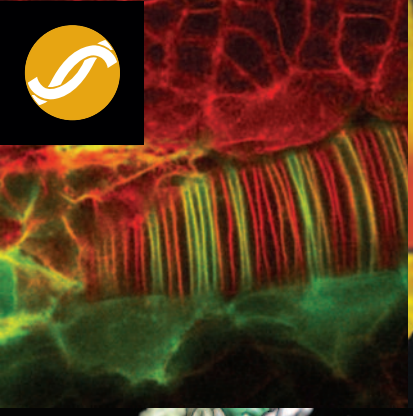
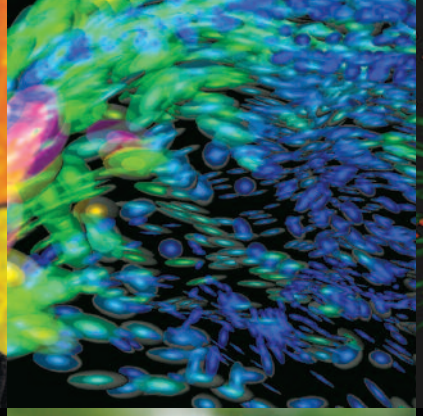
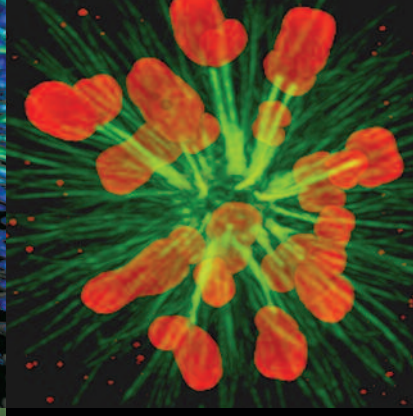
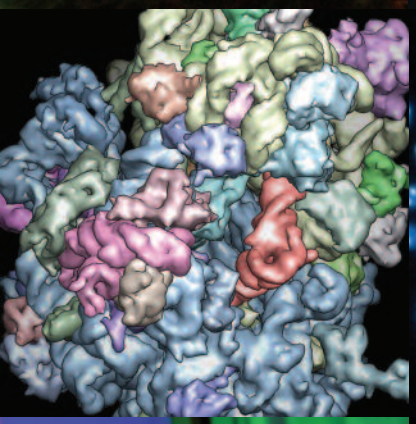
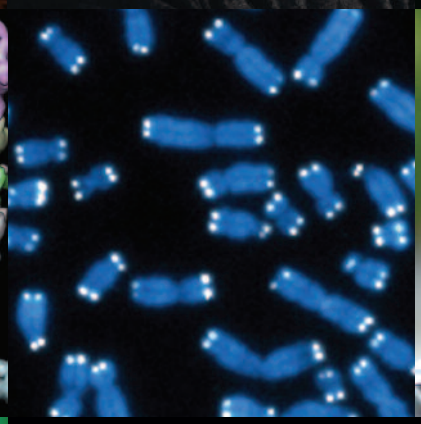
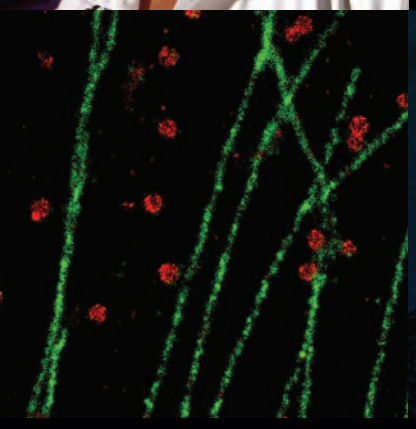


Investing in Discovery

National Institute of General Medical Sciences

Strategic Plan 2008–2012




U.S. DEPARTMENT OF
HEALTH AND HUMAN SERVICES
National Institutes of Health
National Institute of General Medical Sciences

COVER

Top row (left to right)
Neural tube formation in a developing zebrafish, an organism commonly used for genetic research. *Courtesy of Alexander Schier, Harvard University.*

Alejandro Sánchez Alvarado studies tissue regeneration in aquatic flatworms. *Photo at the University of Utah by William K. Geiger.*

Image created using computational biology to show differences between two human brains. *Courtesy of Arthur Toga, University of California, Los Angeles.*

Fluorescent dyes highlight chromosomes and microtubules during cell division. *Courtesy of Edward Salmon, University of North Carolina at Chapel Hill.*

Second row (left to right)
Structure of a ribosome, the site of protein production. *Image by Catherine Lawson, Rutgers University and the Protein Data Bank.*

White dots mark telomeres, which protect the tips of chromosomes. *Courtesy of Hesed Padilla-Nash and Thomas Ried, National Institutes of Health.*

