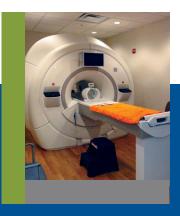






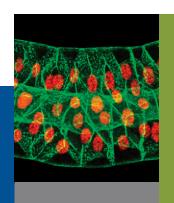
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## List of Abbreviations

| AIDS        | Acquired Immune Deficiency Syndrome   | NIDDK National Institute of Diabetes and Digestive and Kidney |  |  |
|-------------|---|---|--|--|
| AFIP        | Animal Facility Improvement Program   |   | Diseases   |  |
| BDSC        | Bloomington Drosophila Stock Center   | NIGMS   | National Institute of General Medical Sciences   |  |
| CSR         | Center for Scientific Review  | NIH   | National Institutes of Health  |  |
| DCI         | Division of Construction and Instruments  | NIMH  | National Institute of Mental Health  |  |
| DCM         | Division of Comparative Medicine  | NIMHD   | National Institute on Minority Health and Health Disparities   |  |
| DPCPSI      | Division of Program Coordination, Planning, and Strategic Initiatives           | NINDS   | National Institute of Neurological Disorders and Stroke  |  |
|             |   | NPRCs   | National Primate Research Centers  |  |
| <b>EPMC</b> | Extramural Program Management Committee   | NSRRC   | National Swine Resource and Research Center  |  |
| HEI         | High-End Instrumentation Grant program  | OAR   | Office of AIDS Research  |  |
| ICs         | Institutes and Centers (at the NIH)   | OD  | Office of the Director   |  |
| MMRRC       | Mutant Mouse Resource and Research Centers                                      | ORIP  | Office of Research Infrastructure Programs   |  |
| NCATS       | National Center for Advancing Translational Sciences                            | OSE   | Office of Science Education  |  |
| NCI         | National Cancer Institute   | P-12  | Pre-kindergarten through grade 12  |  |
| NHGRI       | National Human Genome Research Institute  | RFI   | Request for Information (used by NIH to solicit broad input on an issue)  Biomedical research support shared instrumentation grant mechanism |  |
| NHP         | Nonhuman primate  |   |  |  |
| NIA         | National Institute on Aging   | <b>S10</b>  |  |  |
| NIAID       | National Institute of Allergy and Infectious Diseases                           |   |  |  |
| NIAMS       | National Institute on Arthritis and Musculoskeletal and Skin Diseases           | SBIR  | Small Business Innovation Research   |  |
| MIMIN       |   | SEPA  | Science Education Partnership Award grant program  |  |
| NIBIB       | National Institute of Biomedical Imaging and Bioengineering                     | SIG   | Shared Instrumentation Grant program   |  |
| NICHD       | Eunice Kennedy Shriver National Institute of Child Health and Human Development | STEM  | Science, Technology, Engineering, and Mathematics  |  |
|             |   | STTR  | Small Business Technology Transfer   |  |
|             |   | ZIRC  | Zebrafish International Resource Center  |  |



#### From the ORIP Director

The National Institutes of Health (NIH) established the Office of Research Infrastructure Programs (ORIP) in December 2011 when the appropriations bill for Fiscal Year 2012 was passed by Congress and signed into law. ORIP provides research infrastructure and related research programs and coordinates NIH's science education efforts. ORIP is located in the NIH Office of the Director's (OD) Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI), which identifies and enhances trans-NIH research in critical areas of emerging scientific opportunities and reports on knowledge gaps that merit further research through its scientific offices. The trans-NIH nature of ORIP activities demands close collaborations between ORIP divisions (DCM, DCI, SEPA), DPCPSI offices, and the entire NIH to optimize support of all disease areas and across the basic, translational, and clinical research continuum.

The activities directed by ORIP, consistent with DPCPSI's mission, include assisting the NIH Institutes and Centers (ICs) to strengthen existing programs, develop resources, advance areas of emerging science, and develop new initiatives to move medical research forward. Biomedical research, like other complex human endeavors, benefits from a robust infrastructure. ORIP's research infrastructure includes the physical, intellectual, and human resources that advance biomedical research at NIH ICs. ORIP partners with NIH ICs to create and support a variety of research infrastructures. These partnerships reinforce ORIP's focus on activities that are of interest to two or more disease- or system-specific ICs. Additionally, ORIP will continue to develop and explore creative ways to partner with other Federal agencies and nongovernmental organizations.

ORIP's unique position and concentrated effort to collaborate across NIH ICs benefits NIH awardees and the extramural scientific community. This allows for the pursuit of evolving scientific opportunities within the currently supported infrastructure areas and expansion into emerging disciplines. ORIP will continue to develop new initiatives that advance and enhance resources to benefit the biomedical research community.

