plan at the NIH Council of Councils meeting.

# Implementation of ORIP's Strategic Plan

ORIP is responsible for the stewardship of investments in the programs and resources it supports to meet the evolving needs of the biomedical research community. ORIP strives to continually improve and increase access to these resources to help drive science forward and respond to the priorities outlined in the NIH-Wide Strategic Plan while meeting budgetary requirements. Effective management of ORIP-supported programs is essential to achieving these goals.

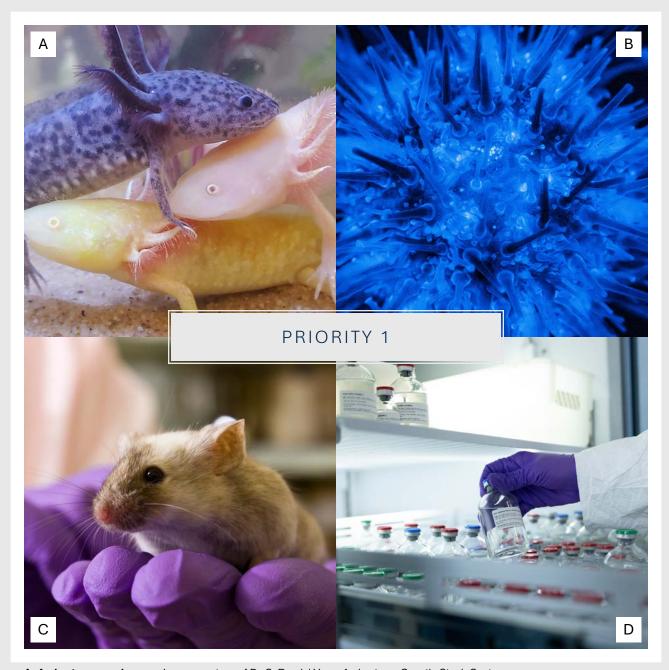
Continued support and management of research infrastructure and associated resource and training programs will require that ORIP build and sustain strong relationships with NIH ICOs—including other offices within DPCPSI—and other federal research agencies. ORIP also will collaborate with the biomedical research community, including users of ORIP-funded infrastructure and resources, to ensure the alignment of ORIP activities with the community's research needs.

ORIP's collaborations will provide opportunities to enhance existing resources, support new resources, encourage innovation, leverage existing infrastructure, recruit and develop additional expertise, retain a talented workforce, and support programmatic priorities. ORIP staff will continue to serve on NIH-wide committees and working groups and collaborate with other federal agencies to advance ORIP's mission and strategic priorities, as well as those of NIH and the wider research community.

Effective partner engagement will require ongoing communication regarding the goals, outcomes, and impacts of ORIP's support for research infrastructure and resources. ORIP will communicate with NIH ICOs and scientific societies on topics of mutual interest related to its programs. ORIP also will communicate the benefits of ongoing investment in its programs to ensure that community partners, policymakers, and the public maintain a thorough understanding of the fundamental importance of these programs to continued scientific progress.

Ongoing collaboration and communication with other NIH and federal entities, as well as with the biomedical research community and other key groups, will allow ORIP to remain current regarding biomedical science and technological innovations as it assesses research needs, identifies gaps in infrastructure, and sets priorities for developing and delivering resources. ORIP will seek community input with respect to research gaps and opportunities at its meetings and workshops, in its requests for information, and through its participation in professional conferences. ORIP will rely on peer review, programmatic review, and input from the NIH Council of Councils and NIH program staff to monitor, evaluate, and prioritize ORIP resources and identify new meritorious resources and resource-oriented projects.

# Capacity Priorities



- A. Ambystoma mexicanum. Image courtesy of Dr. S. Randal Voss, Ambystoma Genetic Stock Center.
   B. A transgenic sea urchin (Lytechinus pictus) with a stable expression of a blue fluorescent protein. Image courtesy of Mr. Erik Jepsen, University of California, San Diego.

  C. A laboratory mouse. Image courtesy of Mr. Dan Port, University of California, Davis.
- D. Experimental vials of specialized antibodies. Image courtesy of Dr. Diogo Magnani, Nonhuman Primate Reagent Resource.

# **Priority 1: Model Resources to Advance the Study of Human Diseases**

Models that enable researchers to study complex human diseases are essential for biomedical discovery. These include a broad spectrum of approaches, from *in vivo* systems and animal models to NAMs, such as organoids, advanced cell cultures, microphysiological systems, computational modeling, and artificial intelligence/machine learning (AI/ML). Aligning with the NIH Director's initiative to prioritize human-based science and reduce animal use wherever possible, these models and related resources play an essential role in biomedical discovery by allowing scientists to better evaluate, prevent, diagnose, and treat human diseases.

Often serving as a bridge between basic science and clinical medicine, models for human diseases have led to numerous major medical advances—including blood transfusions, medications, joint replacements, tissue engineering and organ transplantations, and cancer treatments. These models also have shortened the timelines to diagnosis and reduced the need for invasive clinical procedures, such as bypass surgeries. To study, understand, and develop treatments for complex diseases in humans, scientists need access to a broad array of model systems that mimic the pathobiology of disease while acknowledging the translational limitations often associated with animal models and investing in NAMs that have the potential to better represent human biology and pathophysiology. To fully realize the potential of these resources, researchers need access to robust and reproducible models; integrated multi-omics data; and comprehensive and curated data on mechanistic, genomic, and phenotypic characteristics, as well as sophisticated computational tools to integrate and analyze this information. Such technologies as AI/ML help researchers predict likely outcomes of human disease, which improves the value of preclinical studies for clinical practice.

ORIP plays a central role in biomedical discovery by providing the critical infrastructure to develop, advance, maintain, and distribute a wide array of research models and related resources. ORIP remains committed to advancing scientific rigor, transparency, and experimental reproducibility across biomedical research. By supporting high-quality resources and ensuring the availability of well-characterized, human-centric models, ORIP ensures that

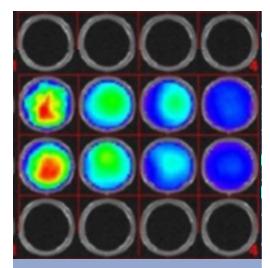


# Models to Advance a New Option for Heart Valve Transplants in Newborns

The National Swine Resource and Research Center supported work leading to a new method for partial heart transplantation in newborns. This technique has been successfully translated to human patients.

→ Full story on the ORIP webpage

Image courtesy of the Medical University of South Carolina.



# Testing Centers for Somatic Cell Genome Editing in Model Organisms

Somatic cell genome editing allows researchers to precisely change the DNA of an organism to correct genetic mutations. A focal point of this effort is the Center for Somatic Cell Genome Editing, which is helping researchers develop innovative treatments for human diseases using both *in vitro* and *in vivo* models.

→ Full story on the ORIP webpage

Image courtesy of the NIH Center for Somatic Cell Genome Editing in Nonhuman Primates.

NIH-funded investigators have the tools they need to drive innovative, transformative science. ORIP's strategic focus is to expand infrastructure and support systems for human-based model development and application, enabling greater relevance, reproducibility, and translational impact across biomedical research.

Priority 1.1: Develop research models, biomaterials, and technologies to address emerging human health needs, prevent disease, promote health, and advance foundational science.

ORIP supports the development of models for human diseases using a comprehensive suite of resources, including animals and NAMs, as well as the infrastructure required to maintain, preserve, distribute, and utilize such models. ORIP also helps ensure the quality, reproducibility, and ethical maintenance of these critical research models. Examples of models for human health and disease include mammalian and non-mammalian species, as well as cells, microphysiological systems, and biomaterials. ORIP supports research centers that maintain well-characterized disease models and other resources. These resources are readily available to NIH-funded researchers to help them meet current biomedical needs and respond to future human health crises.

Both the number and the complexity of models—whether naturally occurring, induced, or genetically engineered—used to study molecular mechanisms of human diseases and test new therapeutics are increasing. Easier, faster access to the most cutting-edge, human-relevant resources allows researchers to quickly generate the data needed to move lifesaving therapies to patients. Innovative methods and technologies are needed to develop and evaluate models and related biomaterials, ensuring they are accurate, reproducible, and capable of producing reliable, meaningful results. To integrate powerful emerging technologies with therapeutic applications—such as genome editing or microbiome therapies—the field will need a new generation of model systems that are patient specific and consider genome, environment, and lifestyle.