NMR expert Michael Summers studies HIV structure and leads an initiative to maximize student diversity at the University of Maryland, Baltimore County. *Courtesy of Michael Summers.*

Third row
Structural biologist Mavis Agbandje-McKenna examines how influenza infects cells. *Photo at the University of Florida in Gainesville by David Blankenship.*

Fourth row (left to right)
Image taken using a new technique called multicolor STORM, which shows individual molecules within cells in unprecedented detail. *Courtesy of Xiaowei Zhuang, Harvard University.*

Gene Robinson studies the molecular basis of honeybee behavior, which is controlled by some of the same genes that regulate daily rhythms in humans. *Photo at the University of Illinois at Urbana-Champaign by L. Brian Stauffer.*

TABLE OF CONTENTS

Top row (left to right)
A DNA-repair enzyme encircling a strand of DNA. *Courtesy of Tom Ellenberger, Washington University in St. Louis School of Medicine.*

Lung damage like that shown here is a focus of teams of critical care specialists and genomic researchers. *Courtesy of Hamid Rabb, Johns Hopkins Medicine.*

A budding yeast cell frozen in time in an X-ray microscopy image. *Courtesy of Carolyn Larabell, University of California, San Francisco, and the Lawrence Berkeley National Laboratory.*

Crystal of the fungal lipase enzyme. *Courtesy of Alexander McPherson, University of California, Irvine.*

Second row (left to right)
Abnormal protein deposits look like balls of steel wool in a micrograph of brain tissue from a person with Alzheimer's disease. *Courtesy of Neil Kowall, Boston University School of Medicine.*

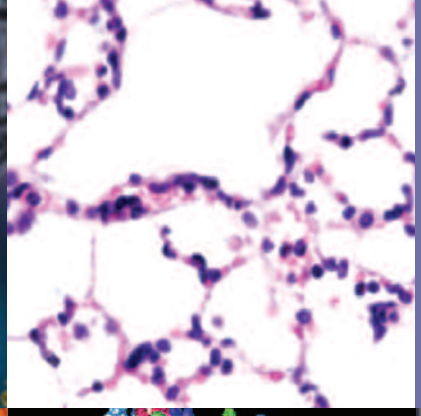
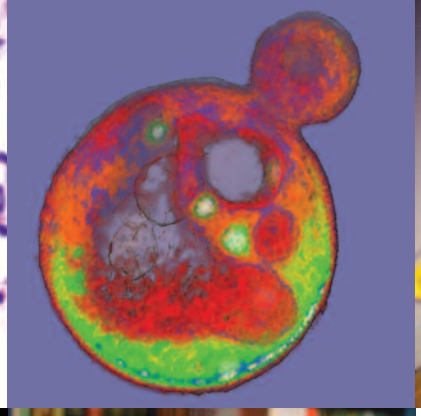
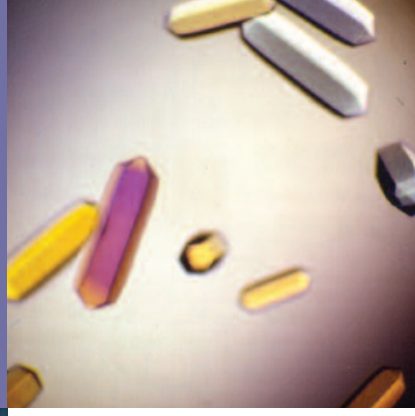
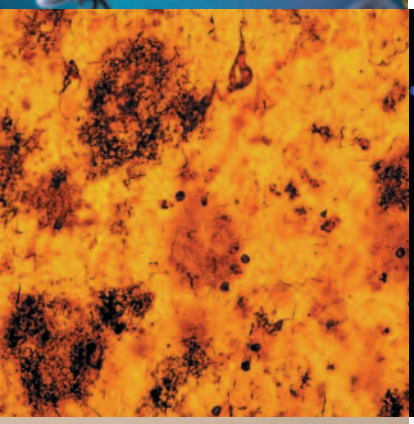
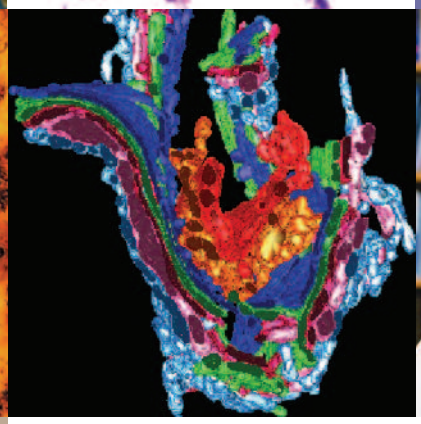
Three-dimensional view of a cell's Golgi apparatus. *Courtesy of Kathryn Howell, University of Colorado Health Sciences Center.*

Organic chemist Amir Hoveyda develops catalysts for chemical reactions that produce biologically active compounds. *Courtesy of the Office of Public Affairs, Boston College.*