ORIP's 2016–2020 Strategic Plan provides the tools needed to forge successful partnerships with NIH ICs, funding agencies, and the scientific community to support the goals of the NIH mission. This 5-year plan presents three thematic areas that were identified during an 18-month planning process. NIH grantees, NIH leadership and colleagues, NIH Council of Councils members, and the general public provided valuable input. The strategic themes define the overall vision, while the outlined strategic goals are ORIP's focus areas. The objective of ORIP's Strategic Plan is not only to build on its significant past investment and existing activities, but also to add new ideas and perspectives to emerging research. Many of the outlined areas build on current programs that have benefited from ORIP's past support. Other areas involve judicious expansion of existing programs and new directions identified as targets for future growth.

To appreciate the new directions in ORIP's Strategic Plan, it is necessary to understand the existing investment in ORIP-supported programs. The section that follows provides a brief overview of ORIP's funded activities and its mission statement. For more in-depth information on ORIP activities, please refer to page 25.



#### **ORIP Thematic Areas**

The ORIP Strategic Plan research infrastructure highpriority thematic areas are:

- I. Developing models of human diseases.
- II. Accelerating research discoveries by providing access to state-of-the-art instrumentation.
- III. Training and diversifying the biomedical workforce.

ORIP supports an intellectual infrastructure for biomedical research through the creation of models of human disease using animals and cultured cells and management of the infrastructure required to maintain, distribute, and utilize these models. Examples of supported animal models include rodents, such as mice and rats; nonhuman primates of different sizes and origins; other mammalian species, such as pigs; aquatic models, such as fish, frogs, and salamanders; and invertebrates, such as fruit flies, nematodes, and protozoa. ORIP maintains these resources at specific centers that make these critical disease models readily available to researchers.

ORIP's shared instrumentation program provides researchers, funded by any NIH IC, state-of-the-art instruments essential for biomedical research. Without access to appropriate modern tools and equipment, it is impossible to conduct pioneering research, to bring forward basic science discoveries, or to design the translational implementation of these studies. This program provides funding for expensive shared instruments that otherwise would not be available to many researchers.

ORIP also supports human infrastructure for biomedical research by investing in the next generation of creative minds. ORIP provides support for veterinary scientists to join the biomedical research enterprise and supports science education for pre-kindergarten through grade 12 (P–12) students, with an emphasis on reaching students from underserved communities.

ORIP will gauge progress towards these thematic areas in reports describing its strategic investments and accomplishments. ORIP will continue to enlist the help of NIH colleagues and the research community as it works to achieve the vision outlined in this plan.

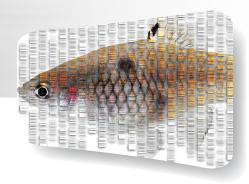


#### **ORIP Mission Statement**

ORIP advances the NIH mission by supporting research infrastructure and research-related resource programs and by coordinating NIH's science education efforts. The NIH's goals are explained in detail in the NIH-Wide Strategic Plan. Specifically:

- ORIP's Strategic Plan supports the NIH-Wide Strategic Plan by funding the "scientific human and physical resources that will help to ensure the Nation's capability to prevent disease."
- ORIP awards grants to support research resources, such as animal models of human disease and state-ofthe-art biomedical instrumentation.
- ORIP plans, organizes, and conducts workshops, both independently and in collaboration with NIH ICs, to identify and pursue scientific opportunities.
- ORIP supports research-training opportunities
  for veterinary scientists to capitalize on their
  distinct perspective and expertise based in a deep
  understanding of comparative medicine and insight into
  animal models of human diseases.
- ORIP supports strategies that bring high-quality science, technology, engineering, and mathematics (STEM) educational opportunities to P–12 students, with an emphasis on underserved communities and the goal of diversifying the next generation of biomedical scientists.



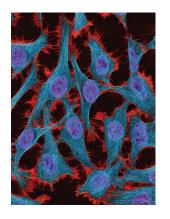


#### **ORIP Theme I**

# **Developing Models of Human Diseases**

Scientists use nonhuman models of human diseases when they are trying to learn about basic disease mechanisms and therapies from experiments that could not be conducted in humans. Evolving technologies and tools for genetic modification will allow currently used animal models to be complemented by new models that will be more focused and predictive of the actual human disease. Even with this new precision, no single animal model will ever recapitulate human disease with complete fidelity. This fact is becoming ever more apparent as we learn about the complexity of human physiology and pathology using the same molecular tools that have allowed us to build better animal models. These new tools and technologies enable scientists to probe deeper into the molecular origins of the clinical symptoms (phenotypes) observable in human diseases. To study, understand, and eventually cure complex diseases in humans will require the use of multiple extensively phenotyped models that mimic the different pathogenic events leading to the disease. Using complementary models may provide the highest predictive capacities, but it will also require new and more in-depth knowledge of disease processes in both models and humans. Additionally, functional alignment of models will require new efforts to integrate data and map phenotypes across model species and into humans. Coupled with a careful choice from among different model systems, this approach should lead to an increased level of predictive power, a decrease in new drug attrition rates, and an increase in the efficacy of new treatments.