These models will help researchers identify new biomarkers of disease progression and address safety concerns for new diagnostics and therapies proposed for human use.

Meanwhile, assessing emerging research needs and evaluating programs that support research resources will help identify resource gaps and opportunities. As new requirements and challenges are identified, novel technologies will play an increasingly important role. To ensure the development and availability of high-quality, suitable models and related resources that will advance research on human diseases, ORIP will—

- Use advanced technologies and tools to improve existing animal models where alternatives do not currently exist, develop new human biology–based models to study human health and disease, and develop novel therapeutics.
- Make strategic investments in studies using human data to support new tools and applications of AI/ML in systems biology that promote data integration, improve predictive value, and enhance the translational relevance of models.
- Solicit applications for ORIP's SBIR/STTR programs to enable new technologies for development, maintenance, preservation, and characterization of models.
- Accelerate the translation of these innovations to practical use, enhancing ORIP-supported resources.

Priority 1.2: Expand access to a broad range of research models, resources, and services—with high transparency standards and comprehensive data—to strengthen rigor and reproducibility in biomedical research.

ORIP supports a wide variety of biorepositories, distribution centers, translational research projects, and resources that develop and enhance access to biomaterials, NAMs, and animal models. ORIP also supports the mechanistic, genomic, and phenotypic characterization of these models to maximize their usefulness in biomedical research.

Evaluating the utility and impact of current research resources is necessary when selecting models for specific studies, ICO-specific and NIH-wide initiatives, and new resources. For example, in specific circumstances, researchers may require access to pathogen-free animal models with well-defined genomic and phenotypic

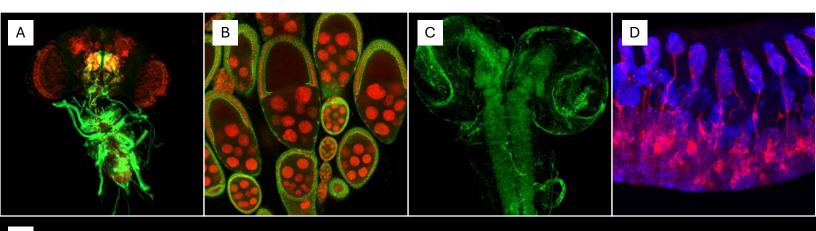


The Jackson Laboratory Center for Precision Genetics is leading a revolution in genetic disease solutions, giving patients and their families hope for the future. The center is generating *in vitro* and mouse models to develop precision therapies for genetic disorders.

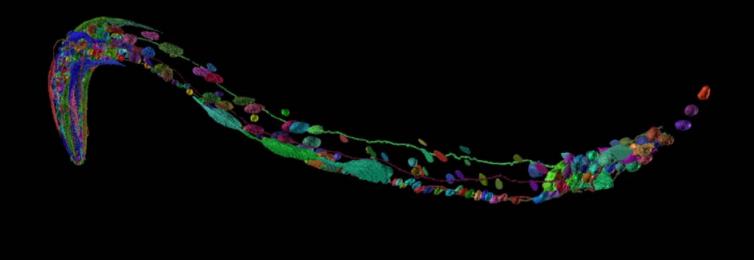
► Full story on the ORIP webpage

Image courtesy of Ms. Tiffany Laufer,
The Jackson Laboratory.

information to understand and cross-compare the biological similarities and differences among models that best mimic the underlying mechanisms of human diseases. Researchers also require access to well-characterized and standardized complex human cell-based models. ORIP will continue to expand its infrastructure to include biorepositories for human cells and tissues, hubs for NAMs and human data, organoids, and other technology development centers that include computational systems models and agentic AI networks (i.e., autonomous AI agents that can achieve specific goals with minimal human oversight) coupled with complex experimental systems.







- A. Drosophila brain. Image courtesy of Dr. Oguz Kanca, Baylor College of Medicine.
- **B.** Egg chambers of *Drosophila*. Image courtesy of Dr. Oguz Kanca, Baylor College of Medicine. **C.** *Drosophila* larval brain. Image courtesy of Dr. Oguz Kanca, Baylor College of Medicine.

- D. Neurons in a *Drosophila* embryo. Image courtesy of Dr. Shinya Yamamoto, Baylor College of Medicine.

  E. A 3D model of a larval *Caenorhabditis elegans* where each cell is annotated based on full-length electron microscopy reconstruction. Image courtesy of Dr. Nathan Schroeder, University of Illinois Urbana-Champaign.

Robust and consistent maintenance and full characterization of models help improve their reliability, reproducibility, and predictive value for human disease studies. To improve access to next-generation, well-characterized model systems with greater translatability to human diseases, ORIP will—

- Implement program assessments and analyze community needs to identify resource gaps in human-relevant systems and create new opportunities.
- Support and enhance research resources that operate under rigorous conditions and maintain well-characterized and curated mechanistic, phenotypic, and genomic data on models and biological materials.
- Strengthen research capacity and infrastructure for current and future human health crises, including acquisition and characterization of models for chronic diseases and the required support spaces at resource centers.
- Use new technologies and extend services to improve the generation, maintenance, preservation, and distribution of models.
- Provide training and share best practices and related data with the biomedical research community.

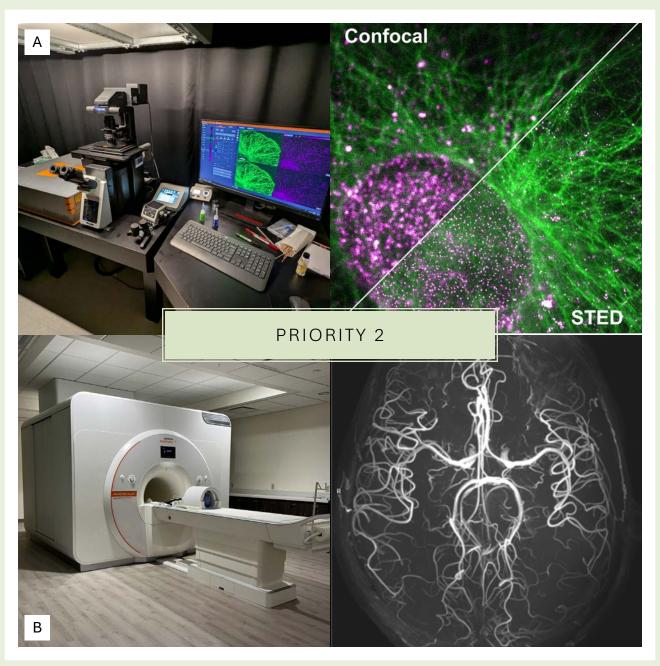


# BioGRID: Supporting Research Through Data Sharing

The Biological General
Repository for Interaction
Datasets (BioGRID) collects
information from scientific
literature for researchers. This
tool allows researchers to
explore deeper questions more
efficiently and cost effectively
with fewer animal studies.

→ Full story on the ORIP webpage

Image courtesy of NicoElNino/Shutterstock.



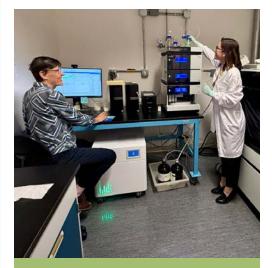
A. Stimulated emission depletion (STED) fluorescence microscope and images of immunostained cells (right) captured by conventional confocal and STED microscope (left). Images courtesy of Dr. Avital Rodal, Brandeis University.
 B. Whole-body human 7T magnetic resonance imaging system (left) and a magnetic resonance angiographic image of human cerebral vasculature (right). Images courtesy of Dr. Hongyu An, Washington University in St. Louis.

# Priority 2: Modern Physical Infrastructure to Accelerate Research Discoveries in Human Health and Diseases

New technologies are a key catalyst for scientific research success. Scientific discoveries, in turn, drive the need for novel tools that enable the next generation of innovative research. This interplay of technological advances and scientific discoveries makes access to modern physical infrastructure—including instruments that generate data, as well as equipment and shared-use research facilities—a critical component of research progress.