Third row
Biophysicist Margaret Gardel studies how the cytoskeleton helps the cell move and change shape. *Photo at the University of Chicago by Lloyd DeGrane.*

Fourth row (left to right)
Scanning electron micrograph showing two types of bacteria. *Courtesy of Tina Carvalho, University of Hawaii at Manoa.*

Bioinformatician Atul Butte analyzes the genomic relationships between diseases and investigates new uses for existing medicines. *Courtesy of Atul Butte, Stanford University.*

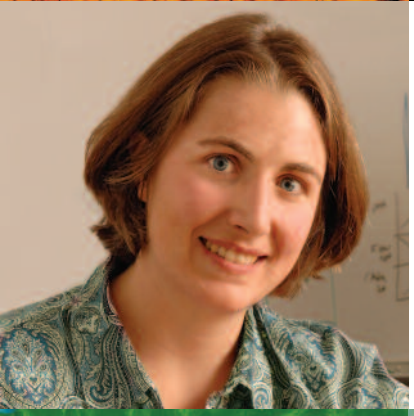


Table of Contents

Investing in Discovery

The investments of the National Institute of General Medical Sciences (NIGMS) in broad and diverse areas of basic research have built a strong foundation of knowledge for biomedicine. Because science is an activity driven by human insight, the Institute has always believed that providing career stability and workforce diversity are key strategies for maintaining a healthy research enterprise.

I, personally, have been fortunate to experience the benefits of these investments throughout my scientific career. As an undergraduate, graduate student, and postdoctoral fellow, my training and research were supported through research grants to my advisors. When I started my independent career, my research projects were funded through a then-new program directed to beginning faculty members.

As with most basic scientists, my research followed a winding path of discovery. Early in my career, I was fortunate to get to work on grant-supported projects to explore a diversity of scientific topics. These ranged from the development of new physical methods to analyses of the fundamental chemical basis of enzyme action, the study of metalloprotein structures, and biological approaches to understanding gene regulation. Much of this research was greatly enhanced by the molecular biology revolution, which itself had been driven substantially by earlier NIGMS-funded studies.

As a faculty member, I saw first-hand the tremendous impact of NIGMS-supported training grants at my academic institution, as well as the influence of these and other programs on the recruitment of a diverse group of students into research. Later in my career, I witnessed how NIGMS-directed programs could bring together larger groups of scientists to tackle important problems using emerging concepts and technologies.

As Director of NIGMS, my job now is to look ahead. I have been entrusted to assure that NIGMS makes its financial investments with a careful eye toward their long-term impact on the research enterprise and the scientists who do the research.

What lies ahead? The incredible complexity of biology is something that tantalizes and challenges us. We recognize that most biological processes involve large numbers of components, interacting directly and indirectly. But we do not yet have all the tools, both technical and intellectual, to understand such systems in a predictive sense. Biological complexity, nuances of our genomic lexicon, and many other mysteries of biomedicine are waiting to be solved to improve health and fight disease.

NIGMS Core Principles

Sponsor and promote basic research as an essential aspect of science to improve human health.

■ ■ ■

Foster innovation and discovery to unveil new knowledge that will lead to future transformations in medicine.

■ ■ ■

Employ integrative and interdisciplinary approaches in the pursuit and dissemination of scientific knowledge.

■ ■ ■

Develop a biomedical research workforce representative of American society at large and actively support training of the next generation of scientists.

■ ■ ■

Ensure stability and rigor in the nation's basic biomedical research enterprise and infrastructure.

■ ■ ■

Communicate openly with the scientific community and the public about the needs, value, and impact of the biomedical research enterprise.

Furthermore, we know that fundamental discoveries are yet to be made. While no one can predict which basic findings will be the ones that shift paradigms or create the medical breakthroughs of tomorrow, I am confident that such discoveries will be made over the period of time covered by this plan.