"...ensure that animal models are all readily available for distribution in research studies..."

#### Expand and ensure access to animal models.

ORIP's disease models program supports the development of new and improved animal models that complement those traditionally used to study human diseases. In addition to the generation of new model systems, it is equally important to ensure that animal models are all readily available for distribution in research studies today, as well as preserved for use by future scientists.

The number and complexity of disease models—naturally occurring, induced, and genetically engineered—are increasing much faster than our ability to effectively access and use the new information to speed life-saving therapies to the clinic. A critical need exists for the creation of innovative knowledge generation and retrieval systems to give translational researchers the ability to analyze the full spectrum of clinically relevant model systems (animal models, cell and organ cultures, tissue and organ chips, and computational methods) and select the most appropriate models for their research. To facilitate the development and ensure the availability of critical animal models, ORIP will:

- Continually evaluate the utility of and provide sustained support for valued traditional and nontraditional animal models.
- Evaluate and promote the application of new technologies to improve generation, preservation, and distribution of rodent, nonhuman primate (NHP), aquatic, and other models.
- Partner with NIH ICs to create information retrieval platforms, knowledge systems, and data repositories to assist scientists in the selection and use of models of human disease.



# Continue to develop and enhance human disease models and research-related resource programs to advance medical research.

Today's biomedical researchers have a wide variety of model systems from which to choose when studying human biology and disease states. Therapeutic approaches can be tested for effectiveness in animal models prior to their introduction into human clinical trials. The advent of new technologies that permit the construction of a mouse with a human immune system has resulted in opportunities to further develop model systems that are more precise and predictive of human pathologies. To ensure that disease models co-evolve with technologies, knowledge of human biology, and the needs of the research community, ORIP will:

- **Identify opportunities and challenges** for animal models to become precise and predictive models of human pathologies.
- Promote phenotyping and annotation of human disease model systems.



"Therapeutic approaches can be tested for effectiveness in animal models prior to their introduction into human clinical trials."





"Make strategic investments... to enhance the reproducibility of specific disease models..."

#### Explore ways to improve the reproducibility of research using disease models.

Reproducible research is essential for scientific progress. Preclinical investigations are particularly susceptible to reproducibility issues, as many factors are experimentally manipulated to understand the biological system under study. Examples include experimental design factors, such as environmental (diet, temperature) and biological qualities (genetic background, sex), that can affect the reproducibility of animal- and cell-based disease models. To enhance the reproducibility of biomedical research, ORIP will:

- **Develop research resources** to train investigators on protocols that influence reproducibility and validation of models of human diseases.
- Explore the use of online learning and the Small Business Innovation Research/ Small Business Technology Transfer (SBIR/STTR) programs to promote training in reproducibility.
- Foster relationships between intramural and extramural groups with expertise in improving the rigor of research using animal models.
- Make strategic investments into infrastructure tools to enhance the reproducibility of specific disease models.



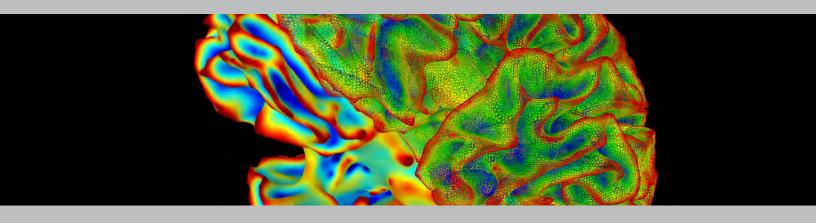
# Support the modernization and improvements of animal research facilities to enhance animal maintenance and care.

Biomedical researchers require high-quality, disease-free animals and specialized animal research facilities. ORIP's Animal Facility Improvement Program (AFIP) provides funds to institutions to modernize animal research facilities through alterations and renovations and to purchase equipment for animal resource centers. To ensure modernization and improvement of animal research facilities, ORIP will:

- Continue to support the AFIP in collaboration with NIH ICs and other Federal agencies.
- Provide support for specialized animal facilities, such as a gnotobiotic facility or surgical suite, to meet the emerging research needs of NIH-supported investigators.
- Solicit applications for SBIR/STTR to bring new animal care technologies to biomedical research.



"...specialized animal research facilities...to meet the emerging needs of NIH-supported investigators."