ORIP plays a unique role by supporting programs that provide the NIH biomedical research community with access to physical infrastructure resources. Instruments drive research by generating the data behind scientific discoveries. Modern equipment is needed to improve research-supporting functions and ensure that laboratories and research facilities operate efficiently. Placing equipment and instruments in shared-use facilities promotes efficiency and collaboration, enables broad access by the research community, ensures assistance from high-quality technical support, creates stimulating scientific environments, and magnifies the impact and return on investment of the strategic programs. By supporting projects that construct and modernize facilities, ORIP invests in physical infrastructure that meets engineering regulatory requirements and enables and sustains biomedical research programs. These infrastructure projects will enhance research operations and capabilities for key scientific areas; streamline workflows for innovation; and facilitate the production of high-impact, cutting-edge data.

Building on its accomplishments and experiences, ORIP will continue to provide funding for advanced scientific instruments, modern laboratory equipment, and the construction or modernization of research facilities. ORIP will maintain the vitality of its physical infrastructure programs and the essential role they play in advancing biomedical research by partnering with NIH ICOs and the biomedical research community. Through these collaborations, ORIP will adapt its programs to meet the changing needs of the research community, ultimately contributing to improved human health.

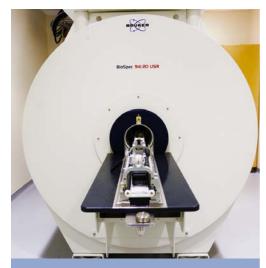


# Mass Spectrometers Accelerate Collaborations on Aging and Women's Health Research

Scientific and health innovations rely on continuous access to cutting-edge technology and instruments. Investigators from the Schilling lab are using S10-funded instruments for research on aging and women's health.

→ Full story on the ORIP webpage

Image courtesy of Dr. Birgit Schilling, Buck Institute for Research on Aging.



# SORDINO: A Silent MRI Technique for Functional Neuroimaging

One of the challenges in animal magnetic resonance imaging (MRI) is that the noise of the machine panics the animals into moving. Researchers developed a novel sampling strategy that minimizes acoustic noise during scans, eliminating interferences to the subject's brain functions and motion artifacts.

→ Full story on the ORIP webpage

Image courtesy of Dr. Yen-Yu Ian Shih, The University of North Carolina at Chapel Hill.

# Priority 2.1: Support the acquisition of state-ofthe-art scientific instrumentation.

ORIP supports the Shared Instrumentation Programs, which fund grant awards for the acquisition of modern scientific instruments. ORIP-supported instruments are placed in hundreds of core facilities at research institutions, benefiting thousands of biomedical investigators nationwide. Each instrument is used on a shared basis, which makes research operations efficient and cost effective and facilitates or enhances multidisciplinary collaborations, technology dissemination, and scientific rigor. ORIP supports all scientific instruments and technologies that can be justified and that align with the NIH-Wide Strategic Plan and the NIH Director's initiative to prioritize human-based science.

To meet the needs of distinct scientific fields and different research communities at all research institutions, ORIP supports the implementation of both established technologies and emerging technologies that have entered the market recently. To ensure continued access to the scientific instruments needed to accelerate biomedical discoveries that lead to improved human health, ORIP will—

- Provide a wide range of advanced instruments that are essential for driving progress across all areas of biomedical research.
- Respond to the evolving modern instrumentation demands of the scientific communities at academic and research institutions nationwide.
- Facilitate the adoption of emerging commercially available instruments and novel technologies that accelerate technological innovations and scientific discovery.

# Priority 2.2: Support the acquisition of equipment for the modernization of laboratories and other shared research-supporting facilities.

ORIP supports the modernization of laboratories and research resource facilities by providing funds for institutions to acquire and install new equipment and tools that will improve or streamline operations. Any

such modernization project must be located at an institutional biomedical research resource, core facility, or other shared space and must align with the demands of biomedical research and related activities. ORIP's Modern Equipment Program provides the research community with access to high-quality facilities and services.

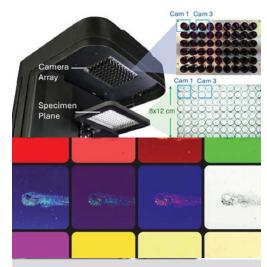
Every research facility employs a broad range of technical solutions to create a well-controlled environment furnished with equipment and tools that enable a wide array of research and research-related activities. In addition to supporting the acquisition of instruments or equipment used in core or shared research facilities, ORIP's SBIR/STTR programs support technological development projects that may benefit the resources and research communities aligned with ORIP's mission.

As science progresses, the infrastructure and equipment needs of research laboratories and research-supporting facilities continue to evolve. To ensure that ORIP's programs meet the changing infrastructure and equipment needs of these laboratories and facilities, ORIP will—

- Support the acquisition of laboratory equipment to improve the operations and management of research facilities.
- Facilitate the procurement of equipment to enhance operations in life sciences and complementary research and support the development of high-quality human-based models and resources.
- Sponsor innovative SBIR/STTR projects to develop technologies that will strengthen the research resources and facilities supported by ORIP's programs.



State-of-the-art metabolic phenotyping system. Image courtesy of Dr. Brian Finck, Washington University School of Medicine.



# A Novel Multi-Camera Array Microscope: Expanding the View of Optical Microscopy

From a prototype concept to a commercial research tool, the new Multi-Camera Array Microscope allows researchers to observe small organisms at high resolution and high speed. This technology was developed with the support of ORIP's Small Business Programs.

→ Full story on the ORIP webpage

Image courtesy of Ramona Optics.



**State-of-the-art metabolic phenotyping system.** Image courtesy of Dr. Gregory Morton, University of Washington.

# Priority 2.3: Construct or modernize biomedical research facilities.

ORIP supports the construction, renovation, and modernization of shared-use research facilities to provide long-term infrastructure for cutting-edge basic, translational, clinical, and behavioral research. ORIP's Extramural Construction Programs provide the research community with a way to address infrastructure gaps in areas of national interest, such as AI/ML and high-priority biosafety level 3 and 4 facilities. Key research areas in human health—including women's health and chronic diseases—will be promoted through the development of collaborative, shared-use research space, with an emphasis on human-based models.

Because physical infrastructure must meet engineering requirements to sustain and support the advancement of NIH-funded biomedical research for at least the next 10 years, these infrastructure investments will benefit all areas of biomedical research. To ensure that these programs meet the infrastructure needs of research and resource facilities, ORIP will—

- Provide long-term infrastructure support for highly impactful collaborative human biology-based research activities.
- Establish frameworks to foster the implementation and use of emerging technologies to support priority research areas.
- Increase research capacities that will advance biomedical research for the health of all people.

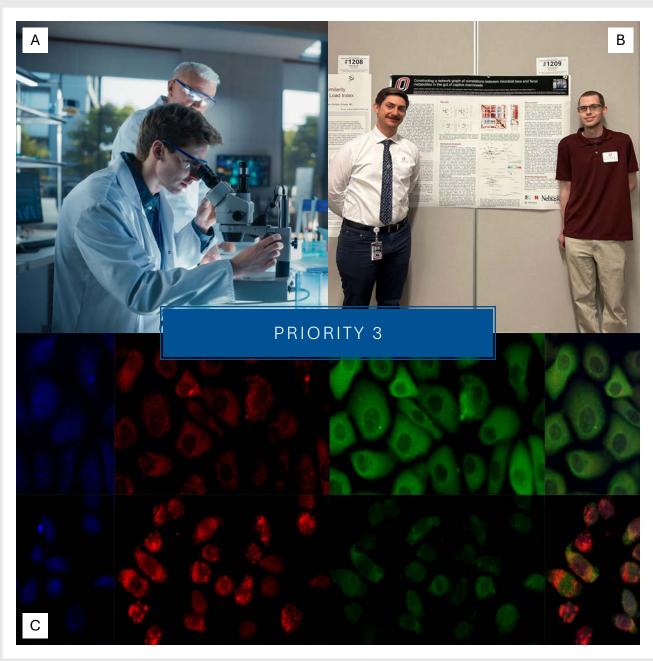


# Oklahoma Medical Research Foundation Research Tower

The Oklahoma Medical Research Foundation (OMRF) research tower adopts environmentally conscious architecture and supports forward-thinking scientific initiatives. With ORIP funding, OMRF has expanded the breadth of its research and fostered new collaborations.

→ Full story on the ORIP webpage

Image courtesy of Ms. Jenny Lee, Oklahoma Medical Research Foundation.