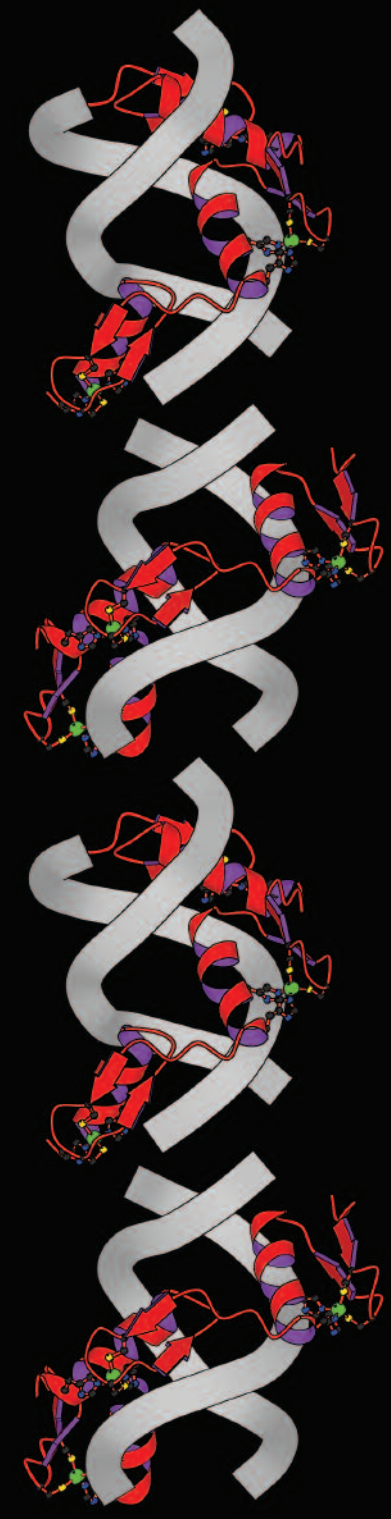
All of us see science evolving at an ever-increasing rate as new advances build on those from the past, and it is critical that the support of science adapts to this rapidly changing landscape. We must take stock of the overall system of biomedical research funding and examine how precious taxpayer resources allocated to NIGMS can be used to support the scientific enterprise—today and into the future, harnessing the creativity of a broad group of scientists.

What lies ahead? The incredible complexity of biology is something that tantalizes and challenges us.

We developed the NIGMS Strategic Plan 2008–2012 through a comprehensive consultation process that gathered perspectives and opinions from scientists, policymakers, scientific and professional societies, the general public, and Institute staff. The plan articulates the Institute's core principles and shows how it will make its strategic investments to ensure that a stable basic research environment will endure to provide the knowledge needed to prevent disease and improve health.

Importantly, this plan is not a call for change for change's sake. In developing it, we saw an opportunity to examine critically our own values and progress, and we intend the plan to serve as a tool for helping us map a course toward solving the great challenges facing biomedicine. Through existing programs and new initiatives, NIGMS aims to maximize the benefit of the public's basic research investments in human health.

Jeremy M. Berg, Ph.D.
Director, NIGMS
November 2007

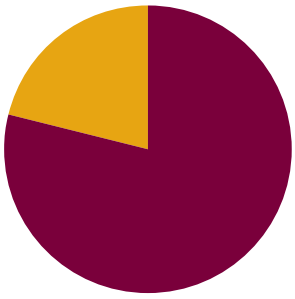


Opposite: NIGMS Director Jeremy M. Berg. *Courtesy of Ernie Branson, National Institutes of Health*.

The structure of a gene-regulating zinc finger protein bound to DNA. *Courtesy of Jeremy M. Berg.*

NIGMS Mission

The NIGMS mission is to support research that increases understanding of life processes and lays the foundation for advances in disease diagnosis, treatment, and prevention. NIGMS-funded researchers seek to answer important scientific questions in fields such as cell biology, biophysics, genetics, developmental biology, pharmacology, physiology, biochemistry, chemistry, bioinformatics, computational biology, and selected cross-cutting clinical areas that affect multiple organ systems. NIGMS also provides leadership in training the next generation of scientists to assure the vitality and continued productivity of the research enterprise.



79 percent of Americans agree that basic science research should be supported by the Federal Government, "even if it brings no immediate benefits."[3]

Why Basic Research?

The National Institute of General Medical Sciences is committed to encouraging and supporting basic biomedical and behavioral research in which scientists explore the unknown. Important medical advances have grown from the pursuit of curiosity about fundamental questions in biology, physics, and chemistry.[1] For example:

- A scientist studying marine snails found a powerful new drug for chronic pain.
- Studying how electricity affects microbes led to a widely used cancer medicine.
- A total surprise in a roundworm experiment yielded RNA interference, a gene-silencing method that has revolutionized medical research.
- Basic research on how bacterial "scissors" chop up DNA from invading viruses spawned the biotechnology industry.

At the outset, none of these discoveries related directly to a specific medical or practical problem—and some of them took decades to come to fruition. While basic research sometimes leads directly to health applications, the usual outcome of basic research is knowledge, rather than a product. That knowledge is common currency for all biomedical scientists—those researchers working on specific diseases, as well as biomedical explorers who strive to understand basic principles of the human body and mind.

Scientists conducting basic biomedical research often use model organisms to answer questions. Many processes that are fundamental to health and disease are very similar in humans, animals, and even single-celled organisms such as bacteria and yeast. Studies directed at addressing simple questions in these model organisms can often provide insights that have considerable relevance to human health.

