ORIP

OFFICE OF RESEARCH
INFRASTRUCTURE PROGRAMS

Fiscal Year 2025 State-of-the-Science Report

National Institutes of Health
Division of Program Coordination, Planning, and Strategic Initiatives

EXECUTIVE SUMMARY

The National Institutes of Health (NIH) Office of Research Infrastructure Programs (ORIP) supports the national biomedical research community and NIH's mission by providing a variety of research infrastructure and training programs that benefit human health both directly and indirectly. In recent years, ORIP has prioritized investment in critically needed cutting-edge biomedical infrastructure and resources to meet current and emerging challenges. ORIP's two divisions, the Division of Comparative Medicine (DCM) and the Division of Construction and Instruments (DCI), work closely together to ensure that their activities align with the office's mission to provide infrastructure across the country to support research in all scientific disciplines. To that end, ORIP fosters collaborations, works to ensure rigor and reproducibility, enables gold-standard science, supports the development of and access to models and related biomedical resources, assists the research community in acquiring advanced scientific instrumentation, modernizes research facilities through physical infrastructure programs, provides specialized research training for biomedical scientists, and assists small businesses in developing new technologies.

ORIP leveraged resources to the fullest in fiscal year 2025 (FY25) to meet its mission and optimize infrastructure support to enhance the nation's competitiveness in biomedical research. By establishing cofunding partnerships with 18 NIH institutes, centers, and offices (ICOs), as well as with an NIH-wide initiative, ORIP was able to maximize its impact on research, further increase its broad array of resources, organize a series of focused sessions on cryopreservation, and finalize the research framework of the *ORIP Strategic Plan 2026–2030*. These efforts were in alignment with NIH's key priority areas—such as chronic diseases research and new approach methodologies (NAMs)—among other crosscutting activities that support basic, translational, clinical, and behavioral research to advance knowledge on human health and diseases and ultimately enhance the health of all people. This state-of-the-science report highlights the many accomplishments and successes that ORIP achieved in FY25 in providing infrastructure for innovation for the nation's biomedical research community.

INTRODUCTION

ORIP supports infrastructure and resources that enable NIH ICOs and the external biomedical research community to conduct innovative research. ORIP's investments—including models for human disease, training and career development, construction and instrumentation, and small business programs—advance foundational infrastructure that supports research outcomes and enables progress across the research continuum, from basic discovery to real-world implementation. ORIP plays an NIH-wide role in infrastructure and discovery by supporting model integration, emerging technologies, instruments, and facilities, as well as developing future generations of the biomedical workforce.

This report highlights recent accomplishments and collaborations that have advanced ORIP's mission and supported NIH and its ICOs in achieving their goals through novel infrastructure. ORIP's FY25 activities support the office's core guiding principle of "Infrastructure for Innovation," advance reproducibility and rigor in research, and build research capacity. Stakeholders—including NIH and ICO leadership, Congress, ORIP grantees, and the public—will find this report useful in understanding ORIP's substantial impact on basic, translational, clinical, behavioral, and population health research. Building on recent accomplishments, ORIP aims to enhance collaborations within and beyond NIH and promote outreach to the broader biomedical research community and public. ORIP is uniquely positioned to foster collaborative science with advanced technology and cutting-edge instruments while supporting research capabilities in less resourced institutions.

STRATEGIC PLANNING

Throughout FY25, ORIP continued to develop its next strategic plan, which was approved by NIH leadership and published in early FY26. As a part of this effort, ORIP staff participated in a comprehensive consultation process and sought input from a broad spectrum of individuals, including biomedical scientists, members of professional organizations, and NIH senior program staff. The *ORIP Strategic Plan 2026–2030* is aligned with NIH's key strategic themes, including a focus on improving human health and an emphasis on replicability and generalizability of research.

ORIP's new strategic plan is built on four priorities: (1) model resources to advance the study of human diseases, (2) modern physical infrastructure to accelerate research discoveries in human health and diseases, (3) innovative cross-disciplinary research training in model systems for human health and diseases, and (4) outreach and awareness of ORIP resources and programs. The strategic plan also identifies four crosscutting themes: (1) responsible stewardship for maximum impact; (2) commitment to transparency, rigor, and reproducibility; (3) strategic investment in translational infrastructure; and (4) advancing research training and broad engagement.

While developing this strategic plan, ORIP used the best available metrics to review and evaluate its research projects and resource programs to ensure efficient management and transparent stewardship. ORIP rigorously assessed the contribution of its resources in a data-driven manner and balanced its portfolio to continually improve its resource centers and projects, thereby encouraging innovative research resources. Program officers and senior staff assessed the alignment of ORIP's programs with emerging and continuing high-priority research needs, especially with new NIH initiatives.

Looking ahead, ORIP will focus on translating its priorities into concrete actions that advance NIH's research infrastructure mission. ORIP will engage proactively through regular communications, joint planning meetings, and participation in NIH-wide initiatives, ensuring that its priorities remain aligned with broader NIH objectives. Additionally, ORIP will foster partnerships with scientific societies and professional organizations, creating forums for dialogue and collaboration that extend the engagement initiated during the strategic planning process. By combining structured assessment, continuous engagement, and adaptive planning, ORIP will ensure that the strategic plan guides its activities effectively and delivers tangible impact on the research infrastructure landscape.

ORIP'S CORE PROGRAM AREAS

ORIP is one office in the Division of Program Coordination, Planning, and Strategic Initiatives within the NIH Office of the Director. ORIP's two divisions support and help accelerate biomedical innovations. DCM helps biomedical researchers by bridging the gap between basic science and human medicine, increasing access to critical research tools, and providing scientific foundations for human health. DCI advances biomedical research infrastructure, optimizes research operation and laboratory environments, and supports high-quality research facilities through its instrumentation, equipment, and extramural construction programs. Both divisions drive rigor and reproducibility in research and also support small business programs by providing grants to support innovation and entrepreneurship in the areas of technology development and commercialization to ensure that researchers have access to technologies critical to their work. Through their activities and commitments, these divisions enhance the nation's competitiveness in biomedical research and scientific discovery.

Infrastructure for Innovation

ORIP's investments in the S10 Shared Instrumentation Grant Programs, S15 Modern Equipment Program, and C06 Biomedical Research Facilities Program have enabled research institutions nationwide to acquire cutting-edge equipment and modernize facilities, with a deliberate emphasis on expanding capacity in under-resourced institutions. These strategic infrastructure investments have enhanced priority research areas by increasing support for human-based research, chronic diseases, NAMs, and other strategic areas that align with the NIH mission and the administration's priorities.

