



NCRR: A Catalyst
for Discovery

NCRR Fact Sheet

Comparative Medicine research has made critical contributions to our understanding of human health and disease. Most of the major medical advances of this century—including effective vaccines, improved cancer treatments, and anti-HIV therapies—depended on the insights gleaned from basic and applied studies of animal and nonanimal models. The Division of Comparative Medicine of the National Center for Research Resources (NCRR) supports the biomedical research community through grants that fund research resources and research projects to create, develop, characterize, preserve, and study a broad array of high-quality animal and animal-related models. This funding also supports research that safeguards the health and welfare of laboratory animals and provides career-development opportunities for graduate veterinarians and postdoctoral-level training for research students who use laboratory animals.

The extramural comparative medicine program at the National Institutes of Health (NIH) began in the early 1960s with the establishment of seven National Primate Research Centers located primarily at academic institutions throughout the country. Since then, comparative medicine research has evolved to include many other vertebrates as well as invertebrates; whereas the use of the nonhuman primate for biomedical research has become limited by practical and social concerns. Now, studies of complex biological processes and human disease are most effectively advanced by applying a combination of cellular, animal, mathematical, computer, and physical models.

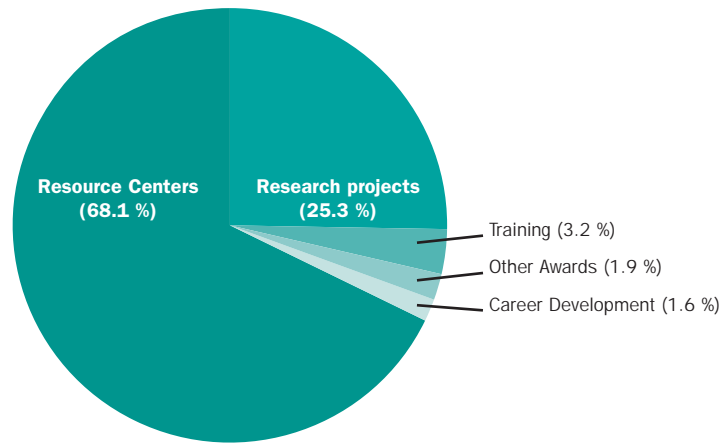
Nonmammalian models—such as bacteria, yeast, worms, fruit flies, and fish—are making important and cost-effective contributions to biomedical science. With comparative gene mapping between humans and these organisms,

researchers can identify potential functions of specific human genes to better understand the underlying basis of genetic disorders. These models are invaluable to studies of gene function, protein interactions, and pathological processes related to humans. The mouse model and other genetically altered animals with defined mutant genes also provide a wealth of information on protein functions and enable preclinical testing of gene therapies.

New comparative medicine tools and techniques have greatly improved the quality and efficiency of creating and preserving animals needed for biomedical studies. For example, pluripotent stem cell technology can be used to create genetically homogeneous populations of laboratory animals. Although the isolation and study of these cells is a relatively new and fast-moving frontier, stem cell research is expected to facilitate advancements in areas such as gene

NCRR is a catalyst for discovery for NIH-supported investigations throughout the nation. NCRR creates, develops, and provides a comprehensive range of human, animal, technological, and other resources to enable biomedical research advances.

NCRR Comparative Medicine Awards – FY 1998



Comparative Medicine
FY 1998 budget:
\$95,716 million

Comparative Medicine
FY 1999 budget:
\$112,238 million

therapy, tissue repair, organ regeneration, and vaccine formulation.

Improved cryopreservation, another powerful and efficient tool in comparative medicine, preserves sophisticated research models and reduces costs for breeding, housing, and maintaining laboratory animals.

Through interactions with its NIH partners and the scientific community, NCRR’s Division of Comparative Medicine determines the scientific priorities that best meet the broad needs of the multidisciplinary biomedical research community. These priorities are achieved by utilizing a variety of grant award mechanisms to support specific scientific opportunities.

Research Resources

• *Animal Models; Animal and Biological Materials*—Well-characterized animal models, model systems, and biological materials are key to many important biomedical discoveries that protect human health. To ensure that such resources are available and accessible to the biomedical research community, NCRR supports institutions—engaged in on-going, peer-reviewed, and health-related research—to establish special laboratory animal colonies, genetic stocks, cell lines (tissue and organs), microorganisms, culture repositories, and more. Continuous research activities of core scientists at these resources generate new knowledge. This enhances the resources’ overall value to the biomedical research community. NCRR supports information resources as well. These include registries, resource-related refer-

ence centers, and newsletters that broadly collect and distribute news and other information to improve the quality, use, care, and breeding of laboratory animals.