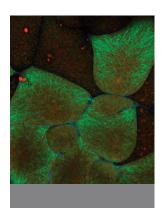




# Accelerating Research Discoveries by Providing Access to State-of-the-Art Instrumentation

The two categories of ORIP's S10 program, the Shared Instrumentation Grant (SIG) and the High-End Instrumentation (HEI) programs, are unique at the NIH, as they support purchases of commercially available instruments to enhance the research of NIH-funded investigators. Without access to appropriate modern tools and equipment, it is impossible to conduct pioneering research, to bring forward basic science discoveries, or to design the translational implementation of these studies. The S10 program provides funding for expensive shared instruments which otherwise would not be available to many researchers. The program funds a broad spectrum of technologies that are used in all areas of biomedical research, from fundamental scientific investigations in biophysics and biochemistry to implementation of novel medical procedures and treatments. Every instrument awarded by the S10 program is used on a shared basis, so that thousands of investigators in hundreds of research institutions nationwide have benefited over the years. ORIP will maintain the vitality of the S10 program and the essential role it plays in supporting the NIH research community and advancing the forefront of biomedical research.





"...necessary
that the
instrumentation
program remains
responsive to...
evolving needs of
the community..."

## Optimize the instrumentation program through forward-looking program management.

Over the years, the demand for different technologies has changed, both as new tools have become available and as the particular focus of scientific efforts has shifted. It is necessary that the instrumentation program remains responsive to these evolving needs of the community. To ensure that ORIP's S10 program continues its broad reach and important benefits, ORIP will:

- Implement improved metrics to evaluate the S10 program.
- Modify the S10 program requirements and administration to augment its costeffectiveness and utility for the biomedical research community.
- **Update program guidelines** to serve the needs of all of the S10 program users (both SIG and HEI).

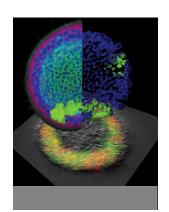


Strategy 2

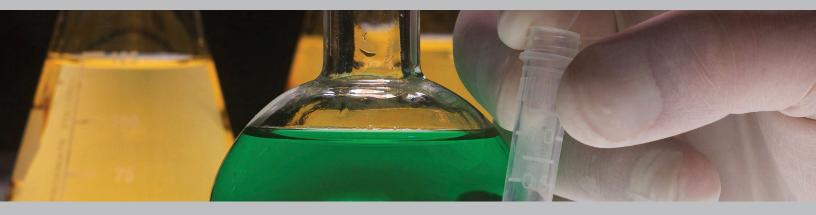
# Continue to accelerate research discoveries by providing access to state-of-the-art instrumentation.

ORIP's S10 program has served the extramural NIH research community well for more than 25 years. Instruments funded by the S10 program enable work conducted by all NIH ICs at hundreds of research institutions nationwide. The importance of the S10 program for advancing basic science discoveries and their translational implementation is well recognized by the biomedical research community. To continue this record of accelerating research discoveries, ORIP will:

- Provide support for technologies needed by the biomedical research community.
- Partner with NIH ICs to leverage resources and extend the reach of the S10 program.



"Instruments funded by the... S10 program enable work supported by all NIH ICs at hundreds of institutions..."





## **Training and Diversifying the Biomedical Workforce**

The most important ingredient in biomedical science is the inquisitive mind of the well-trained scientist. Maintaining this "human infrastructure" requires careful investments, in both time and money, to ensure that the next generation of biomedical researchers reaches its full potential. To continue the advancement of human health, the NIH must attract some of the best minds from the full diversity of each generation into medical research. ORIP will support activities designed to complement other NIH programs, to improve scientific training at all levels, and to advance a diverse research workforce.





"Veterinary scientists... offer a distinct perspective and expertise to translational biomedical research..."

## Train veterinary scientists as translational researchers.

Veterinary scientists, biomedical scientists with a veterinary degree, can offer a distinct perspective and expertise to translational biomedical research through their comparative understanding of disease models. Veterinary scientists can make unique recommendations regarding the development, refinement, and reproducibility of disease models and optimize laboratory animal maintenance and care. However, because hurdles continue to impede the entry of veterinarians into basic and applied research careers, ORIP will:

- **Identify and address challenges and opportunities** for veterinary scientists to acquire the skills needed to participate in biomedical research.
- Collaborate with NIH ICs to develop programs that capitalize on the specialized
  expertise of veterinary scientists (e.g., pathology, emerging infectious diseases, and
  epidemiology).
- Promote biomedical research collaborations between physicians and veterinary scientists.
- **Train veterinary scientists** to lead activities that integrate biomedical findings across model species (e.g., multidisciplinary training programs).
- Support dual-degree training programs for veterinary scientists.