For example, a gnotobiotic facility at the University of California (UC), San Diego, funded through ORIP's C06 mechanism, enabled researchers to study the role of an altered gut microbiome, a condition known as "leaky gut," in which the intestinal lining becomes more permeable, allowing undigested food particles, toxins, and bacteria to enter the bloodstream, which may contribute to chronic liver diseases, such as alcohol-associated hepatitis and metabolic dysfunction–associated steatotic liver disease. Researchers at UC San Diego have identified a toxin-producing gut bacterium as a key driver of alcohol-associated hepatitis. The team has since developed a targeted bacteriophage therapy—using small viruses that selectively kill disease-associated bacteria—and screened for the most effective phage combination. This approach has now received U.S. Food and Drug Administration (FDA) approval for Phase 1 clinical trials, bringing the experimental treatment one step closer to patients.

Scientific Foundations for Human Health

ORIP continued to play a vital role in FY25 in developing and sustaining models for human disease while also supporting such next-generation approaches as organoid systems, tissue chips, and computational models. Together, these complementary platforms expand opportunities for precision medicine and translational research.

For example, ORIP supported a variety of research activities in FY25 that positively impact the development of models

for human disease, from cryopreservation of biological samples to enhanced experimental designs. These projects included the development of a reproducible repository system for community-driven cryopreservation, a 3D zebrafish microanatomical and gene expression atlas for disease modeling, the production and validation of monoclonal antibodies to enhance the rigor and reproducibility in a vertebrate research model, and the generation and validation of antibodies and antibody-based biosensors for the zebrafish research community.

Driving Translational Research with Rigor and Reproducibility

In FY25, ORIP led NIH-wide efforts to strengthen reproducibility by integrating research on extrinsic factors with advanced instrumentation, standardizing model resources, and promoting such preservation technologies as cryopreservation. These initiatives provide investigators with more reliable tools to ensure robust and reproducible science. State-of-the-art scientific instruments generate reliable, reproducible, and rigorous measurements, which serve as quantitative gold-standard references and maintain the nation's top position in biomedical research.

With the rise of multi-omics and high-dimensional datasets, researchers increasingly face a large dimensional limit, at which the number of variables exceeds the number of observations. This poses risks, including model instability and irreproducible findings. An ORIP-supported grant tackles a critical need in modern biomedical research by addressing these risks. Research on reproducibility statistics and machine-learning (ML) methods for systematic phenotyping and model integration across models, organs, and technologies will help in developing statistical frameworks and ML pipelines that incorporate reproducibility metrics directly into data analysis workflows and enhance the transparency and reliability of biomedical discoveries. Ultimately, the project strengthens community standards for rigorous, reproducible research and ensures that findings derived from complex research model studies remain robust, interpretable, and translatable.

ORIP supported FY25 efforts to enhance rigor and reproducibility in *Drosophila* disease modeling and functional genomics, enabled a major FlyRNAi.org 2025 update, and expanded standardized datasets and integrated new technologies to provide reproducible and accessible resources for the research community. Furthermore, ORIP supported the development of a phage-displayed synthetic nanobody library and screening platform, which replaces traditional camel immunization with a scalable, reproducible pipeline. This tool generated nanobodies for immunostaining and immunoblotting, and the library has been made available for nonprofit use, promoting widespread adoption of rigorously tested reagents. ORIP also supported the development of tools to improve reproducibility by standardizing data interpretation and enabling cross-species validation of critical reagents. Through these achievements, ORIP's investment directly advanced the creation of community-wide resources that ensure rigor, reproducibility, and translational value in biomedical research.

Technology Translation and Entrepreneurship: Small Business Programs

Through its Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs, ORIP supports innovative technologies that accelerate biomedical discovery and enhance reproducibility. These investments enabled advanced breakthroughs in cryopreservation, high-resolution imaging, and novel approaches to disease modeling.

During FY25, ORIP continued supporting the advancement of several important technologies through Phase II awards, including those that align with an important focus area—cryopreservation. These projects include a cryopreservation technology platform to produce better cryoprotectants to preserve cells and tissues for the next generation of cell-based therapeutics in regenerative medicine and drug discovery and a rat sperm cryopreservation and artificial insemination system to improve the preservation and revival of genetic stocks.

Also in FY25, Ramona Optics Inc.—an ORIP-supported company—successfully brought a new microscope concept called the Multi-Camera Array Microscope (MCAM™) to the national and international marketplace. This instrument is challenging the limitations of current microscopes, with new capabilities that allow behavioral phenotyping of model organisms. Another ORIP small business grant recipient, SPOC Proteomics, Inc., aims to revolutionize proteomics by developing a first-of-its-kind high-throughput proteomic kinetic profiling platform that addresses the challenges of interrogating protein interactions at scale for research and clinical applications. This technology will advance the screening of protein interactions and significantly reduce cost and time compared with traditional methodologies for drug discovery, vaccine development, and biomarker identification.

ORIP's small business programs collaborated with a number of NIH ICOs—including the National Institute of General Medical Sciences (NIGMS), National Institute of Arthritis and Musculoskeletal and Skin Diseases, and National Institute of Neurological Disorders and Stroke—to fund technologies related to cryopreservation, transplantation, cell therapy, and gene replacement therapy to bring technologies to the marketplace to support the research community at large and advance human health.

Together, these small business initiatives directly benefit patients, including those with rare diseases that often receive less attention because of limited demand for therapies, providing hope for new diagnostics and treatments.

RESEARCH RESOURCE SUPPORT, DISSEMINATION, AND ENGAGEMENT

In FY25, ORIP expanded its efforts to disseminate scientific resources; update digital platforms and fact sheets; and engage the research community through meetings, workshops, and outreach. Enhanced web resources and improved communications are making ORIP-supported infrastructure more visible and accessible.