The power of this remarkable unity of biology—a consequence of the fact that all organisms on Earth are descendants of a common ancestor—has been greatly enhanced by the success of the Human Genome Project and other genome-sequencing projects that were enabled by many years of NIGMS funding. Through the common language of DNA, results from model organisms can be more readily, and rapidly, related to human health than ever before.

Of the above examples, one in particular—the $40 billion biotechnology industry[2]—has produced tangible economic benefit to the nation through increased productivity and job creation. Biotechnology has proven to be a major force in modern medicine, having enabled drug manufacturers to create novel and effective treatments, such as therapeutic antibodies, that have few side effects and that have revolutionized the way physicians treat some types of lymphoma and breast cancer.

Through these and other dividends of the Federal research investment, scientists have made great strides in helping Americans live longer and healthier lives. Yet our work is far from done. To attack complex diseases of today such as cancer, heart disease, arthritis, depression, Alzheimer's disease, diabetes, and many other chronic conditions, we need more knowledge. We need basic research to understand the full complexity of disease processes, including what happens in the body years before symptoms show up.

No matter how counter-intuitive it may seem, basic research has proven over and over to be the lifeline of practical advances in medicine.

— NOBEL LAUREATE ARTHUR KORNBERG

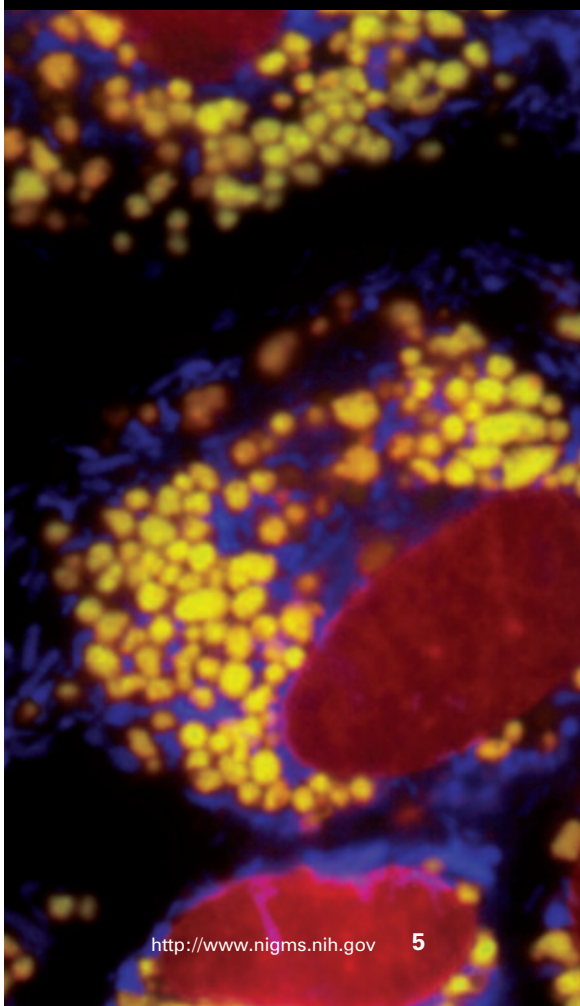
Many of today's therapies have significant limitations. Treatments that are applied after the onset of serious disease — kidney transplants and dialysis, bypass surgery for coronary artery disease, surgical removal of tumors — though often lifesaving, are not optimal. Treating disease before such interventions are needed would likely improve both outcomes and quality of life. Basic biomedical research has the power to move treatments in this direction, and in the coming years, emerging biotechnology and nanotechnology tools will give researchers unprecedented precision to detect and derail disease at its earliest stages.

As an example of how basic research helps to fuel rapid progress in developing new and safer treatments and prevention strategies, one recent analysis[4] suggested that a $1 increase in public basic research stimulated approximately $8 of pharmaceutical research and development investment in less than a decade.

In 2006, the National Institutes of Health (NIH) budget allocation totaled $28 billion, roughly half of the pharmaceutical industry's $55 billion research and development spending in the same period.[5] Since the private sector spends the vast majority of its research dollars on translational and clinical research, NIH spending on basic research — roughly two-thirds of the NIH budget — is a critical balancing factor for the health of the overall national research enterprise.

James Thomson derived the first human embryonic stem cell line and recently reprogrammed skin cells to act like embryonic stem cells. *Photo by Jeff Miller, University of Wisconsin-Madison.*

Fluorescently labeled cells confirm computational predictions about where various medicines and chemicals accumulate inside cells. *Courtesy of Gus Rosania, University of Michigan.*



Institute Profile

NIGMS Authorizing Language

"The Surgeon General is authorized, with the approval of the Secretary, to establish in the Public Health Service an institute for the conduct and support of research and research training in the general or basic medical sciences and related natural or behavioral sciences which have significance for two or more other institutes, or are outside the general area of responsibility of any other institute, established under or by this Act."