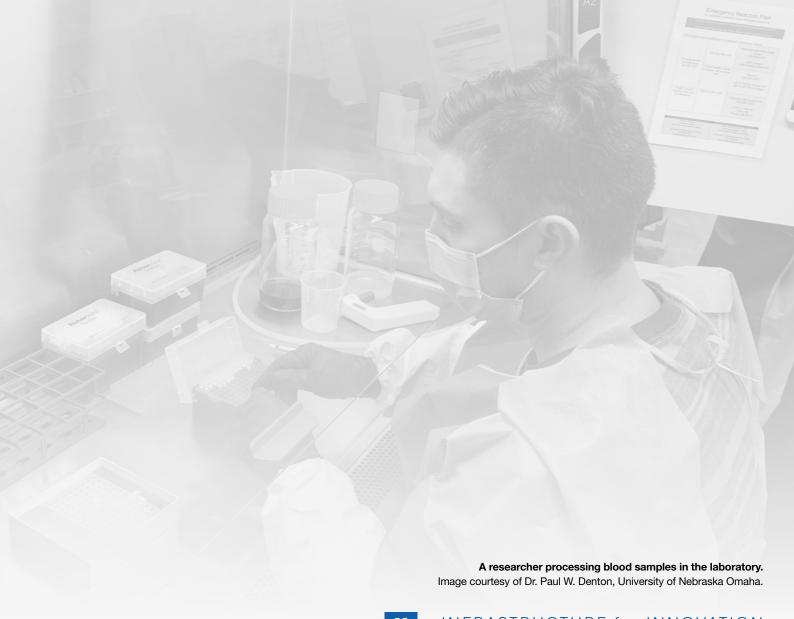


- A. Research training in the laboratory. Image courtesy of Gorodenkoff/Shutterstock.B. Scientists at the University of Nebraska Omaha's Annual Research Creative and Activity Fair. Image courtesy of Dr. Jonathan B. Clayton, University of Nebraska Omaha.

  C. MYC-inhibited human Meibomian gland epithelial cells. Image courtesy of Dr. Cornelia Peterson, Tufts University.

# Priority 3: Innovative Cross-Disciplinary Research Training in Model Systems for Human Health and Diseases

Biomedical researchers must be equipped with the skills to develop and interpret human-based models. To improve human health, ORIP is committed to training and career development that will prepare both early-career and established scientists to become independent investigators, research team members, resource directors, and mentors who sustain the biomedical research enterprise. ORIP will expand its existing strengths in training and career development to incorporate interdisciplinary training that bridges biology, engineering, data science, and public health. By building a strong pipeline of scientists with multidisciplinary expertise across model systems, through targeted recruitment, training, and support, ORIP will ensure that these professionals are empowered to drive innovation in biomedical research, ultimately translating their expertise into meaningful improvements in human health and disease prevention.





# Supporting the Next Generation of Veterinary Scientists

Rachael Wolters, D.V.M., Ph.D., an early-stage veterinary scientist, received a Special Emphasis Research Career Award that supported her ability to pursue academic research.

→ Full story on the ORIP webpage

Image courtesy of Dr. Rachael Wolters, Vanderbilt University.

# Priority 3.1: Promote innovative approaches for integrated career development of biomedical researchers involving interdisciplinary teams.

ORIP supports programs that develop leaders in human-based models—including biology-centered *in vivo* modeling, AI/ML, bioinformatics, tissue engineering, organoids, and organ-on-chip technology—and to retain them in human health and disease–focused research. ORIP offers training and career development opportunities for early-career scientists, enabling them to become independently funded researchers who engage in collaborative and interdisciplinary cutting-edge science and publish novel research findings.

Scientists from a variety of disciplines can make unique contributions to the development, refinement, maintenance, and reproducibility of research that utilizes animal models, where necessary, and NAMs for human diseases. ORIP's training programs provide dedicated mentors and project funding for scientists, helping them to overcome challenges, such as limited access to protected research time due to service obligations. To ensure quality training of these essential scientists in new and emerging research areas, ORIP will—

- Invest in training, mentorship, and interdisciplinary collaborations for scientists developing capacities in human-based approaches to serve as independent researchers and collaborative team scientists.
- Support career development and training that prepares these scientists to pursue and secure support for cutting-edge research that fills major gaps in biomedical and biobehavioral science while expanding knowledge in emerging areas critical to human health.
- Encourage interdisciplinary collaborations and cross-training in essential and emerging areas, such as computational biology/bioinformatics, biostatistics, AI/ML, science communication, science policy, and other relevant fields.

# Priority 3.2: Advance the career development of scientists to align with the management and use of comparative medicine resources.

ORIP supports technical training in the use of model systems and related resources. ORIP's resource centers provide critical support for investigators interested in biomedical research careers that use animal models where necessary; human-based models, such as complex *in vitro* microphysiological systems or organoids; and related resources. Furthermore, in collaboration with other NIH ICOs, ORIP supports workshops and other focused events designed to educate biomedical researchers about the use of specific models and related resources in emerging research areas.

The ongoing training of the biomedical research workforce is necessary to ensure that investigators fully understand the advantages and the limitations of individual research models and related resources. Such training promotes reproducibility of research findings, as well as the use of human-based NAMs in research. As part of its evolving training and career development efforts, ORIP will—

- Maintain the highest integrity of research resource training and operations.
- Expand and promote available resource-related training and expertise at ORIP-supported centers and programs.
- Support early-career investigators, with a goal to create a workforce pipeline for new comparative medicine resource directors and leaders.

ORIP is committed to advancing the career development of scientists by integrating interdisciplinary training in emerging areas that align with the future sustainability of ORIP-supported research resources.

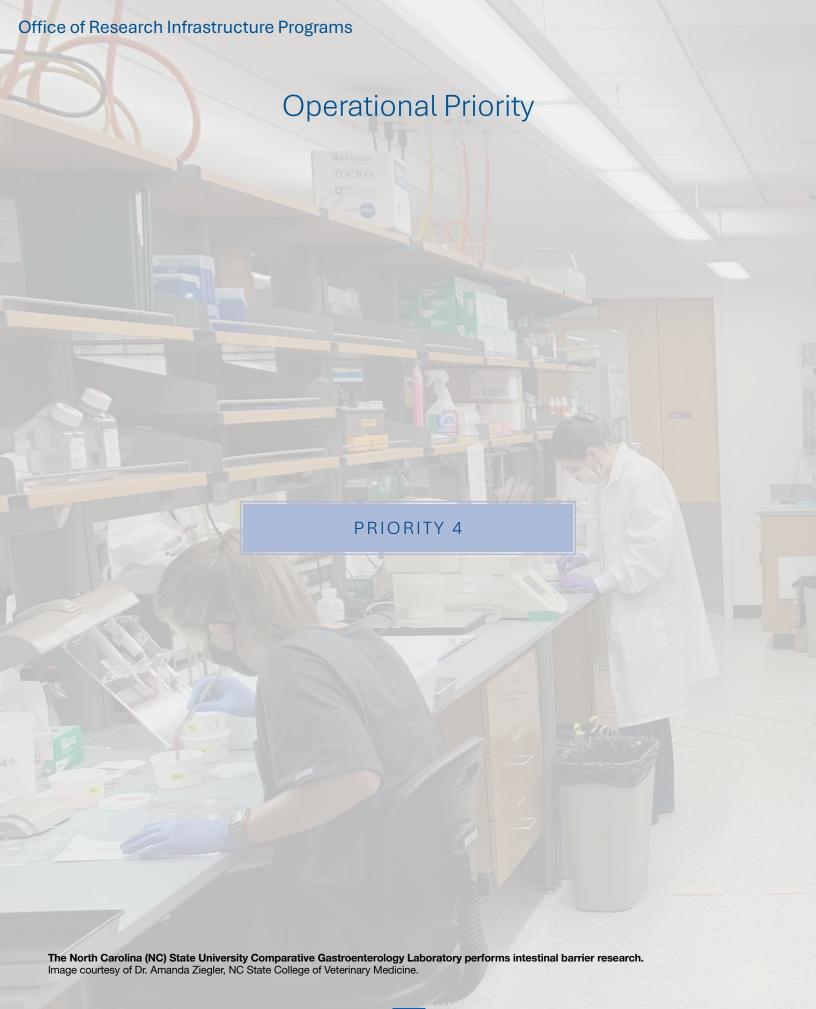


# Facilitating the Career Development and Research Advancements of Veterinary Scientists

Kelly Metcalf Pate, D.V.M., Ph.D., Director of the Division of Comparative Medicine at MIT, obtained several ORIP grants that played a pivotal role in her independent research training and early-career development.