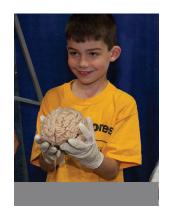


Strategy 2

## Support workforce diversity through P–12 STEM education.

The NIH is committed to attracting biomedical researchers from a diverse range of cultural and ethnic backgrounds. To recruit individuals from groups underrepresented in biomedical research, ORIP will:

- Use the Science Education Partnership Award (SEPA) program to provide information on career opportunities, educational resources, and training for targeted P–12 students and teachers.
- **Support the development of approaches** that introduce children to scientific thinking and problem solving early in their education.
- Support the development of mobile apps and Serious STEM Game resources for P–12 students to foster scientific thinking and problem solving.



"SEPA...provides information on career opportunities, educational resources, and training...for students and teachers..."





"...encourage SEPA grant recipients to conduct increasingly rigorous evaluations of their programs."

## Promote rigorous educational evaluations of SEPA grants.

Federally sponsored STEM education programs, at all levels, are increasingly being asked to demonstrate evidence of effectiveness. ORIP will require SEPA grant recipients to conduct increasingly rigorous evaluations of their programs. A description of each project's evaluation plans will be required in the application and will be considered by the study section when determining an impact score. To encourage grantees to go beyond "traditional" evaluation measures, ORIP will require SEPA grant recipients to:

- Conduct rigorous assessments that can demonstrate the effectiveness of their projects.
- Publish the outcomes of their evaluations.



## Help teachers, mentors, and parents improve student interest in science.

Teachers, mentors, and parents all make important contributions to student interest in science. To facilitate contributions from a diverse group of role models and mentors by providing specific opportunities and support for teachers, college students, and others, ORIP will:

- Support the placement of students and teachers into research laboratory settings that facilitate better science teaching and learning when they return to the classroom.
- **Support the development of programs** that engage graduate students in teaching part time as a means of exploring alternate careers as P–12 educators.
- Encourage the participation of mentors who are similar in age, gender, and race to the participating students.
- **Develop materials and resources** for the SEPA website (http://www.nihsepa.org) that help teachers and parents enhance STEM education.



"encourage the participation of mentors who are similar in age, gender, and race to the participating students."

## ORIP's Strategic Plan: Supporting the NIH-Wide Strategic Plan

The NIH's mission is to seek fundamental knowledge about the nature and behavior of living systems and to apply that knowledge to enhance health, lengthen life, and reduce illness and disability. This mission, outlined in the NIH-Wide Strategic Plan, is accomplished through the goals described in the strategic plans of each of the 27 NIH Institutes and Centers (ICs). Similarly, ORIP's Strategic Plan supports the NIH-Wide Strategic Plan by funding the "scientific human and physical resources that will help to ensure the Nation's capability to prevent

disease." This research infrastructure, and associated research-related resource programs, are used by the NIH ICs to expand the knowledge base and expertise needed in medical research. Specifically, ORIP develops and enhances access to the animal models of human diseases that are essential for translational medicine and helps to train a diverse biomedical workforce; together these efforts improve the rigor and reproducibility of the biomedical research that is *Turning Discovery Into Health*.

#### NIH-Wide Strategic Plan Framework

#### **Advance Opportunities in Biomedical Research**

#### Fundamental Science

- Foundation for progress
- Consequences often unpredictable
- Technology leaps catalyze advances
- Data science increases impact/efficiency

## Health Promotion/Disease Prevention

- Importance of studying healthy individuals
- Advances in early diagnosis/detection
- Evidence-based reduction of health disparities

#### **Treatments/Cures**

- Opportunities based on molecular knowledge
- Breakdown of traditional disease boundaries
- Breakthroughs need partnerships, often come from unexpected directions
- Advances in clinical methods stimulate progress



#### Description of ORIP Activities

## Human Disease Model Resource and Research Centers

ORIP's comparative models program supports the development of new and improved animal models that complement those more traditionally used to study human diseases. The precision and predictability of these models can be rapidly enhanced through new and developing biological engineering approaches. The number and complexity of disease models—naturally occurring, induced, and genetically engineered—are increasing much faster than our ability to effectively access and use the new information to speed life-saving therapies to the clinic. A critical need exists for innovative information resources that provide translational researchers with the tools required to identify the full spectrum of clinically relevant model systems (animal, cell culture, and molecular) and to select the most appropriate model systems for their research.