Other resources provide a variety of valuable genetic tools to the research community. These include a number of invertebrates such as defined strains of the fruit fly *Drosophila melanogaster* and the nematode *Caenorhabditis elegans*. Moreover, resources for consistent and standardized biological models, such as cephalopods and *Aplysia*, offer researchers alternative invertebrates that are suitable for a wide range of molecular investigations, especially in neurophysiology.

• *National Primate Research Centers (NPRCs)*—Nonhuman primates’ close molecular, immunological, reproductive, and neurological relationships to humans make them essential surrogates for humans in biomedical studies that require an integrated understanding of a whole individual. For more than three decades, a national network of NPRCs has provided nonhuman primates as models of human health and disease for basic and clinical biomedical studies. These highly specialized facilities, supported by NCRR’s NPRC Program, are closely affiliated with U.S. academic institutions. The centers are strategically located across the country to offer convenient access for large numbers of biomedical investigators. In 1998, the NIH categorical institutes awarded approximately \$115 million in research project grants to scientists who collaborated with NPRC researchers to use NPRC resources. In this way, the NPRCs enhance the effectiveness of federally appropriated biomedical research funding.

Collectively, the NPRCs provide a special environment for more than 18,000 nonhuman primates, mostly macaques but representing more than 20 different monkey species. These animals—of known pedigree and health status—have broad applications to biology, medicine, behavior, and health.

Each NPRC is staffed by a core of scientific experts in nonhuman primate research and by technical-support professionals. Led by the center director, each NPRC’s core investigators

Summary of NCRR Comparative Medicine and Research Grant Opportunities

RESEARCH RESOURCES	RESEARCH PROJECTS	CAREER DEVELOPMENT AND TRAINING	OTHER GRANT OPPORTUNITIES
<ul style="list-style-type: none"> • Animal (mammalian and non-mammalian) Models; Animal and Biological Materials • National Primate Research Centers • Other Primate Resources 	<ul style="list-style-type: none"> • Resource-Related Projects • Investigator-initiated Research Projects • Exploratory/Developmental Projects 	<ul style="list-style-type: none"> • Special Emphasis Research Career Awards • Midcareer Investigator Awards in Mouse Pathobiology Research • National Research Service Awards and Training 	<ul style="list-style-type: none"> • Small Business Technology Transfer – Phases 1 and 2 • Small Business Innovation Research – Phases 1 and 2

conduct biomedical research—supported by grants from other institutions, including NIH—that utilizes, defines, and develops the nonhuman primate as an animal model for studying human diseases.

The multidisciplinary environment at each NPRC stimulates innovative collaborations on studies of major human diseases. Each year, approximately 1,400 investigators, supported by their individual grant funding, collaborate with NPRC core scientists and use NPRC resources. The NPRCs also provide thousands of nonhuman primate blood and tissue specimens to investigators at research institutions worldwide. This is a valuable service, since few researchers could afford to use scarce and expensive nonhuman primates solely to obtain a specimen needed for a research project.

A Visiting Scientist Program administered by the NPRCs provides participants research opportunities coupled with advanced training in nonhuman primate biology necessary to conduct research at an NPRC. In 1998, more than 350 scientists participated in this program. Through another initiative, the centers annually train several hundred graduate students and postdoctoral scientists associated with the NPRCs’ host institutions.

How To Access an NPRC: (1) Submit a research proposal to an NPRC director, who will determine project feasibility and resource availability. (2) Once feasibility and availability are established, the NPRC will provide cost information to the researcher for inclusion in a formal research proposal. (3) The scientific merit of the proposal is evaluated through the NIH peer-

review process or through a similar process elsewhere. (Small pilot projects funded by other sources may be considered and evaluated by a research advisory committee of an NPRC.)

(4) In addition to the scientific evaluation, animal care and use protocols and possible biosafety concerns must be approved. (5) Once funding for the proposed project is approved, both the investigator and the NPRC director are notified; at this time, NPRC resources required for the proposed project are reserved.

Note: Contact NPRC program directors to: (1) inquire about the research emphasis and objectives of a center; (2) request biological materials such as blood samples, organ tissues, and biological fluids; and (3) obtain information about the Visiting Scientists Program. NPRC contact information is available electronically through the *Comparative Medicine Resources Directory*: <http://www.ncrr.nih.gov/ncrrprog/cmpdir/cmdirectory.asp>

• *Other Primate Resources*—In addition to the NPRCs, NCRR’s Division of Comparative Medicine supports several research resource facilities that provide natural environments for specially bred nonhuman primate colonies. These resources, which include baboons and rhesus and squirrel monkeys, advance multidisciplinary research of human social and sexual behavior, geriatrics, reproductive biology, genetics, spontaneous diseases, vaccine development for childhood diseases, hypertension, AIDS, cancer, and more.