→ Full story on the ORIP webpage

Image courtesy of Erin Mathieu Photography.



# **Priority 4: Expanding Outreach and Awareness of ORIP Resources and Programs**

ORIP provides essential resources—including models and related biomaterials; instrumentation and equipment; construction, renovation, and modernization of research spaces; and training opportunities—that are critical for conducting cutting-edge basic, clinical, and translational research. In addition to shared resources and infrastructure, ORIP grants empower investigators at large and small institutions across the United States to conduct innovative research resulting in new fundamental knowledge, as well as potentially new diagnostic tools and treatments that advance patient care and benefit human health. However, many investigators who could benefit from ORIP programs are unaware of these valuable resources. Strengthening outreach and expanding awareness will amplify the impact of ORIP-supported programs, promote collaborations, accelerate biomedical advancements, expand our understanding of health and disease, and maximize the return on investment of NIH-funded initiatives.

ORIP is committed to raising awareness about and improving access to its valuable resources within NIH and across the research community as a whole. To support the distribution of its resources and infrastructure, ORIP will maintain productive collaborations while also engaging in new partnerships with NIH ICOs, other federal agencies, and investigators in the broader research field. ORIP continues to raise awareness of its programs through meetings and workshops involving NIH-wide collaborators and expands the research community's knowledge of available programs and services through broad communication channels. Additionally, ORIP remains committed to translating complex research into clear, actionable insights that can be effectively communicated to various audiences, including the general public.

### Priority 4.1: Strengthen outreach to the biomedical research community.

ORIP actively engages with investigators to foster awareness and facilitate access to its resources. Through workshops, conferences, site visits, publications, and virtual platforms, ORIP maintains open dialogues with researchers, institutions, and other key partners. Regular updates and feedback mechanisms ensure that ORIP-supported programs remain responsive to community needs and scientific advancements. To enhance outreach and engagement to the biomedical research community, ORIP will—

- Expand communication with the biomedical research community via workshops, resource directors' meetings, requests for information, webinars, conferences, and social media.
- Increase the visibility of ORIP funding opportunities and grant programs to enhance the office's impact across the biomedical research community.
- Enhance the outreach efforts of ORIP's SBIR/STTR programs to attract innovative entrepreneurial projects with commercial potential.
- Highlight the scientific breakthroughs and successes resulting from ORIP-supported programs to encourage broader participation and utilization.
- Promote open communication with ORIP-supported resource centers to identify challenges and enhance operational efficiency.
- Enhance feedback mechanisms to understand current gaps and meet the needs of investigators.



#### Priority 4.2: Expand collaborations with NIH ICOs and other federal agencies.

ORIP is highly collaborative in supporting research resources and infrastructure that benefit multiple NIH ICOs and other federal agencies. By building strong interagency partnerships and investing in shared research priorities, ORIP strengthens vital biomedical research resources and helps respond to scientific challenges.

ORIP's collaborative efforts across agencies improve the efficiency, accessibility, and impact of NIH-funded resources, ensuring that researchers from diverse fields have the tools and support they need to drive scientific discoveries and advance public health. Additionally, ORIP is committed to expanding collaborations with NIH ICOs and federal agencies to strengthen the biomedical research ecosystem and drive innovation. To further increase collaboration and resource utilization within NIH and across the federal landscape, ORIP will—

- Conduct focused outreach to NIH program staff to emphasize the benefits of ORIP-supported resources and encourage cross-institute investments.
- Develop joint initiatives and collaborative projects with NIH ICOs that align with shared research priorities and address NIH-wide needs.
- Strengthen partnerships with other federal agencies to enhance the strategic impact of ORIPsupported research resource centers and state-of-the-art instruments.



#### Priority 4.3: Promote ORIP's impact to the public and strategic partners.

Public awareness and partner engagement are essential to ensuring ORIP's programs receive the recognition and support necessary for sustained success. By leveraging digital platforms, social media, and focused outreach campaigns, ORIP effectively communicates how its programs advance the translatability of preclinical research and contribute to human health. To enhance public and strategic partner engagement, ORIP will—

- Develop strategic alliances by forming new partnerships with key collaborators.
- Promote the importance of ORIP-supported research resources and infrastructure and highlight how the resulting scientific accomplishments allow advances in human health.
- Enhance transparency and accountability by continuing to communicate the importance, impact, and success of ORIP's priorities, programs, processes, and policies.



Conducting Responsible Stewardship to Maximize Research Efficiency



**Enhancing Scientific Transparency, Rigor, and Reproducibility** 



Investing in Resources and Infrastructure for Translational Research



Promoting Research and Training Opportunities

# Crosscutting Themes

ORIP has identified four crosscutting themes that span the priorities and goals of the office's strategic plan to enable biomedical discoveries: Conducting Responsible Stewardship to Maximize Research Efficiency; Enhancing Scientific Transparency, Rigor, and Reproducibility; Investing in Resources and Infrastructure for Translational Research; and Promoting Research and Training Opportunities. The many scientific challenges and opportunities that ORIP will address to advance its mission are not unique to any one priority of the strategic plan. These four crosscutting themes highlight key areas that are essential to achieving ORIP's strategic goals and mission.

# **Conducting Responsible Stewardship to Maximize Research Efficiency**

ORIP contributes to the NIH mission by supporting shared resources and promoting crosscutting research. By contributing significantly to health research through grants for resources and physical infrastructure, and by sharing expertise and promoting the training of biomedical scientists, ORIP displays scientific stewardship. ORIP has successfully leveraged collaborations across NIH and other federal agencies to fund research that focuses on shared strategic priorities and maximizes the return on scientific investments. By launching joint initiatives and fostering new collaborations, ORIP demonstrates responsible stewardship of the investment that is allocated to biomedical research.

Responsible use of funding allocations includes continuous evaluation of models to ensure the research conducted is most appropriate for the scientific questions being addressed. By identifying current research gaps and recognizing opportunities for growth, ORIP is effectively managing and maximizing the investments in biomedical research. ORIP monitors innovative opportunities in which to invest, including NAMs, that will advance its mission in an efficient and cost-effective manner. By funding resources that distribute biological materials, microbiome information, and antibody reagents, ORIP continuously promotes the use of NAMs.

ORIP's physical infrastructure programs support the acquisition of instruments and equipment, as well as the construction and renovation of shared-use research facilities. By facilitating access to state-of-the-art physical infrastructure, these programs will enhance research operations and capabilities for key scientific areas and improve the efficiency and sustainability of biomedical research programs across the United States. Through these programs, ORIP helps foster collaborations among investigators and meet their research needs, with the ultimate goal of advancing research to improve human health.

Outreach and communication efforts are also vital for sharing trustworthy scientific information and advocating the importance of maintaining scientific integrity and accountability of continued funding in biomedical research. Research highlights and selected grantee publications demonstrate how ORIP funding has resulted in innovative research methods and groundbreaking discoveries while displaying accountability and transparency when sharing research outcomes.

ORIP will continue to optimize operations and promote data-driven decision-making to enhance efficiency and program effectiveness. Policies have been implemented to expand the office's communication capabilities with a variety of audiences—including website updates, pre- and postfunding application webinars, and analysis of engagement metrics—to reduce time needed for addressing redundant inquiries and redirecting queries to available resources online. For example, ORIP developed the instrument Schedule Management, Access Requesting and Tracking (iSMART) tool to

improve operational efficiency of resources and to alleviate administrative burden on PIs. Additionally, a data visualization and management tool allows ORIP staff members to track progress reports and associated publications, extract data automatically, and generate visualizations that offer insights into the outcomes of the office's programs.

### **Enhancing Scientific Transparency, Rigor, and Reproducibility**

The transparency, rigor, and reproducibility of research studies is key to ultimately improving outcomes in public health. Opportunities for improving transparency in research studies and publications have been identified (e.g., detailed methodology instructions in reports). Policies will be implemented across the funding cycle—through the steps of grant application, peer review, award distribution, and manuscript publication—to improve transparency, rigor, and reproducibility.