Resource Support and Dissemination

The S10 Shared Instrumentation Grant Programs within ORIP's DCI provide a cost-effective mechanism for researchers to obtain cutting-edge instrumentation. These innovative instruments must be used on a shared basis, which allows thousands of researchers in hundreds of institutions across the United States to advance their research and ensures responsible stewardship of taxpayer dollars. In FY25, DCI made 111 awards to 79 institutions in 34 states, funding work across a broad range of academic and research institutes, including those in Institutional Development Award (known as IDeA) states that historically have received less funding from NIH and whose awards help build their research capacities. These awards supported a wide assortment of emerging methodologies and technologies—including automated cell culture systems, -omics sequencers, high-performance computing clusters, and robotic frozen storage units for biobanking **(Figure 1a).** The S10-funded instruments assisted with more than 2,200 NIH-funded research projects across basic, translational, and clinical research that were funded by 24 NIH ICOs and two other federal agencies (U.S. Department of Veterans Affairs [VA] and FDA) **(Figure 1b).**

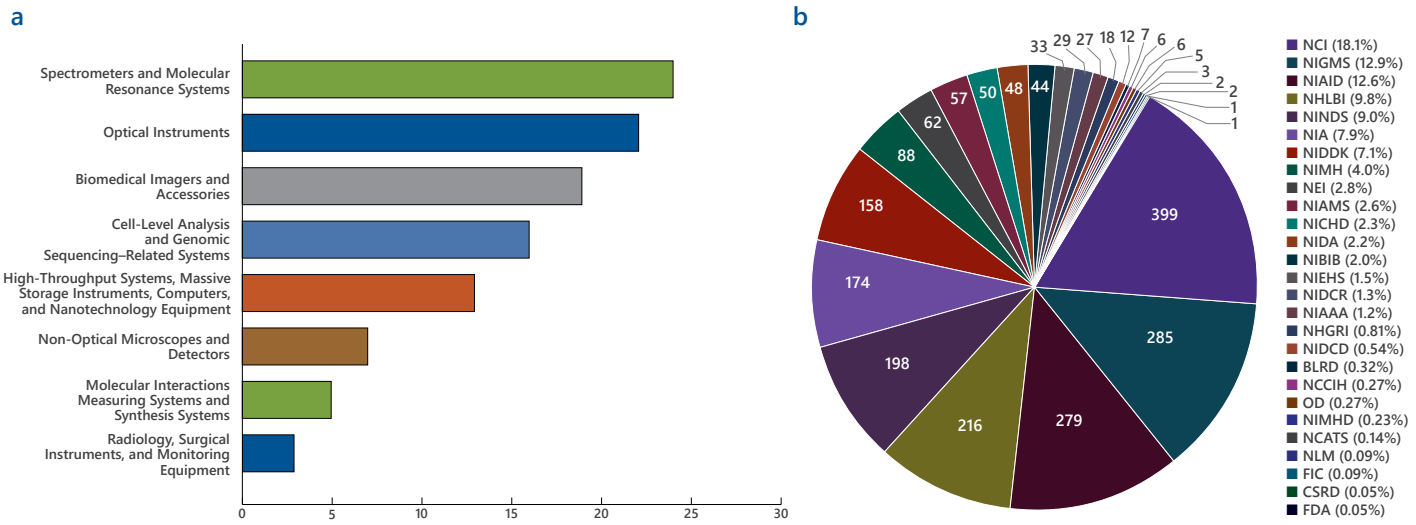

Figure 1. S10 instruments support all areas of NIH-funded research. (a) The number and types of instruments funded by S10 programs in FY25. (b) Percentage of research projects from different NIH ICOs, the VA, and the FDA supported by S10 instruments in FY25. The number in each pie piece represents the number of federally funded research projects.

Of special note, one ORIP-funded mass spectrometer is being used to provide a quantitative method for measuring concentrations of the HIV drug lenacapavir in patient plasma samples, which enables therapeutic monitoring and personalized modifications to treatment regimens in clinical settings. Proper drug dosage is critical to ensure the efficacy of a treatment. Objective drug titration validates the immunology effect by quantifying drug concentration and provides evidence and guidance supporting lenacapavir dosage and the twice-a-year pre-exposure prophylaxis (known as PrEP) regimen.

An ORIP-funded hyperpolarizer enables clinical-grade magnetic resonance imaging probes to be produced in one-tenth of the time when compared with previous versions of the system. This allows researchers to complete real-time, whole-body imaging to study metabolic flux in a broad range of diseases—including cancer and Alzheimer's disease.

The S15 Equipment Program within ORIP's DCI facilitates the acquisition and installation of modernized equipment to optimize operational workflows in biomedical research facilities. In FY25, DCI administered S15 grants to

20 institutions across 15 states, supporting modernized equipment—including 3D printers that create physiologically relevant multicellular tissue constructs that mimic human tissue to create more realistic models—that will advance ORIP's strategic initiatives.

DCI continues to support C06 programs, which help institutions construct new or update existing shared-use research facilities to expand research capacities. In FY25, DCI awarded 14 C06 projects, including many that fall within NIH priority categories. For example, one of the largest positron emission tomography (PET) research centers in the world, Yale PET Core, actively supports more than 120 clinical research protocols and is using ORIP support to modernize its radiochemistry infrastructure. The Rockefeller University will use ORIP-supported funds to expand its Gruss Lipper Precision Instrumentation Technologies Resource Center to meet demands from researchers at Rockefeller and regional institutions for instrument prototyping and fabrication technologies—such as photolithography, soft lithography, microfluidics, and film and particle deposition—for *in vivo*, *ex vivo*, *in vitro*, and *in chemico* studies. Coriell Institute for Medical Research will expand its biobanking and cell engineering center, which will increase its offerings of products and services in induced pluripotent stem cells (iPSCs), 3D organoid models, and cell gene engineering by 20-fold. The funded C06 grants also support population health and the real-world data initiatives of NIH. For example, the Institute of Living, a psychiatric hospital in Connecticut, will enable a neuroscience biotyping facility to collect data from psychiatric patients and subtype them to discover the translational potential for personalized psychiatric medicine. Emma Pendleton Bradley Hospital, the nation's only psychiatric hospital devoted to children and adolescents, will construct a center to integrate clinical services and research spanning many developmental and neurobehavioral/neuropsychiatric conditions (e.g., autism, obsessive-compulsive disorder/anxiety, depression, psychosis).

ORIP's DCM supports a broad range of translational research projects and resources that help in developing and increasing access to preclinical models. ORIP collects annual statistics on the Biomedical Resource and Research Centers' stock collections, services, and distribution that are supported by NIH grants. **Table 1** displays the statistics reported in FY25 for the most-used biomedical research models. Because investigators may not acknowledge or cite these specific resources, the information shown in this table on grants and references is underestimated.