Under the recently established NIH Chimpanzee Management Program, a few chim-

panzee colonies are maintained by U.S. research institutions for research purposes. These facilities are required to meet stringent Federal requirements for laboratory animal care and use and provide a favorable environment for the chimpanzees. The future use of chimpanzees for research—including appropriate breeding-colony size, genetic factors, and long-term care—will be managed and coordinated by the Chimpanzee Management Office in NCRRC's Division of Comparative Medicine, with the advice of several extramural comparative medicine experts.

Research Projects

• *Resource-Related Projects*—An investigator-initiated, resource-related research project grant supports applied studies to characterize and develop new comparative medicine resources or to improve existing ones. Such a project would, for example, expand the current knowledge base for an existing model system to make it more useful and accessible to the biomedical research community. Or, it would create a new model of human biology and disease or a new model system, such as cell cultures or computerized/mathematical integrated systems. Creation of a new model supported by this funding mechanism must span the interests of at least two NIH categorical institutes. A resource-related research project also may seek to improve biotechnology in the comparative medicine field—transgenic and cryopreservation methods; animal genetics, nutrition, and reproductive physiology; laboratory animal health to eradicate or minimize diseases that compromise research and animal welfare; or methods to monitor and enhance animal welfare.

• *Investigator-Initiated Research Projects*—Grants awarded for comparative medicine research projects support basic research related to a particular animal species, stock, or strain as a model for studies of disease processes or other biological phenomena related to human health. These research projects establish, preserve, and improve the quality of laboratory animals and the utility of an animal model or model system. Animal models created and developed with sup-

port of this funding should have broad biomedical applications. As with resource-related research grants, proposed projects must span the research interests of at least two of the NIH categorical institutes.

Areas of interest in comparative medicine research include, but are not limited to:

- Improvements in laboratory animal welfare.
- Development and characterization of natural and induced mammalian and non-mammalian models of human biology and disease.
- Improvements in transgenic technology, cryopreservation methods, and reproductive biology.
- Studies of animal genetics and behavior, identification and characterization of non-traditional species for biomedical research, improvements in animal nutrition, and research in reproductive physiology.
- Detection and characterization of diseases that affect laboratory animals and could interfere with research or compromise animal welfare.
- Development of animals genetically resistant to disease.
- Development of vaccines for prevention of intercurrent diseases in laboratory animal colonies.

• *Exploratory/Developmental Projects*—Research projects supported by an exploratory/developmental research grant should challenge existing paradigms and encompass novel ideas at the edge of new frontiers or should improve our understanding of a biomedical research problem. NCRRC's Division of Comparative Medicine first utilized this funding mechanism in 1998 to stimulate new uses of animal models.

This funding mechanism offers investigators an opportunity to collect preliminary data to support future grant applications for basic, investigator-initiated research projects.

Applications for an exploratory/developmental grant are generally accepted in response to a public request by NCRRC's Division of Comparative Medicine

For additional information**contact:**

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NCCR Home Page:

<http://www.nccr.nih.gov>

Other available NCCR**publications:**

Comparative Medicine
Resources directory

NCCR Highlights magazine

NCCR Reporter magazine

National Center for Research
Resources brochure

that specifies this award mechanism. The Division of Comparative Medicine may also agree to accept an application following programmatic staff consultation with a potential applicant. Because this grant supports an innovative hypothesis, no supporting preliminary data—as evidence of project feasibility—are required. However, the proposed research plan must be sound and must undergo competitive peer review.

Career Development and Training

• *Special Emphasis Research Career Awards (SERCA)*—The SERCA in Pathology and Comparative Medicine provides five years of support to assist veterinarians motivated toward research careers to develop new skills and knowledge necessary to become independent biomedical investigators in multicategorical, animal-based research. Candidates for the SERCA must have post-graduate experience in animal medicine and plan to direct their careers to biomedical investigations that explore animal models. The SERCA offers in-depth research experiences in a variety of research areas—basic, applied, and clinical—related to a wide range of biological disciplines. The overall training effort should be focused on a central research question. The question, for example, may involve the elucidation of disease mechanisms of induced and spontaneous mutant animals—such as mice, rats, or zebrafish. Examples of current research needs in comparative medicine and of training opportunities provided by a SERCA include, but are not limited to, the following:

- Discovering and developing natural and induced animal models of human biology and disease.
- Using molecular and immunological techniques to pursue basic mechanisms of disease and identifying and characterizing alterations in embryonic and postnatal development resulting from genetic alterations in laboratory animals.
- Using and improving transgenic animal technology to address questions in biology and disease.
- Identifying and characterizing non-tradi-

tional species for biomedical research, improving animal nutrition, or studying reproductive physiology.