ORIP supports independent replication studies and validates new technologies to enhance research impact through collecting, maintaining, and distributing well-characterized research resources and providing services for basic, preclinical, and translational research studies. ORIP also supports the development of Research Resource Identifiers (RRIDs) and actively promotes the use of RRIDs by researchers to identify and cite the key biological resources used in experiments. These efforts will help researchers, reviewers, and funding agencies accurately track and verify the resources, leading to more reliable and replicable research outcomes.

ORIP's centralized repositories provide research resources that help optimize and enhance scientific rigor, transparency, and reproducibility of biomedical research using robust infrastructure, well-trained personnel, and biomedical expertise to ensure health and genetic quality control and assurance standards. Furthermore, ORIP supports research to better understand the effects of extrinsic factors on study results and address current limitations in understanding the role of extrinsic variables in animal models. In addition, the instrumentation obtained by investigators to conduct this monitoring and reporting will be integrated into resource centers and core facilities to ensure widespread utilization, which maximizes rigorous and reproducible study designs.

# **Investing in Resources and Infrastructure for Translational Research**

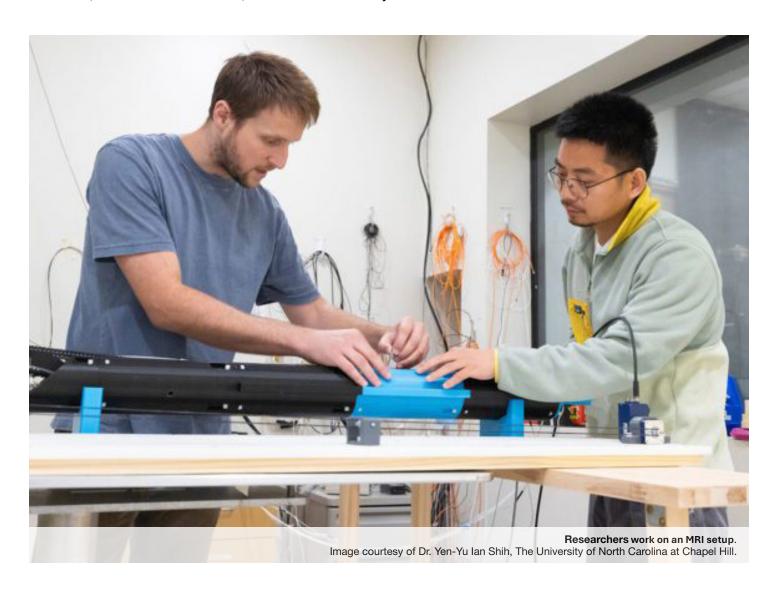
ORIP invests in model resources that are critical for explaining the complex biological mechanisms underlying many chronic diseases across populations, such as age-related disorders (e.g., Alzheimer's disease), infectious diseases (e.g., hepatitis B), and women's health conditions (e.g., endometriosis). ORIP emphasizes research advancements in health outcomes by supporting the infrastructure needed to conduct these studies. ORIP will continue to uphold and support the highest standards of animal welfare and public safety in all aspects of its programs and initiatives. ORIP also invests in research that studies the effects of intrinsic factors—including sex, age, and genetic background—by supporting reproducible data–generating instruments and modernizing biomedical research facilities.

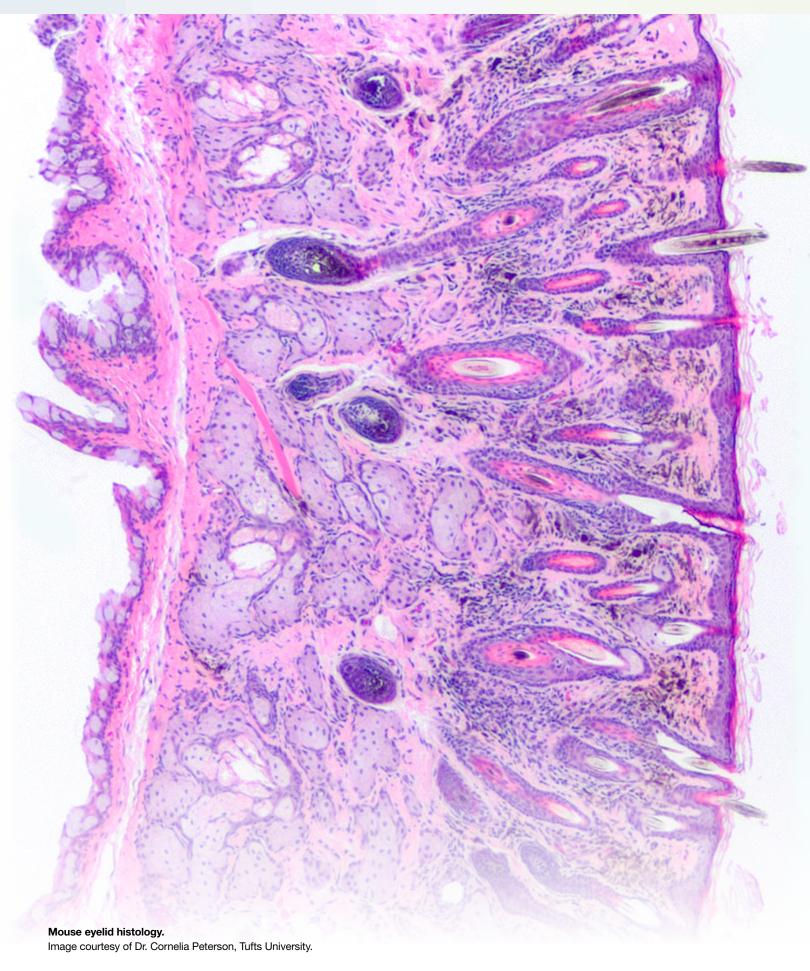
ORIP will continue to collaborate with the Office of Research on Women's Health (ORWH) to pursue research that clarifies mechanisms underlying sex as a biological variable in disease manifestation and severity. Furthermore, by continuing to collaborate with ICOs, ORIP has strengthened the nation's biomedical research enterprise by modernizing equipment and instrumentation through the <u>S10</u> Instrumentation Programs to support research on healthy aging and common conditions in older adults. ORIP-funded researchers will have access to state-of-the-art technologies and instruments to facilitate scientific studies that span these critical areas of human health.

### **Promoting Research and Training Opportunities**

The next generation of scientists brings innovation and dedication to address new or continuing complex biomedical issues. ORIP invests in multiple programs to advance the careers of scientists engaged in basic and translational comparative research. These researchers possess specialized expertise in the application of models and related resources. ORIP, in collaboration with many other NIH ICOs, understands the importance of training this next generation of investigators who will enhance our nation's research competitiveness, foster scientific innovation, improve research rigor, develop robust learning environments for future generations of researchers, and strengthen public trust in evidence-based science.

ORIP also recognizes the role that all higher learning institutions play in contributing to the nation's biomedical research capacity. The office facilitates research training by supporting infrastructure updates to shared resource centers, outreach to the biomedical research community to spread awareness of programs and resources, and policy implementation to foster new collaborations among investigators across institutions. Through these efforts, ORIP promotes training at all levels, including investigators, students, research technicians, and other laboratory staff.





## Description of ORIP Activities

## **Comparative Medicine Resources**

Each year, several thousand researchers use ORIP-supported resource centers for biomedical research. These centers support both NIH-funded researchers and investigators funded by other government entities, foundations, and the private sector. Examples of some of these valuable resource and research centers are provided below.

Human Tissues and Organs for Research Resource (HTORR): Established more than 30 years ago, HTORR provides biomedical investigators with donated normal and diseased human tissues and organs recovered using project-specific procurement, processing, preservation, and distribution protocols. This resource, which is managed by the National Disease Research Interchange in Philadelphia, Pennsylvania, and is supported by ORIP through a U42 grant—in partnership with the National Eye Institute; National Heart, Lung, and Blood Institute (NHLBI); National Institute of Allergy and Infectious Diseases (NIAID); National Institute of Arthritis and Musculoskeletal and Skin Diseases; and National Institute of Diabetes and Digestive and Kidney Diseases—facilitates human tissue research across the gamut of noninfectious and infectious diseases, including diseases that are public health priorities and rare diseases, including rare genetic disorders.