Table 1. FY25 Statistics on the Most Utilized Biomedical Research Models

Repository	Research Model	Items in Repository	Distributed Strains/ Biospecimens	Number of NIH Grants Supported by Orders	Publications by User Community	Number of NIH Grants Cited in Publications	Number of NIH ICOs Funding Research Cited in Publications
Human Tissues and Organs for Research Resource	Human Biospecimens	2,148[a]	2,148	77	88	283	23
Bloomington *Drosophila* Stock Center at Indiana University	Flies	93,494	138,171	714	2,180	1,057	26
Mutant Mouse Resource & Research Centers	Mice	69,021	1,816	189	629	1,079	25
Zebrafish International Resource Center	Zebrafish	46,290	66,899	77	97	101	19
Caenorhabditis Genetics Center	Worms	26,810	27,175	597	1,905	436	23
National Primate Research Centers	Nonhuman Primates	22,890[b]	6,315[c]	447	478	963	17

[a] This resource is not a biobank, biorepository, or tissue bank but is a tissue interchange that utilizes a prospective rather than retrospective procurement model. Thus, items in repository also are represented by distributed biospecimens.

[b] Reflects total nonhuman primates supported across all seven National Primate Research Centers, including breeding colony animals; this does not include tissue samples distributed.

[c] For nonhuman primates, this number is production count.

Note: The numbers for the National Primate Research Centers are for FY24 (reported in FY25). Research performance progress reports (RPPRs) for the National Primate Research Centers are received in March of each fiscal year. Consequently, RPPRs report on the previous fiscal year.

DCM also developed the ORIP Precision Disease Modeling Initiative, which provides the biomedical research community with advanced, next-generation preclinical models and cell systems to replicate human disease variants. The current initiative focuses on linking human multi-omics data with predictive preclinical models to understand disease causality, reduce the failure rate of drug candidates, and support precision therapies. **Table 2** features the pilot centers' areas of progress in FY25.

Table 2. Pilot Centers for Precision Disease Modeling Initiative FY25 Progress

Center, Institution	Overall Number of Submitted Variants[a]	Accepted Number of Submissions/ Variants	Number of Models to Be Created	Number of Models Established	Number of Collaborating Institutions	Publications	Investigational New Drug/ Preclinical Testing
BCM Center for Precision Medicine Models, Baylor College of Medicine, Texas	156	63/79	219	203	31	12	9
The Jackson Laboratory Center for Precision Genetics, The Jackson Laboratory, Maine	162	66/117	124	87	52	18	13
UAB Pilot Center for Precision Animal Modeling, The University of Alabama at Birmingham, Alabama	186	103/112	139	127	28	48	2

[a] A "variant" refers to a difference in the DNA sequence of a particular gene between individuals, essentially a variation in the genetic code within a person's genome compared to a reference sequence.

Engagement

ORIP engages with the biomedical research community through meetings and workshops, and the office had many engagement successes in FY25. For example, ORIP was instrumental in facilitating the Cryopreservation and Other Preservation Approaches for Animal Models Workshop. The goal of the workshop was to examine current practices, challenges, and emerging opportunities in preserving preclinical models for biomedical research. The workshop discussed key topics, including protocol standardization, training in preservation methods, data management, quality control, logistical difficulties, and infrastructure needs. In addition to safeguarding supported repositories, enhancing cryopreservation methods by addressing these gaps allows ORIP to strengthen rigor and reproducibility while minimizing variations among experiments.

ORIP has continued to maintain a visible presence on social media platforms, including X, to connect with both the biomedical research community and the public, which allows the office to communicate important biomedical research findings. In October 2024, findings from a clinical trial that used ORIP-funded instrumentation and led to FDA approval of a breakthrough monoclonal antibody treatment for Alzheimer's disease received more than 1,200 views on X. A January 2025 tweet about ORIP-supported research that highlighted the development of precision medicine models to end the diagnostic odyssey for patients with rare diseases received more than 525 views. Several other tweets about ORIP-supported findings also have received hundreds of views, likes, reposts, and total engagements.

DCI has conducted an inaugural series of informational webinars across all award stages to ensure that investigators understand the federal requirements of an S10 award, as well as to share best practices and provide a live opportunity for investigator inquiries to be answered. In addition, DCI initiated weekly "office hours" to provide an ongoing opportunity for potential applicants to ask questions. This well-received event attracted more than 60 visitors in its first 3 months. Short videos also have been released as an additional resource to help people learn about the S10 Instrumentation Programs. ORIP's efforts have significantly reduced administrative burden and increased efficiency in resolving investigator queries while ensuring that current and potential investigators have access to the latest information about the resources and programs the office supports. In addition, updates to digital platforms have improved the visibility and user-friendliness of ORIP communications.

To maximize ORIP's impact on the biomedical research landscape, the office continues to foster a collaborative science ecosystem and strengthen its partnerships with NIH ICOs to enhance the NIH mission. ORIP has active partnerships with 20 NIH ICOs, including collaborations with the National Institute of Dental and Craniofacial Research and *Eunice Kennedy Shriver* National Institute of Child Health and Human Development to understand genomic variants associated with a broad range of

congenital defects. Through effective outreach, ORIP has maintained partnerships with six ICOs to provide data-driven decisions for S10 instrument investments to ensure that areas of national priority, such as artificial intelligence (AI) and deep ML, are supported. Through such mechanisms as DCI's Seed Instrument Support program, ORIP has built roadmaps and strategically planned how to address several gaps facing research and instrument communities, broadly boost instrument support nationwide, establish instrument support in less-resourced institutions, and promote research innovations in all institutions. In addition, ORIP continues to collaborate with other NIH ICOs to support biomedical research facilities to improve human health.

SCIENTIFIC HIGHLIGHTS AND PUBLICATIONS

ORIP strives for excellence within its areas of investment, such as next-generation model systems, disease applications, crosscutting discoveries, training and career development, and instrumentation and construction. A number of FY25 scientific highlights and publications showcase ORIP's success in these areas, such as an ORIP-supported publication that was selected as Editor's Choice in *Biology of Reproduction* for reporting a new model for endometriosis. Below are other select examples.