ORIP invests in the development of human disease models that make use of rodent species, such as mice and rats; nonhuman primates and other mammalian species such as pigs; aquatic species, such as fish, frogs, and salamanders; and invertebrate species, such as fruit flies, worms, and protozoa. ORIP also supports resource-related research projects that develop animal-based reagents such as antibodies and critical genetic resources, such as maps, microarrays, and sequences. Additionally, ORIP supports a variety of centers that provide animal models of human biology and disease to biomedical researchers around the

world. Depositing animals with rare and useful mutations at repositories can protect them from loss due to disease or accident and can lower the costs of maintaining them. These centers have the expertise and technical resources available to ensure that the genetic backgrounds of mutant animals do not change over time, thereby improving the reproducibility of preclinical studies.

Each year, several thousand researchers use ORIP-supported resource centers for biomedical research. In addition to NIH-funded researchers, these centers also support investigators funded by other governmental sources, foundations, and the private sector. Examples of some of these valuable resource and research centers are provided on the pages that follow.

#### Mutant Mouse Resource & Research Centers (MMRRC):

ORIP funding supports both the development of new genetically engineered mouse models and the facilities that maintain and distribute these research mice (and other biological materials) for understanding mammalian biology and human genetic disorders. The MMRRC (https://www.mmrrc.org) consist of four geographically distinct centers that collectively operate as a one-stop shop to serve the biomedical research community. This national network of mouse breeding and distribution facilities also serves as an information-coordinating group for genetically engineered mouse strains and mouse embryonic stem cell lines valuable for all types of biomedical research. The MMRRC accept, cryopreserve, maintain, and distribute transgenics, knockouts, and all other kinds of induced mutant mouse lines at no cost to the

researchers who developed them and for a nominal fee to other academic researchers. The MMRRC distribute more than 200,000 live mice to scientists yearly. Their collections contain approximately 4,600 specific mutations in mice and tens of thousands more saved as frozen embryonic stem cells.

The MMRRC index and maintain data characterizing strains; this enables researchers to seek out mouse strains, cell lines, or cryopreserved materials and to make an informed purchase. MMRRC scientists also provide valuable technical expertise to researchers around the world.

National Primate Research Centers (NPRCs): NHPs, such as rhesus and African green monkeys, are critical for biomedical research because of their close anatomic, physiologic, and genetic similarities to humans. NHPs facilitate discoveries that may directly apply to studies of human health and help scientists test treatments for such conditions and infectious diseases as AIDS, malaria, drug addiction, obesity, and Parkinson's disease. ORIP's NHP programs fund animals, technologies, specialized facilities, and expert services that support and enhance research. Each year, the seven NPRCs (http://nprcresearch.org) facilitate more than 1,000 individual research projects involving thousands of investigators who help bring safe and effective therapies to patients.

#### **National Swine Resource and Research Center**

(NSRRC): Swine have many anatomic and physiologic characteristics that make them unique models for research on human diseases. The NSRRC (http://nsrrc.missouri.edu) serves as a repository and distribution center for swine models used in transplantation, reproductive, cardiovascular, and other types of biomedical research. The NSRRC also creates new genetically modified pig lines requested by the research community and performs research aimed at improving swine models. Models generated by scientists working at various institutions are imported into the resource center and rederived to a pathogen-free status, and gametes and embryos are cryopreserved.

Zebrafish International Research Center (ZIRC): The ZIRC (http://www.zebrafish.org) makes available more than 19,000 zebrafish lines for use by geneticists and other biomedical researchers. The transparency of young zebrafish allows researchers to directly observe developing organs—a characteristic that has proven extremely useful in studying vertebrate development. Zebrafish, useful for

understanding the function of many of the genes identified by the Human Genome Project and in the study of regenerative medicine, can produce hundreds of progeny and are easy to maintain.

Other Aquatic Model Resources: ORIP also supports a range of aquatic model species, such as marine slugs (*Aplysia*), frogs (*Xenopus*), and salamanders (*Ambystoma*) for use in biomedical research. ORIP funds research and resource centers to develop and maintain critical genetic stocks, biological materials, and online information for researchers. The aquatic animals are used as models for studying human development, behavior, and disease.

Bloomington Drosophila Stock Center (BDSC): Fruit flies (Drosophila spp.) are inexpensive to maintain in the laboratory, have short lifespans, reproduce prodigiously, and have well-understood genetic characteristics. Drosophila have provided key understandings of the genetic basis of mutations. Numerous techniques for studying the inheritance and production of mutations have been developed. ORIP support for the BDSC (http://flystocks.bio.indiana.edu) enables the collection, maintenance, and distribution of genetically defined strains of Drosophila melanogaster that provide experimental tools useful to a broad range of investigations. The BDSC provides strains with mutant alleles of identified genes, including a large number with transposable elements. As with other ORIP resources, BDSC scientists can share available strains, their expertise on Drosophila genetics, and the use of Center resources, such as databases.