Mutant Mouse Resource and Research Centers (MMRRC): The MMRRC Consortium operates repositories for the acquisition, maintenance, and distribution of mouse models, germplasm, and embryonic stem cells (ESCs) for biomedical research. Four MMRRC centers and one Informatics, Coordination, and Service Center work together to preserve, protect, and ensure the quality of these models for scientists worldwide. Models available from the MMRRC have well-defined and stable genetic backgrounds that allow investigators to generate robust and reproducible results. The MMRRC includes more than 60,000 unique mutant alleles available in one or more forms as living mice, frozen germplasm, or ESCs. The MMRRC also offers the research community numerous services, such as quality-control testing for mouse pathogens, mutagenesis, and ESC isolation. The MMRRC's holdings and associated services have promoted the discovery of new diagnostics, treatments, and prevention strategies for almost every field of biomedical research.

Rat Resource and Research Center (RRRC): The RRRC provides the biomedical community with ready access to valuable rat strains and stocks, ESCs, and other related services that enhance the use of rats in research and maintain high standards of genetic quality control and health monitoring to maximize research reproducibility. There are more than 600 rat models in the RRRC inventory. These include single mutations on standard genetic backgrounds, "tool" rats (e.g., Cre-driver strains, fluorescent protein–expressing reporter strains), models with unique or complex genetic backgrounds, and collections of congenic strains. In addition to repository, cryostorage, and distribution functions, the RRRC facilitates acquisition of rat strains from other international repositories and provides specialized services, consultation, and technical training to investigators using rat models. Research efforts at the center are focused on improving cryopreservation and *in vitro* fertilization in the rat, generating new rat models needed by the research community, and characterizing the gut microbiota of rat models to better understand its impact on model phenotypes.

National Gnotobiotic Rodent Resource Center (NGRRC): The NGRRC is a nationwide resource for germ-free and gnotobiotic mice and associated services. Gnotobiotic means "known life" and refers to the

selective colonization of germ-free mice with microbes. The NGRRC provides germ-free and gnotobiotic mice and expertise, including germ-free rederivation, to investigators across the country whose research focuses on such areas as diabetes, cancer, metabolic syndrome, atherosclerosis, arthritis, and intestinal biology and disease. Transplanting human fecal microbial samples into gnotobiotic mice is a popular approach for testing *in vivo* functional properties of dysbiotic bacterial communities from diseased patients and enhance clinical relevance of murine preclinical therapeutic models. These insights from gnotobiotic mice have been used to develop novel therapies that have been tested in clinically relevant mouse models colonized with human complex bacteria and led to several Phase 2 clinical trials in human subjects. During the past 5 years, the NGRRC provided 15,000 gnotobiotic mice to more than 200 principal investigators in 100 universities and NIH intramural programs.

Centers for Somatic Cell Genome Editing: The broad applicability of targeted and programmable genome editing approaches, including those based on CRISPR-Cas9, raise the potential of new ways to treat a variety of rare genetic diseases, as well as common diseases. This initiative focuses on creating better models for assessing genome editing *in vivo* and has already produced and validated state-of-the-art rodent and pig reporter strains to allow detection of on-target and off-target genome editing in individual cells. ORIP supports four centers that specialize in major mammalian model species (rodents, pigs, and nonhuman primates [NHPs]) and are designed to develop new genome editing technologies, conduct preclinical testing of therapeutics to treat human diseases, and provide resources and testing services to a growing biomedical community. The testing centers are also assisting NIH-funded investigators in assessing the efficacy and safety of *in vivo* genome editing and delivery technologies, determining genome editing thresholds for specific diseases associated with minimal off-target effects, and ascertaining feasibility parameters in a model system.

National Primate Research Centers (NPRCs): Collectively, the seven NPRCs complement and enable the missions of other NIH ICOs by providing NHPs, state-of-the-art equipment, and scientific and technical expertise to study a wide range of diseases. The NPRCs facilitate 700–800 research projects per year, involving investigators from all areas of biomedicine. Areas of investigation supported by the NPRCs include metabolic, cardiovascular, neurological, and other chronic diseases, as well as regenerative medicine, reproductive health, medical genetics, aging, HIV/AIDS, and other infectious diseases. Because many studies in aging, chronic diseases, and HIV/AIDS require NHPs, the Office of AIDS Research and National Institute on Aging provide partial support for specialized colonies at the NPRCs. Most researchers who use the NPRC facilities and intellectual resources are funded by the NIH institutes and centers (ICs) and other federal agencies.

National Swine Resource and Research Center (NSRRC): Supported by ORIP, in partnership with NIAID and NHLBI, the NSRRC is the only national repository that supports swine-based research across multiple disciplines. The NSRRC provides invaluable services to the research community by creating new genetically engineered swine models as requested by investigators. The center has facilities with top-quality biosecurity to ensure these animals remain free of 13 defined pathogens. In addition, the NSRRC serves as a stock center by importing, maintaining, and preserving swine models and wild-type animals and by distributing them (including biomaterials) to investigators throughout the nation. The center's inventory consists of approximately 400 live animals representing more than 21 genetic backgrounds. Examples of swine models created by the NSRRC include transgenic pigs for research on organ transplantation into NHPs; immunocompromised and humanized pigs; the "oncopig" model for cancer research; and models for mammary tumors, congenital muscular dystrophy, Prader–Willi Syndrome, adenomatous polyposis coli, phenylketonuria, and Fanconi anemia group A.

<u>Zebrafish International Resource Center (ZIRC)</u>: ZIRC is a unique resource supported by ORIP in partnership with the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development that broadly

serves the national and international research communities. ZIRC is a repository for zebrafish genetic stocks and research materials (e.g., antibodies, cDNAs/expressed sequence tags). The center provides resources and services to zebrafish laboratories supported by most NIH ICs. Using self-developed or adapted methods, ZIRC maintains more than 13,100 genetically defined lines propagated under stringent quality control and health monitoring to ensure the highest level of reproducibility in research. ZIRC also provides pathology and consultation services (e.g., health, husbandry, cryopreservation), develops diagnostic platforms to screen for the most prevalent pathogens that are potential threats to laboratory zebrafish, and establishes standards for zebrafish research facilities.

Bloomington Drosophila Stock Center (BDSC): ORIP supports the BDSC with co-funding support from the National Institute of Neurological Disorders and Stroke and National Institute of General Medical Sciences. The BDSC enables the collection, maintenance, and distribution of more than 90,000 distinct and genetically characterized strains of fruit flies (Drosophila) used by the national and international research communities. Drosophila are excellent animal models because they are inexpensive to maintain in the laboratory, have short lifespans, reproduce prodigiously, and have well-understood genetic characteristics. Tens of thousands of genetically distinct Drosophila stocks have been produced that support modeling of human health and disease at the molecular level. The BDSC routinely collects transgenic or mutant strains of Drosophila from various projects employing gene knockout with transposable elements, gene knockdown with transgenic RNA interference, and other molecular approaches. As with other ORIP resources, BDSC scientists share available strains; their expertise on Drosophila genetics; and the use of center resources, such as databases.



#### ORIP Initiatives for Developing and Improving Human Disease Models

ORIP seeks to improve and disseminate the best models for human conditions and diseases that are of interest to multiple NIH ICs. The following example highlights ORIP's current areas of emphasis in developing models, making them available to researchers, and ensuring their preservation for future use.

Centers for Precision Disease Modeling Program: Affordable whole-genome sequencing and molecular profiling offers unique opportunities to study the genetics and pathogenesis of myriad human diseases. Nevertheless, genetic variation among individuals and the difficulty of interpreting this kind of information impede development of personalized therapies based on a patient's genetic makeup and molecular phenotype. To overcome these obstacles, ORIP launched the Centers for Precision Disease Modeling Program to provide the biomedical community with the advanced models needed to develop precision therapies for disorders controlled by a single gene, as well as diseases with more complex genetic architectures. ORIP supports three centers that evaluate the likelihood of a particular human genetic variant causing disease in optimized models. The centers then integrate findings into clinical care and clinical trials. The program now has an increased focus on creating cost-effective, high-throughput pipelines for testing human genomic variants linked to diseases in such models as the mouse, rat, Caenorhabditis elegans, zebrafish, and Drosophila, as well as Xenopus embryos and human induced pluripotent stem cells. These centers have developed such techniques as robust phenotyping to determine whether specific genetic changes recapitulate a human phenotype, creating and validating numerous animal models in different species, conducting a wide range of studies that increase the understanding of how gene mutations influence cellular and organismal phenotypes, and supporting large numbers of preclinical studies using assisted precision-directed therapies. Overall, the three centers have published more than 120 research articles and collaborated on numerous projects across the nation. Investigators are actively exploring NAMs by incorporating human clinical data, human organoids, tissues and cell lines, and genomic and proteomic data.