Next-Generation Model Systems

S10-funded state-of-the-art scientific instruments have accelerated research involving NAMs and new technologies **(Figure 2a).** Although the acknowledgement rate for an S10 grant in publications is not 100%, the number of publications stemming from the use of S10-funded instruments clearly shows that these instruments support and impact both established and emerging methodologies and technologies. The S10 instrument support for some types of NAMs has been highly consistent during the last 5 years, but there is a recent upward trend in some of the areas, such as organoids **(Figure 2b).**

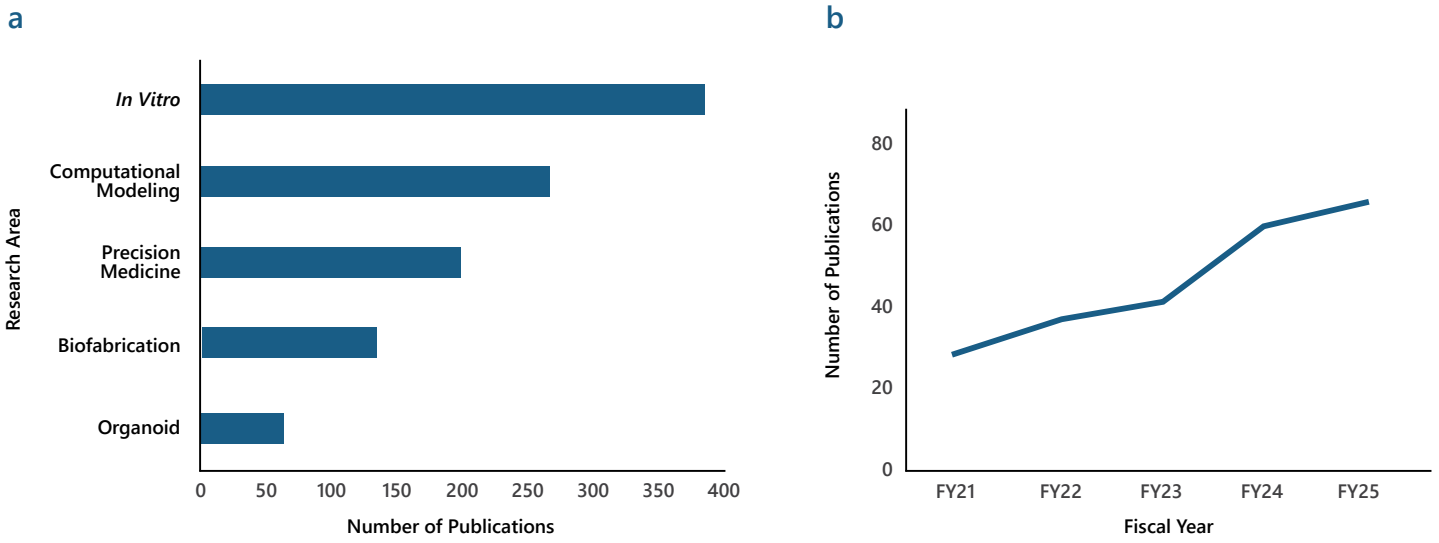

Figure 2. S10 instruments support research utilizing NAMs and new technologies. (a) The number of FY25 publications that stemmed from the use of S10-funded instruments. (b) The number of publications specifically on organoids during the previous 5 fiscal years.

For example, researchers at the Buck Institute for Research on Aging not only used S10-funded instruments to study the roles of protein aggregates in aging-related neurodegenerative disorders but also contributed to the structural and functional validation of a fallopian tube organoid—a 3D tissue model designed to mimic a native fallopian tube—ensuring rigorous study outcomes while minimizing variations among experiments. This model will serve as a gold standard for studying gynecological conditions and diseases—such as ectopic pregnancy and high-grade serous carcinoma—that could have a profound impact on women's health research.

DCM supports the development of next-generation model systems by advancing NAMs that complement and help minimize the use of animal models in biomedical research. A key example is the Human Tissues and Organs for Research Resource (known as HTORR), funded by ORIP with other NIH partners, which provides human tissues that have enabled major initiatives, including the Genotype-Tissue Expression (GTEx) Program, Somatic Mosaicism across

Human Tissues (known as SMaHT) Network, LungMAP (Molecular Atlas of Lung Development Program), and Developmental Genotype-Tissue Expression (dGTEx) project. ORIP's U54 Centers for Precision Modeling leverage patient-derived and engineered iPSCs and organoid platforms for comparative genomics, multi-omics analyses, and therapeutic screening, integrating human data with research models to enhance translational relevance and reduce reliance on animals. DCM-funded investigators also use immunodeficient or immunosuppressed fish, mice, pigs, and nonhuman primates as hosts for human cell transplantation in regenerative medicine studies. Additional efforts include establishing cross-species correlations using human kidney organoids and rhesus kidneys, developing AI models that identify drug candidates for liver fibrosis through human iPSC-derived hepatic organoids, and applying ML via the BioGRID database to define conserved pathways relevant to neurological and cancer biology.

Disease Applications

Chronic Diseases

Acquiring fundamental knowledge on the causes of chronic diseases is critical to developing new therapeutic and preventive strategies, and ORIP directly supports the NIH priority of combating chronic diseases. Results obtained from S10-funded instruments were included in more than 2,200 FY25 publications and have advanced the understanding of numerous diseases, such as diabetes, obesity, and heart disease, across populations **(Figure 3).**

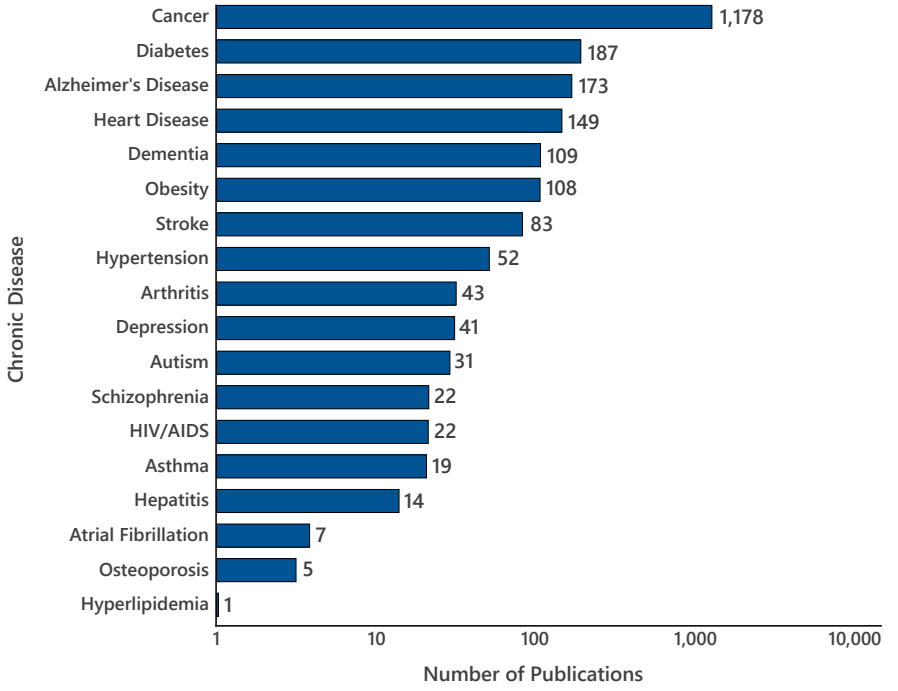

Figure 3. Number of FY25 publications by disease area resulting from S10-funded instrument–supported research.