#### Current Areas of Emphasis for Developing and Improving Human Disease Models

ORIP seeks to provide better models of human disease conditions of interest to multiple NIH ICs. Today's biomedical researchers have a wide variety of model systems from which to choose when studying human biology and disease states. Therapeutic approaches can be tested for safety and effectiveness in animal models prior to human clinical trials. New technologies that permit the construction of a mouse with a human immune system and other such constructs have resulted in model systems that are more precise and predictive of human pathologies. Examples of two current areas of emphasis are provided on the next page.

Stem Cells/Regenerative Medicine: To evaluate potential risks and benefits of stem cell-based therapy and understand the full spectrum of the stem cell actions in animal-based preclinical studies, ORIP initiated the program for Improvement of Animal Models for Stem Cell-Based Regenerative Medicine. This initiative focuses on comparisons of animal and human stem cells to provide information for the selection of the most predictive and informative model systems; the development of new technologies for stem cell characterization and transplantation; and the improvement of animal disease models for stem cell-based therapies. For example, ORIP supports the creation of transgenic pigs to enable the study of adult stem cells and their progenitors. These pigs also will be useful for studies of cancer, regenerative responses, and intestinal, hepatic, renal, and skin diseases.

Precision Modeling: ORIP has funded Pilot Centers for Precision Disease Modeling. Each Center consists of an interdisciplinary research team of scientists and physicians organized to address specific medical problems by creating new animal models to more precisely mimic patient-specific disease processes and to develop innovative treatment options. Current technology permits specific genetic modifications in model animal species, as well as the ability to replace specific cells and tissues, resulting in phenotypes that are closely analogous to human patients. These new animal models will accelerate the generation of precision diagnostic and therapeutic approaches for such diseases as cancer, Parkinson's disease, and diabetes.

## Animal Facility Improvement Program

Biomedical researchers require high-quality, disease-free animals and specialized animal research facilities. ORIP's Animal Facility Improvement Program (AFIP) provides funds to institutions to modernize animal research facilities through alterations and renovations. In addition, AFIP also supports purchases of equipment for animal resources, diagnostic laboratories, and other related infrastructure. Although AFIP does not offer direct support for research activities, it plays an essential role by funding awards to enhance the physical conditions of conventional and specialized animal research facilities. Safe and well-controlled environments and up-to-date standards of care are necessary for the healthy, well-characterized animals needed to ensure the accuracy of experimental

protocols. AFIP also assists in complying with the United States Department of Agriculture Animal Welfare Act and the Department of Health and Human Services policies related to the care and use of laboratory animals.

Commercially available biomedical methods and technologies are needed to improve animal models of human disease, as well as the care, use, and management of laboratory animals. ORIP's SBIR/STTR program stimulates the development and commercialization of novel tools and equipment for the care and monitoring of research animals. Once commercially available, such tools become an option for researchers seeking to upgrade their facilities. Novel technologies that promise more accurate and uniform maintenance of environmental conditions and more precise assessment of the well-being of research animals will be of great use to biomedical scientists. Better tools in laboratories will help control experimental conditions and contribute to more exact, and more reproducible, scientific outcomes.

#### Provide State-of-the-Art Instrumentation to Accelerate Research Discoveries

ORIP's S10 program is unique at the NIH, providing support for the purchase of commercially available state-of-the-art instruments. Such instruments are essential for the conduct and advancement of scientific investigations, but are too expensive for a single researcher to own and operate. Without access to appropriate modern tools and equipment, it is impossible to conduct cutting-edge research to bring forward basic, translational, and clinical science. This program provides next-generation technologies to NIH-supported investigators.

Grant applications come from groups of NIH-funded investigators who must demonstrate that the requested instrument would advance their research and be used on a shared basis. ORIP does not limit the supported technologies. 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, and biomedical imagers. The program responds to the community needs by funding proportionally to the number of requests for a specific technology. To demonstrate the need for an instrument,

applicants are required to list projects that will be enhanced by the requested instrument. Every application is supported by research projects from 12 to 15 NIH-funded investigators. The research of thousands of investigators—funded by all NIH ICs, from hundreds of institutions coast to coast—has benefited from this program over the years.

The demand for new instruments has remained strong, both as new tools become available and as the particular focus of scientific efforts changes over time. ORIP's S10 program is cost effective, has high impact, and advances the NIH mission.

## Training and Career Development of Veterinary Scientists

ORIP supports training and career development programs specifically for veterinary students and veterinarians. The objective of these programs is to attract highly qualified veterinary students and veterinarians to biomedical and research careers.