- Studying animal diseases that may interfere with biomedical research results.
- Improving laboratory animal welfare.

• *Midcareer Investigator Awards in Mouse Pathobiology Research*—This award was recently established by NCCR's Division of Comparative Medicine in response to great increases in the numbers of genetically altered mice being used by the biomedical research community and to the burgeoning opportunities for mouse pathobiology research in this environment. This award will relieve mouse pathobiologists from time-consuming service obligations to permit protected time for the conduct of mouse pathobiology research. This opportunity expands the potential of mouse pathobiologists to make significant contributions to their fields of research, thus capitalizing on the exciting discoveries being made using genetically altered mice for biomedical research.

NIH and NCCR are especially interested in increasing the number of scientists trained to conduct high-quality mouse pathology. Therefore, candidates supported by this award must develop a mentoring program that will meet their individual needs and capabilities and also train the next generation of mouse pathologists.

Most applicants for this award will hold a degree in veterinary medicine (D.V.M. or equivalent) from an institution recognized by the American Veterinary Medical Association. However, individuals who have other degrees, such as clinical (M.D.) or research (Ph.D.), may also apply if they have been certified or have demonstrated the necessary expertise to perform high-quality, funded research in mouse pathobiology. Applicants should have completed their specialty or research training within 15 years of applying for this award.

Award candidates must be working in a research environment at an institution that has a well-established research and career-development program and is committed to the candidate's becoming a productive, independent investigator. This award provides up to five years of support.

Comparative Medicine permits biomedical investigators to study human health and disease in a variety of animal models and nonbiological systems before moving to patient studies in clinical research.

• **National Research Service Awards (NRSAs) Individual Pre- and Postdoctoral Fellowships:** NIH-supported NRSAs provide postdoctoral and predoctoral fellowships to ensure that an adequate number of well-trained biomedical and behavioral scientists will be available in the future. NCRR's Comparative Medicine area supports up to three years of training for NRSA candidates—U.S. citizens and noncitizen nationals—who possess a degree in veterinary medicine (D.V.M. or V.M.D.), Ph.D. degree, or equivalents, from recognized academic institutions. This training award provides individuals with the knowledge and experience needed to conduct independent research. (For a listing of possible training research areas related to comparative medicine, see “Investigator-Initiated Research” above.) Applicants for these fellowships must arrange their appointments to academic institutions, pursue full-time research activities with the guidance of well-qualified senior experts, and include carefully selected graduate credit courses in their training programs.

Institutional Award: Veterinary Research Training: NCRR's Division of Comparative Medicine offers NRSAs to eligible institutions to support the training of veterinarians for research careers in biomedical areas related to animal-based research. Potential trainees must possess a degree in veterinary medicine (D.V.M. or V.M.D.) and also have at least one year of postdoctoral experience in a discipline related to comparative medicine. Combining a veterinarian's broad knowledge of whole-animal biology with specialized research training gives trainees a strong foundation for a research career in biomedicine and the experience to eventually compete for independent grant funding.

Institutional Awards: Short-Term Student and Health Professional Research Training: The Division of Comparative Medicine offers NRSAs to eligible biomedical research institutions to support two to three months of training for veterinary students in laboratory animal science, laboratory animal medicine, comparative medicine, and comparative pathology. Grantee institutions are expected to seek applications from students for this training by widely advertising

these opportunities. The training must be multidisciplinary in nature and designed to stimulate the student's interest in biomedical and behavioral research. The training experience should provide the student with a sense of belonging to the scientific community.

Other Grant Opportunities

NCRR's Division of Comparative Medicine participates in two federal programs that provide grant support to small businesses. *The Small Business Technology Transfer (STTR) Grant* award and the *Small Business Innovation Research (SBIR) Grant* award both support research designed to provide knowledge in biomedical methods and technologies and to develop their applications to uses in laboratory animal areas of interest. A major difference in the requirements of STTR and SBIR grants is that STTRs require that a small-business applicant organization enter into a collaborative partnership to conduct the research project with a research institution that has the potential to produce commercial products; SBIRs do not require outside collaborative activities. Moreover, the principal investigator for an STTR-supported project must have a formal appointment with or commitment to the applicant small business, whereas the principal investigator (applicant) for an SBIR grant must be employed primarily by the small business concern at the time of the award and throughout the project period. For an SBIR award, investigators or facilities at research institutions may be included under subcontractors or as consultants, but are not required.

The SBIR application receipt dates are April 15, August 15, and December 15 of each year. The STTR application receipt dates are April 1, August 1, and December 1 of each year. Program solicitations and other details are available at the NIH Web site: <http://www.nih.gov/grants/funding/sbir.htm>.