For example, researchers at the Medical College of Wisconsin are using an S10-funded instrument to study how bacterial proteins respond to environmental changes and invade host immune systems. Persistent bacterial infections—aggravated by the increasing prevalence of antibiotic resistance and associated with such chronic diseases as cancer and Alzheimer's disease—pose significant economic and societal burdens. This study has broad implications beyond infections in developing new delivery systems for therapeutic drugs for a broad range of human diseases, including cancer.

Rare Disease Models

DCM actively supports rare diseases research by providing disease expertise and platforms for preclinical studies and development of new personalized therapeutics. In FY25, a number of ORIP-supported projects resulted in important discoveries in rare disease areas. For example, The University of Alabama at Birmingham Center for Precision Animal Modeling identified the cause of X-linked myopathy with excessive autophagy (XMEA) in a patient family and created a preclinical platform that allowed successful drug screening. XMEA causes muscle weakness that can begin in childhood and primarily affects males. People with XMEA may be wheelchair-bound in adulthood. Currently, no specific treatments exist, so screening for successful drug candidates that improve functional outcomes and extend survival represents a significant breakthrough in the treatment of this debilitating disease.

As published in *Neurobiology of Disease*, researchers at The Jackson Laboratory Center for Precision Genetics tested therapeutic strategies for alternating hemiplegia of childhood, a rare disease that causes developmental delays, intellectual disabilities, seizures, and painful involuntary body movements that threaten health. This work offers clear insights into how the rare disease progresses and how it might be stopped. Additionally, patients with rare diseases often wait years for a diagnosis—referred to as the "diagnostic odyssey." The Baylor College of Medicine is looking to end this odyssey by developing models to better diagnose these patients, as well as developing new therapies. ORIP supports collaborative research projects that link current personalized medicine efforts in human subjects with advances in research-model genomics and technologies, providing critical infrastructure and resources for exploring the genetic basis of human diseases and ultimately developing and testing treatments for these diseases.

Regenerative Medicine

ORIP-supported researchers from the aquatic models community achieved important milestones in FY25, including the discovery that retinoic acid breakdown is required for proximodistal positional identity during axolotl limb regeneration. This study investigated the cellular process involved in tissue regeneration that results in correct restoration of missing structures in the axolotl. Studies building on this discovery could identify the chemical signals that unlock early developmental instructions, which are inactive in humans after birth. The *Nature Communications* article describing this discovery received a great deal of media attention, including features in *Popular Science*, *National Geographic*, and *The Washington Post*.

ORIP's Stem Cells and Regenerative Medicine Initiative advances cross-species models and technologies to restore or replace damaged tissues. One recent breakthrough supported by ORIP is the development of pluripotent stem cell–derived arterial grafts that remained patent in rhesus macaques for 6 months, showing strong potential for human vascular repair. Creating a universal vascular graft helps improve surgery for cardiovascular disease. ORIP also supported studies that offer promise for studying regeneration to enable therapeutic discovery for chronic degenerative human diseases, as well as studies advancing translational platforms for human stem cell engraftment, developing pathogen-free colonies, and engineering double-mutant strains to enhance immune system "humanization." Collectively, these ORIP-supported advances demonstrate how regenerative medicine projects are producing clinically relevant grafts, refining regenerative models, and enabling new therapies for human disease.

Immunotherapeutics

As reported in *JAMA*, in June 2025, the FDA approved the twice-yearly injectable lenacapavir (Yeztugo®), the first drug to provide near-complete protection against HIV infection with administration only every 6 months. Extensive support from ORIP-funded resources enabled this breakthrough. Research models supplied by ORIP's U42 programs were central to pivotal preclinical studies demonstrating lenacapavir's efficacy, which informed two large-scale human trials that showed between 96% and 100% protection from HIV infection. ORIP's antibody reagent resources further enabled immune monitoring, and advanced instrumentation funded by ORIP's S10 programs was used to develop methods to measure levels of lenacapavir in plasma. Beyond prevention, ORIP has supported HIV cure research since the late 1990s, laying the scientific foundation for lenacapavir's mechanism of action by elucidating HIV capsid dynamics, assembly pathways, and resistance mechanisms. ORIP-supported computer clusters and structural biology studies also were critical in drug design. Lenacapavir is now a model for next-generation antivirals, underscoring the transformative role of ORIP-funded infrastructure in advancing HIV/AIDS therapeutics from basic discovery to clinical application.

Crosscutting Discoveries

Genomics

In FY25, genomics advances drove biomedical discovery. As part of the nonhuman primate dGTEx project—co-funded by ORIP, the National Human Genome Research Institute, and the National Institute of Mental Health—researchers profiled more than 30 tissues across six developmental stages in rhesus macaques and marmosets. This project produced bulk RNA sequencing and whole-genome data, creating the first developmental single-cell atlases for these species. These datasets are a powerful tool for allowing direct comparison with human development data, offering new perspectives on evolutionary biology and the genetic basis of pediatric disease. Several FY25 publications underscored the genomic advances of dGTEx. A *Nature* review introduced the human and nonhuman primate dGTEx projects as a foundation for developmental genomics.

Other significant studies published in FY25 revealed critical windows of vulnerability in cortical development using human neural stem cells and identified human-specific features of cerebellar synapse development, with implications for neurodevelopmental disorders. Also, a cross-species analysis advanced population genomics by validating a software pipeline that provides a powerful tool to estimate genetic relatedness to elucidate behavior, population structure, and the evolution of biological traits.

Artificial Intelligence

In FY25, the ORIP-supported Enabling AI-Based Mouse Genetic Discovery project demonstrated how advanced AI can accelerate genetic discovery and therapeutic development. Researchers used a common large language model to analyze mouse genomic sequences and identify the genetic basis of hearing loss. This approach was extended to human genomic data, enabling the identification of causal variants in both hearing loss and rare, complex genetic diseases while also showing that AI can analyze large amounts of data effectively. The team then collaborated with Google to create an "AI co-scientist," a virtual scientific collaborator designed to accelerate biomedical discovery and drug development by helping scientists generate novel hypotheses.

To test its use for drug discovery, the AI co-scientist was tasked with identifying therapies targeting epigenomic modifiers for the treatment of liver fibrosis, a disease with limited therapeutic options. In parallel, the team developed a NAM-aligned experimental platform in which human hepatic organoids derived from stem cells were combined with a live-cell imaging system for dynamic monitoring of fibrosis and drug responses. These organoids reproduced hallmark features of human liver fibrosis.