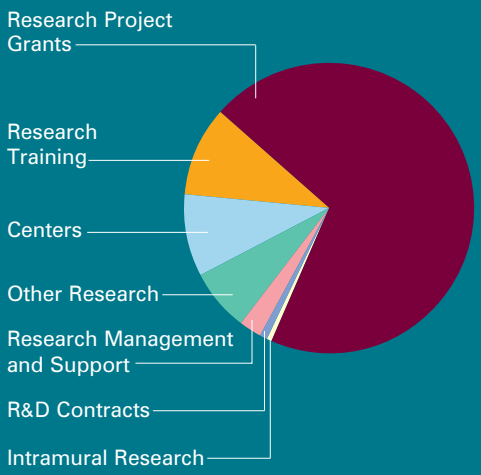
—PUBLIC LAW 87-838, OCTOBER 17, 1962

The Institute was established in 1962 to support basic biomedical research and training. NIGMS-sponsored discoveries build a fundamental body of knowledge that underpins much of the research conducted at other NIH institutes and centers. Most NIGMS research grants fund investigator-initiated projects. NIGMS also provides broad-based, multidisciplinary research training for thousands of scientists nationwide via institutional training grants and individual fellowships, as well as in the context of individual research project grants.

Currently, NIGMS-funded research and training spans a broad spectrum of science, handled administratively by five components:

Division of Cell Biology and Biophysics fosters the study of molecular and cellular structure and function. Significant physics- and chemistry-based technological advances have fueled progress in understanding life at the level of molecules and atoms. Fundamental research in structural biology is the basis for the development of precise, targeted therapies for a range of diseases.

Division of Genetics and Developmental Biology promotes basic research that aims to understand mechanisms of inheritance and development. This research underlies more targeted projects funded by other NIH institutes and centers. A substantial number of these studies are performed in model organisms, an approach that continues to increase understanding of common diseases and diverse behaviors.



Distribution of NIGMS Spending (Fiscal Year 2007)

As has been the case for many years, more than 70 percent of the NIGMS budget is devoted to research project grants (RPGs). Within the RPG pool,[6] approximately 86 percent of the budget goes to R01 and R37 grants, 1 percent to R21 grants, 1 percent to R15 grants, 4 percent to P01 grants, 3 percent to R41/R42/R43/R44 grants, and 2 percent to U01 grants, including the Pharmacogenetics Research Network and the Models of Infectious Disease Agent Study.

About 10 percent of the budget is devoted to research training in the form of institutional training grants and individual fellowships. Within this category, 86 percent of the funds go to institutional training grants while 14 percent go to individual fellowships. Like all NIH institutes and centers, NIGMS also supports a substantial number of students and postdoctoral fellows as part of research project grants.

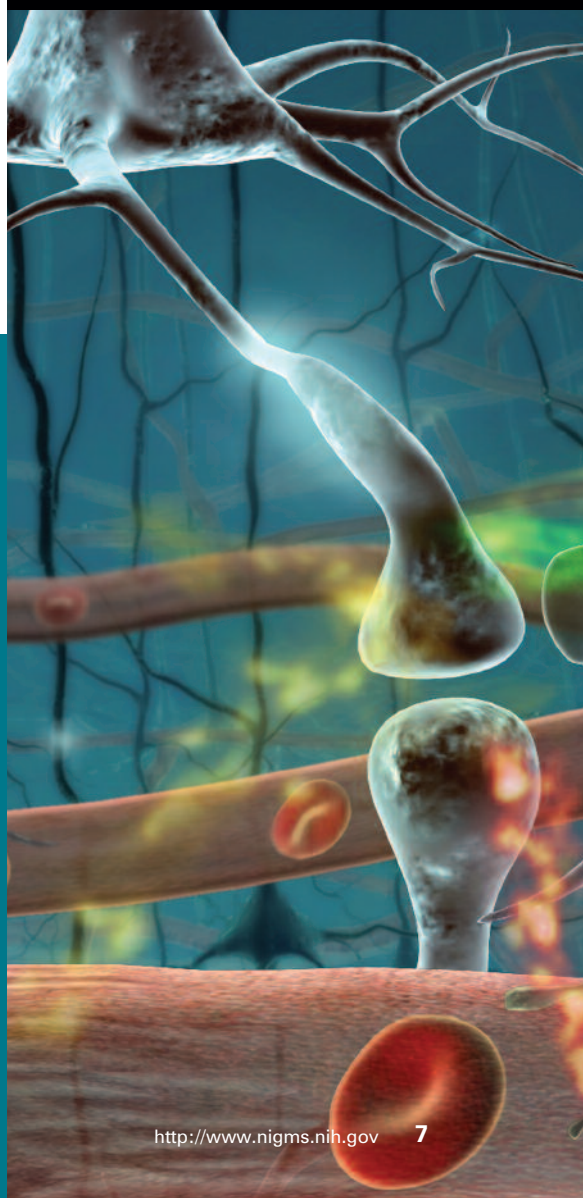
Division of Pharmacology, Physiology, and Biological Chemistry supports fundamental biology, chemistry, and biochemistry studies that deepen understanding of biomedicine and generate knowledge to improve the detection and treatment of disease. This research addresses several clinically relevant areas, including burns, wound healing, the effects of drugs and anesthesia on the body, and the total body response to injury. Investigations range from the molecular to the organismal level and can include clinical studies.