## **Physical Infrastructure Resources**

### **Shared Instrumentation Programs**

ORIP's Shared Instrumentation Programs provide NIH-funded teams of investigators working across a broad range of research areas access to next-generation technologies. The programs support commercially available instruments that are costly but essential to carrying out cutting-edge basic, translational, and clinical research. Examples of funded instruments include X-ray diffraction systems, nuclear magnetic resonance and mass spectrometers, DNA and protein sequencers, biosensors, electron and confocal microscopes, cell sorters, biomedical imagers, computing and informatics clusters, and high-throughput systems. Because all instruments must be used on a shared basis, they are typically installed in core research facilities. The requirement that ORIP-funded instruments be shared ensures the cost effectiveness of instrument use, operation, and management. Applicants must demonstrate that a new instrument will help advance biomedical science, and awards are made for instruments that support at least three NIH-funded research projects.

Shared instrumentation awards advance biomedical research capacities nationwide, including institutions in under-resourced states. Over the years, the Shared Instrumentation Programs have benefited the research of thousands of investigators who work at hundreds of different institutions and are funded by all NIH ICOs. The demand for new instruments has evolved over the years, reflecting advances in biomedical technologies and changes in science and research priorities. Research findings and discoveries resulting from the use of



A high-performance computing cluster. Image courtesy of Dr. Kyle Ellrott, Oregon Health & Science University.

shared instruments obtained through ORIP have supported the mission and goals of NIH by driving biomedical research advances both nationally and internationally.

#### Modernization of Biomedical Research Facilities

ORIP provides funds to modernize biomedical research facilities through the acquisition and installation of equipment and alterations and renovations of existing research space. This ORIP program does not offer direct support for research activities; rather, it funds enhancements of the physical conditions of conventional and specialized biomedical research facilities. These types of modernization projects must be undertaken at an institutional animal research facility, core facility, or other shared-use space that provides access and services to many researchers, so that a sizeable local research community will draw long-term benefits from the updated operations and functions.

Investments in physical infrastructure improve or streamline operating procedures and processes in laboratories and research facilities. Remodeling space and providing access to efficient equipment expand the capacity of essential support services for a broad range of research programs. Refurbishing space, updating building systems, and acquiring and installing novel equipment also are essential to conducting specialized research-related activities.

Research facilities are an important class of infrastructure that receives ORIP modernization support. Safe and well-controlled environments and up-to-date equipment are necessary to ensure the rigor and reproducibility of experimental protocols. Renovations and modern equipment in animal facilities also help institutions comply with the Animal Welfare Act, U.S. Department of Agriculture regulations, and U.S. Department of Health and Human Services policies related to the care and use of laboratory animals.

### **Training and Career Development of Biomedical Researchers**

Biomedical researchers play an important role in public health, particularly as a growing number of human diseases are found at the intersection of human and animal populations in changing environments. These scientists contribute broadly to the biomedical enterprise by conducting comparative medical research, developing models for human diseases, and providing critical clinical expertise on interdisciplinary and translational research teams using various types of biomedical models.

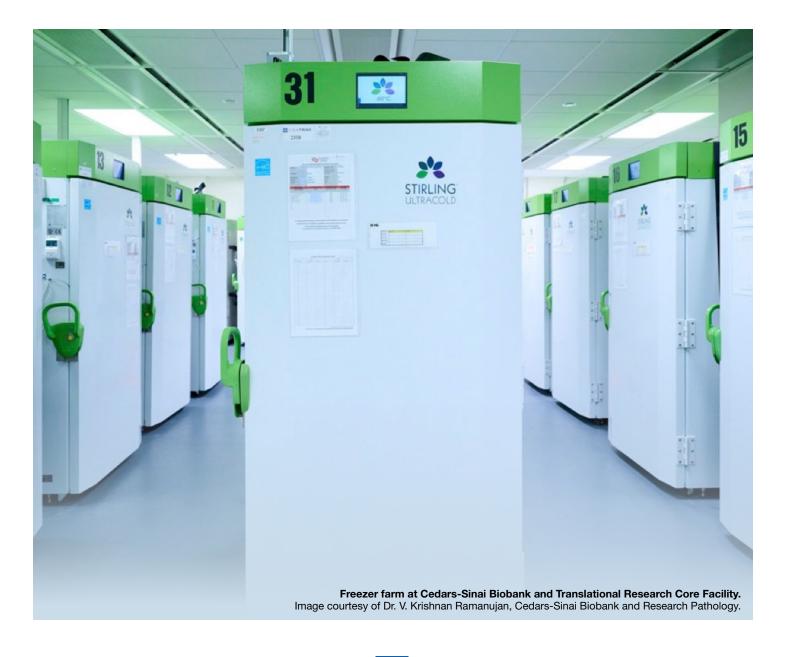
ORIP's training programs support the participation of investigators and trainees in a variety of research experiences in comparative medicine and pathology. The programs are designed to encourage talented scientists to pursue careers in biomedical research and to advance translational research. These programs also provide unique training experiences for students and investigators that are not duplicated by other NIH ICOs.

One of ORIP's training programs supports institutional grants that through multiyear support, help prepare postdoctoral students for successful careers in biomedical and translational research. Another ORIP training program, the <a href="Special Emphasis Research Career Award">Special Emphasis Research Career Award</a> (SERCA), provides "protected time" from clinical duties to early-career scientists so they can obtain the in-depth research experience needed to excel as independent scientists. Graduates from this program have been shown to be more successful in obtaining NIH grants and publishing scientific research papers than those who did not go through the program. ORIP also funds limited-competition small research grants to bring additional research support and increased independence to SERCA recipients.

# Small Business Programs: Improving Methods and Technologies for Research Resources

Advancing biomedical research depends on the availability of innovative, commercially viable methods and technologies to enhance biomedical models for human diseases. ORIP's SBIR/STTR programs aim to attract cutting-edge projects that benefit ORIP-supported resources and align with the office's mission.

SBIR/STTR projects of special interest to ORIP focus on the development and commercialization of novel or emerging technologies in two key areas: (1) technologies that enhance the understanding, preservation, characterization, validation, and refinement of biomedical models, as well as those that support complementary research models, and (2) tools, devices, and systems that improve the operations, efficiency, and functionality of research infrastructure, including facilities involved in the oversight, management, and support of biomedical research programs.





# Appendix: Acronym List

AI/ML artificial intelligence/machine learning

BDSC Bloomington *Drosophila* Stock Center

DCI Division of Construction and Instruments (at ORIP)

DCM Division of Comparative Medicine (at ORIP)

DPCPSI Division of Program Coordination, Planning, and Strategic Initiatives

ESC embryonic stem cell

HTORR Human Tissues and Organs for Research Resource

ICs institutes and centers (at NIH)

ICOs institutes, centers, and offices (at NIH)

MMRRC Mutant Mouse Resource and Research Centers

NAMs new approach methodologies

NGRRC National Gnotobiotic Rodent Resource Center

NHLBI National Heart, Lung, and Blood Institute

NHP nonhuman primate

NIAID National Institute of Allergy and Infectious Diseases

NIH National Institutes of Health

NPRCs National Primate Research Centers

NSRRC National Swine Resource and Research Center

ORIP Office of Research Infrastructure Programs

ORWH Office of Research on Women's Health

RRID Research Resource Identifier

RRRC Rat Resource and Research Center

SBIR Small Business Innovation Research

SERCA Special Emphasis Research Career Award

STTR Small Business Technology Transfer

ZIRC Zebrafish International Resource Center

Front cover images, clockwise from top left:  Positron emission tomography and computed tomography scanner. Image courtesy of Weill Cornell Medicine.  Data graph. Image courtesy of ImageFlow/Shutterstock.  Laboratory mouse. Image courtesy of The Jackson Laboratory.  Tissue bioprinting equipment. Image courtesy of IM Imagery/Shutterstock.	
NIH National Institutes of Health Office of Research Infrastructure Programs	