Two AI-recommended drugs demonstrated strong anti-fibrotic activity on this platform. One of them, vorinostat, an FDA-approved histone deacetylase inhibitor, not only reduced fibrosis but also promoted liver cell regeneration. This finding is a promising new therapeutic strategy for liver fibrosis. The large language model's ability to mine mouse fibrosis studies provided the foundation for these repurposing insights, underscoring how AI can bridge research models and human disease to accelerate translational discovery.

Workforce of the Future: Training and Career Development

In FY25, ORIP strengthened its commitment to training scientists and developing the next generation of biomedical researchers. ORIP's institutional research training grants, awarded to institutions that provide advanced training in comparative medicine, support motivated veterinarians who wish to explore careers in biomedical research. The T32 Postdoctoral Program trains highly qualified veterinarians for research careers in biomedical areas related to comparative medicine. In FY25, ORIP supported 10 T32 training grants, with an average of 4.6 trainees per grant; 48 publications were reported based on these grants. The Special Emphasis Research Career Award (SERCA) provides early-career veterinary scientists with 4 years of protected research time for intensive, supervised career development in the biomedical sciences, leading to research independence. In FY25, ORIP funded 17 SERCA/K01 awards, resulting in 18 reported publications.

ORIP is prioritizing expanding opportunities for cross-training and multidisciplinary training, which emerged as a need during the Comparative Medicine Resource Directors Meeting in August 2024 and in training-related focus groups organized by ORIP in spring 2025. Specific training areas identified through these discussions that ORIP is focusing on include computational biology, data science, AI, statistics, and business disciplines. ORIP also emphasizes training in NAMs to prepare trainees in meeting the challenges of biomedical research. By expanding and strengthening its career development programs in response to a thorough analysis of research needs, ORIP is working to ensure that comparative medicine researchers will continue to advance the biomedical research field for years to come.

Instrumentation

ORIP's S10 instrumentation programs support the acquisition of commercially available, state-of-the-art scientific instruments that are critical for cutting-edge research but are too expensive to be obtained by individual researchers. Shared use of these instruments facilitates advanced scientific studies and maximizes the return on NIH investment and the benefits of these technologies. On average, each S10 dollar supports approximately $20 of NIH research grants, demonstrating the great research-enabling power of the NIH shared instrumentation programs. These awards have proven their value in strengthening the U.S. biomedical research enterprise by modernizing instrumentation and infrastructure at research institutions nationwide and supporting researchers, ranging from Nobel laureates to early-career investigators. The S10 programs have fostered technological advancement within the scientific instrument industry, creating jobs and positively impacting regional and national economies.

Researchers at the Advanced Pulmonary Physiomic Imaging Laboratory at The University of Iowa are using S10-funded instruments to study the links between lung structure and lung function. Over the years, the team has received three S10 awards to support the purchase of computed tomography scanners to study how air moves in and out of tiny peripheral air spaces, how blood flows through the intricate vascular network, and how the delivery of blood and fresh gas are optimized for normal physiologic respiratory processes. The team is working to characterize lung structure (airways, vasculature, parenchyma) and function (regional ventilation/perfusion relationships along with lung mechanics), leveraging new opportunities in the field.

The S10 programs have enabled biomedical research to advance to clinical trials. The Washington University in St. Louis Center for Clinical Imaging and Research used an

S10-funded advanced imaging system in a clinical trial related to Alzheimer's disease, the most common cause of dementia among older adults that is estimated to affect more than 6 million people in the United States. The imaging system was used to test the efficacy and adverse events of donanemab, an antibody designed to clear amyloid plaques in early symptomatic Alzheimer's. The team needed quantitative metrics to demonstrate, with high precision, pathology in the brain before and after treatment with donanemab. The center used its high-quality scanners with more precise measurements, including the ORIP-funded scanner, to show that donanemab slowed clinical progression of the disease in early symptomatic patients. Donanemab was recently approved for use by the FDA.

ORIP FISCAL YEAR 2025 BUDGET AND LEVERAGED FUNDING FOR RESEARCH INFRASTRUCTURE

ORIP contributes to the NIH mission by supporting shared research resources, promoting crosscutting research to enable biomedical discoveries, and leveraging budgeting and co-funding strategies. With a fraction of a percent of the NIH budget, ORIP awards more than 220 new competitive grants each year, sustaining more than 3,000 NIH-funded research projects. The office has successfully leveraged collaborations across NIH to ensure that ORIP maximizes its positive impact on leading-edge biomedical research and accomplishes as much as possible with its modest budget.

For example, in FY25, ORIP secured significant funding levels in support of ORIP-managed awards, amounting to a 10% addition to ORIP's budget. DCM obtained more than $11 million in co-funding from 17 ICOs and the INCLUDE (INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndromE) Project for ORIP grants, cooperative agreements, administrative supplements, and revisions supporting resource centers and research resources **(Figure 4a).** This co-funding was invested across multiple research models **(Figure 4b).**