Division of Minority Opportunities in Research sponsors a range of programs to increase the number of individuals from underrepresented groups engaged in biomedical and behavioral research. This investment aims to enhance the development of biomedical and behavioral researchers and help make the scientific workforce representative of the diverse U.S. population.

Center for Bioinformatics and Computational Biology funds research in areas that join biology with computer science, engineering, mathematics, physics, and statistics. Major emphasis is placed on the development of computational tools, including methods for extracting knowledge from very large data sets routinely amassed by modern biomedical research laboratories.

Angelika Amon deciphers how chromosomes are distributed to daughter cells during cell division. *Photo by Donna Coveney, Massachusetts Institute of Technology.*

Illustration of nerve signaling in the brain showing the interaction of nerve cells, blood vessels, and molecules like glucose and oxygen. *Courtesy of Neal Prakash and Kim Hager, University of California, Los Angeles.*



Centers make up 9 percent of the budget. Most of these centers are associated with initiatives such as the Protein Structure Initiative, the Large-Scale Collaborative Award program, the National Centers for Systems Biology program, the Chemical Methodologies and Library Development program, and centers devoted to specific studies of trauma, burn, perioperative injury, and wound healing.

Other research makes up 7 percent of the budget. The Minority Biomedical Research Support program accounts for 74 percent of this category. Research career awards represent another significant component.

The remaining categories include research management and support, which contributes to administrative costs, such as NIGMS staff salaries and scientific review expenses (2.5 percent of the budget); research and development contracts (1 percent), which fund activities such as the NIGMS Human Genetic Cell Repository; and intramural research (less than 0.2 percent).

Strategic Goals

As history has proven time and again, basic research is an engine of progress. The knowledge that grows from fundamental exploration is essential. The future of America's health depends on it, as does the nation's global economic competitiveness. NIGMS strongly commits to continuing to invest in discovery by using a variety of vehicles to support basic research.

Investigator-initiated research project grants—mostly R01s—will continue to remain the main focus of the overall NIGMS research portfolio.

GOAL I: Enhance the basic biomedical research enterprise through grant support for competitive, investigator-initiated research.

NIGMS recognizes the need to provide scientists sufficient latitude to explore biomedicine in order to improve health. Although many important advances have occurred in a manner that could not have been anticipated, most scientific advances are more deliberate and require years of persistent work. While good research depends on a balance of ingredients, among the most important are adequate financial support and access to state-of-the-art resources and equipment.

NIGMS will pursue this strategic goal through the following objectives:

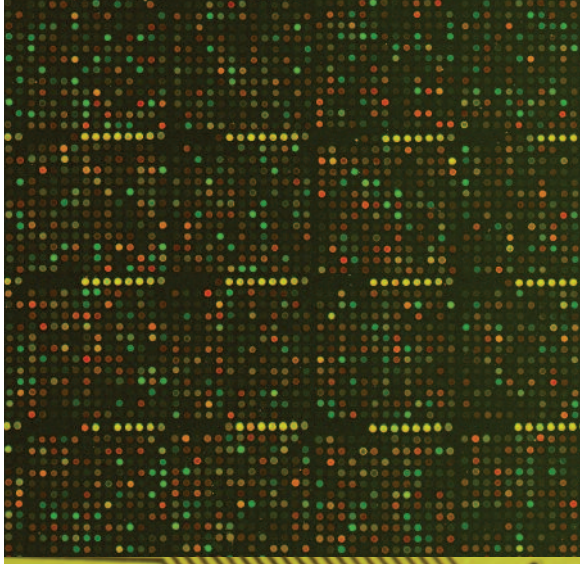
- **Maintain a balanced research portfolio that reflects scientific excellence and variety.** By funding a wide spectrum of scientific topics, the Institute will encourage flexibility to allow emerging areas to be pursued promptly. Investigator-initiated research project grants—mostly R01s—will continue to remain the main focus of the overall NIGMS research portfolio. However, coordinated research programs will also provide an important and responsive avenue for addressing biomedical problems and creating resources for use by the scientific community at large.