Predoctoral training programs support veterinary students for a 1-year immersion in hypothesis-based research in laboratory animal medicine, comparative medicine, or pathology. All research-training activities are conducted on a full-time basis during the student's year away from clinical instruction and progress toward their veterinary degree. Another predoctoral program is the summer research program, which provides research-training experiences for veterinary students. ORIP also supports institutionally based postdoctoral training and educational programs that prepare graduate veterinarians for careers in biomedical and translational research.

The Special Emphasis Research Career Award, with 3 to 5 years of "protected time," supports veterinary scientists early in their careers in obtaining the research expertise necessary to become 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.

#### Science Education Partnership Award

Diversity in the scientific community stimulates the different perspectives and ideas that can foster innovation. A 2011–2012 report on the demographics of the NIH scientific workforce revealed a significant lack of diversity. The SEPA program was established in 1991 to encourage underrepresented minorities and low socioeconomic status students from urban and rural communities to consider careers in basic or clinical research. Included in the target audience are the American Indian, Alaskan Native, and Native Hawaiian/Pacific Islander communities.

SEPA funding supports the development of educational resources targeting STEM for P–12 students and teachers. SEPA's overarching goals are to enhance the training of a diverse workforce to meet the nation's biomedical, behavioral, and clinical research needs and to increase public health literacy and appreciation of NIH-funded research through health-related science exhibits in museums. SEPA also encourages partnerships with NIH's Institutional Development Awards, Research Centers in Minority Institutions, and Clinical and Translational Science Awards programs, as well as with other Federal agencies. All SEPA projects conduct rigorous evaluation to determine their effectiveness and must be aligned with the Next-Generation Science Standards in addition to the published science and math standards from the relevant states.

Some SEPA-funded projects target health disparities, like the SEPA Community-Based Participatory Research projects on prevention issues related to such diseases as obesity and diabetes. SEPA-funded informal science education projects include projects based at science centers, traveling exhibits, and public service announcements on radio and television, as well as documentaries and films. Other outreach activities, such as "Science Cafes" and "Community Health Fairs," are designed to educate students, teachers, and the larger community on the important correlations between lifestyle and health.



#### Pathway to the ORIP Strategic Plan

ORIP was established in December of 2011 and comprises several programs that were included in the former National Center for Research Resources' mission. This is the first ORIP strategic plan and is designed to allow its programs to fully integrate and stand independently, yet enhance trans-NIH opportunities, as a unique research infrastructure effort that drives research discoveries across NIH.

This strategic plan was developed by ORIP staff after considering input from three major arenas: (1) focus groups of IC representatives to provide trans-NIH feedback, (2) public requests for information (RFI), and (3) conferences with the extramural scientific community.

A draft strategic plan was provided to 24 NIH colleagues representing 16 ICs and several organizational units from the NIH Office of the Director. This initial draft was intended to stimulate thinking and guide discussion within the internal focus groups. The draft emphasized future priorities—it was not focused on protecting existing models, resources, repositories, stock centers, or instruments. Three focus groups were assembled in November and December 2014 as venues to collect thoughts from NIH colleagues. Discussions revolved around what should be maintained in light of future priorities and where future emphasis should be placed. An external facilitator served to keep the discussions between IC participants and keep ORIP staff mainly as observers. Discussions were captured by a science writer and audio recording. This initial ORIP Strategic Plan draft also formed the starting point for a discussion held in January 2015 with the Extramural Program Management Committee (EPMC), a group of senior leaders representing

all NIH IC extramural programs. After completion of the focus groups and broad discussion with EPMC members, ORIP staff incorporated major points into a new strategic plan draft.

In February 2015, two RFIs were issued to solicit opinions and ideas from the public at large. Respondents were asked to provide their perspective on any of several topics as they related to the mission and program areas of DCM/ORIP, DCI/ORIP, and OSE-SEPA/ORIP, with the aim of directing the major objectives of ORIP for the next 5 years. Several major categories were considered, each containing several topics: (1) Disease Models, Informational Resources, and Other Resources; (2) Training; (3) Physical Infrastructure; (4) Expanding Career Opportunities in Biomedical and Veterinary Research; and (5) Public Health Literacy and Animal Models in Research. Responses to the RFIs were collected and analyzed in March 2015. ORIP staff incorporated major points to update the strategic plan draft.

In the final phase, 60 extramural participants—mostly scientists who are familiar with or who use ORIP's programs—were provided the updated strategic plan draft for evaluation and comment. Participants returned feedback to ORIP. This feedback was used to design several discussion panels for the conference which was held July 8 and 9, 2015. Council of Councils liaisons Terry Magnuson, University of North Carolina at Chapel Hill, and Keith Reimann, University of Massachusetts, participated and helped provide meeting oversight. IC leadership and staff were also in attendance. The meeting outcome, summarized in a comprehensive report, provided the information to complete the final strategic plan.



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