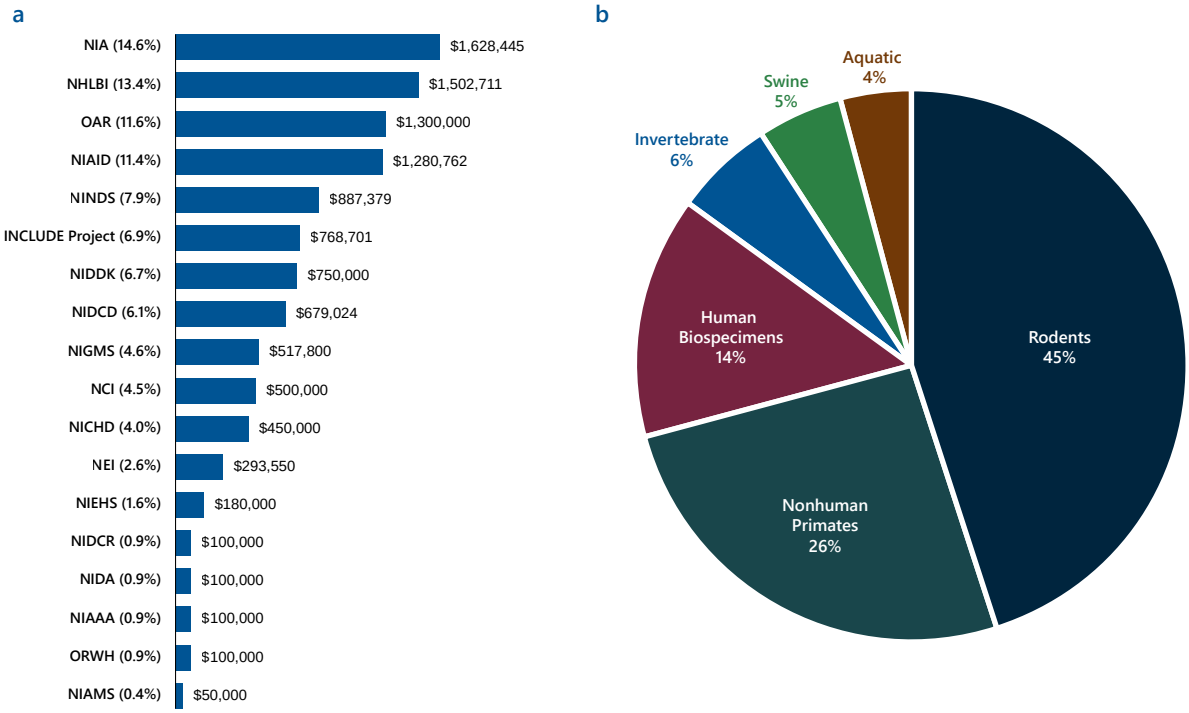

Figure 4. DCM's FY25 co-funding amounts. (a) Percentage of total co-funding amount contributed by each ICO and actual funds provided by each ICO in descending order. (b) Percentage of DCM co-funding invested in different research models.

In FY25, DCI obtained more than $18 million in co-funding from six NIH ICOs and programs for grants **(Figure 5).** In addition, ORIP manages an annual budget of $8 million for the Office of AIDS Research construction program dedicated to modernizing HIV research facilities.

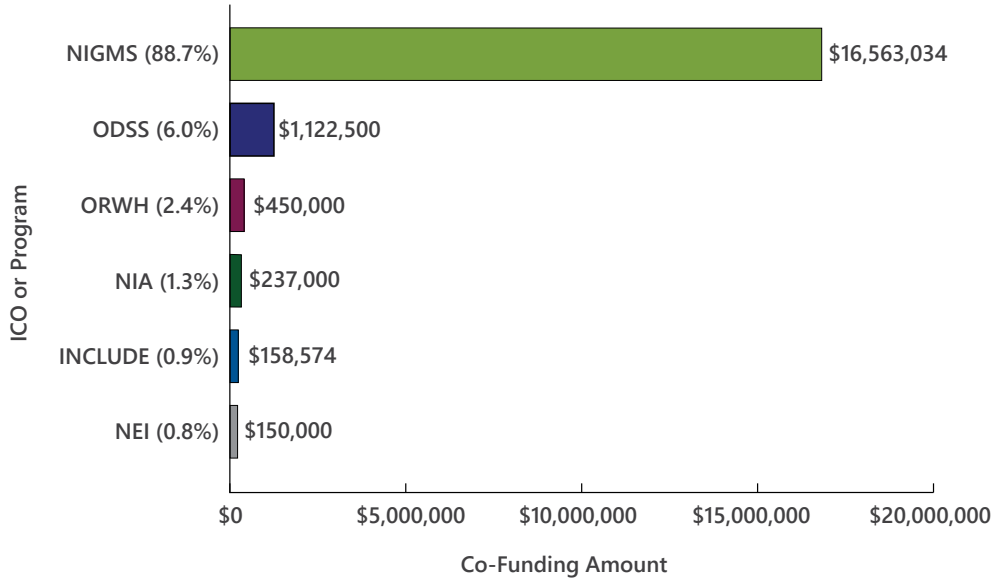

Figure 5. DCI's co-funding partners, percent of total co-funding amount contributed by each partner, and actual funds provided by each partner in descending order.

ORIP's SBIR and STTR programs have a combined annual budget of more than $8 million, including co-funding from NIGMS. In FY25, seven new applications were funded, totaling $3.84 million **(Figure 6).** Additionally, four FY24 Phase II grants totaling slightly more than $4 million were carried over.

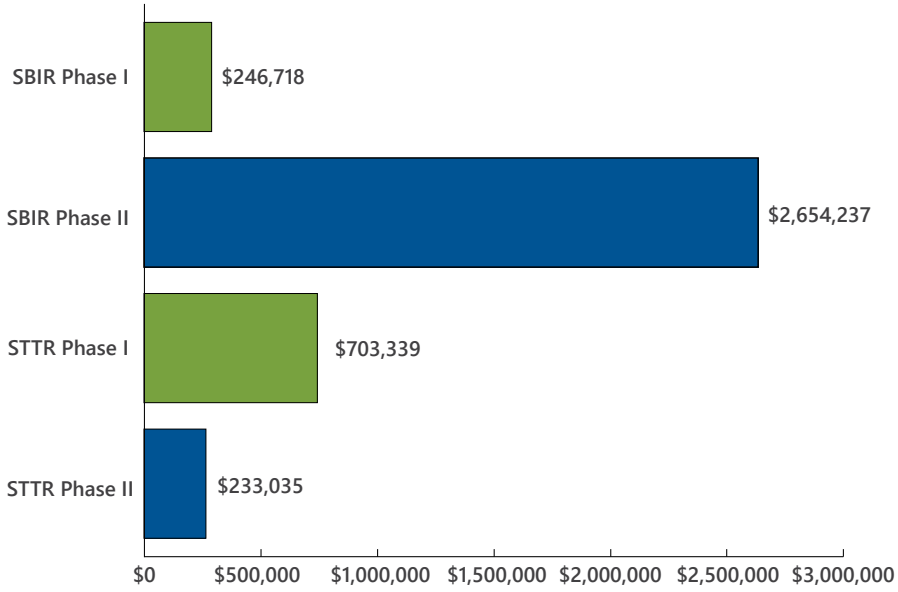

Figure 6. FY25 funding of new SBIR and STTR Phase I (feasibility and proof-of-concept) and Phase II (continuation of the research and development initiated in Phase I) projects.

CONCLUSION

Collectively, these efforts underscore ORIP's unique role as an innovation driver across NIH. By embedding models for human disease within a broader ecosystem of infrastructure, reproducibility, training, and technology translation, ORIP is enabling the biomedical community to address complex health challenges more reliably, effectively, and rigorously.

Looking forward, ORIP remains committed to advancing cutting-edge infrastructure, ensuring reproducibility, promoting broad access to resources, and fostering the workforce of the future. These principles have helped formed the basis for ORIP's new strategic plan, which outlines ORIP's vision to create and maintain resources to advance biomedical research. Ultimately, ORIP is well positioned to catalyze the next era of biomedical discovery and contribute to transformative improvements in human health.