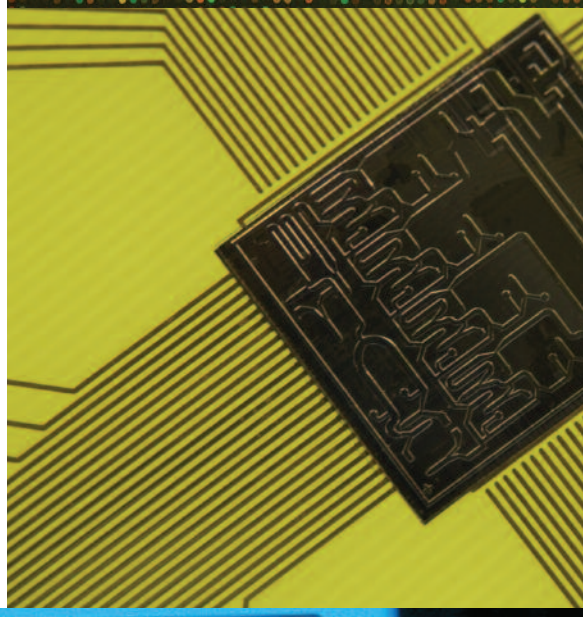
Cynthia Otto is both a critical care veterinarian and a researcher who examines the body's response to traumatic injury. *Photo at the University of Pennsylvania School of Veterinary Medicine by Alisa Zapp Machalek, NIGMS.*

Opposite: A microarray (top) reveals the activity of thousands of genes simultaneously. *Courtesy of Brian Oliver, National Institutes of Health.*

This "lab on a chip" (middle) allows scientists to conduct several liquid-based experiments simultaneously in a space about the size of a postcard. *Courtesy of Maggie Bartlett, National Institutes of Health.*

Carol Greider (bottom) studies how chromosome caps called telomeres and the enzyme that adds them, telomerase, maintain stable chromosomes. *Courtesy of Johns Hopkins Medicine.*





■ **Facilitate career stability in the biomedical workforce.** NIGMS recognizes that scientific investigation, as a human endeavor, requires career stability enabled through steady research funding. The Institute will protect the talent pipeline, especially by addressing the vulnerability of career transition times, as a way to encourage continuity in the research enterprise. While the Institute recognizes that obtaining NIH funding will always be a highly competitive process, NIGMS considers it very important that all investigators have a reasonable chance of success. In particular, NIGMS will make a deliberate effort to fund new investigators. These actions are especially relevant in limited funding climates that can disadvantage applicants who are new to the NIH system. NIGMS will also continue to provide bridge funding for highly meritorious investigators who are especially at risk during constrained budget periods.

■ **Provide support for innovative, high-risk biomedical research initiatives with the potential for achieving significant health impact.** NIGMS will continue to encourage scientists to pursue innovation and risk in biomedical research. For science to move forward in leaps rather than in incremental steps, scientists need opportunities to test unconventional ideas and to try novel methods for solving difficult technical and conceptual problems that stall a field's progress. One current effort initiated by NIGMS is the EUREKA (Exceptional, Unconventional Research Enabling Knowledge Acceleration) award program, in which review criteria focus on potential impact and exceptional innovation in research and/or technology. Through EUREKA and other programs, NIGMS will identify research proposals with the potential to have a significant impact on scientific knowledge and on human health.

■ **At the Institute level, initiate enhancements to the peer review process.** In addition to supporting NIH-wide enhancements to the peer review system,[7] NIGMS will continue to develop alternative in-house review practices and criteria that address review challenges, especially those that affect interdisciplinary research, quantitative biology, new scientific fields, and the entrance of new players into the biomedical research community. As part of the NIH Roadmap for Medical Research, NIGMS administers the NIH Director's Pioneer Award and the NIH Director's New Innovator Award programs. Each of these programs employs a novel, individualized peer review approach. NIGMS will pilot approaches that streamline administrative requirements for research project grants, always striving to ensure quality and consistency in the review of applications.

The Institute recognizes that multiple approaches are needed to solve complex research problems.

■ **Support research that analyzes fundamental mechanisms that traverse multiple organ systems.** NIGMS will continue to fund research on clinically related problems, addressing several selected areas, including burns, wound healing, the effects of drugs and anesthesia on the body, and the total body response to injury. These areas of inquiry will remain an important element of the Institute's research portfolio since they focus on biological phenomena on a systems-wide, organismal level and they are not funded in a comprehensive way by other NIH institutes and centers. Some of these NIGMS-funded research efforts will involve clinical studies, but the Institute will not fund purely outcomes-based research, nor will it systematically examine issues related to health care access and delivery.

NIGMS supports research in selected clinical areas, including trauma, burn, and perioperative injury; sepsis; wound healing; and anesthesiology.

Opposite: As part of the Models of Infectious Disease Agent Study, biostatisticians M. Elizabeth Halloran (top) and Ira Longini (bottom left) develop computational models to study disease transmission and intervention strategies. *Courtesy of the Fred Hutchinson Cancer Research Center.*

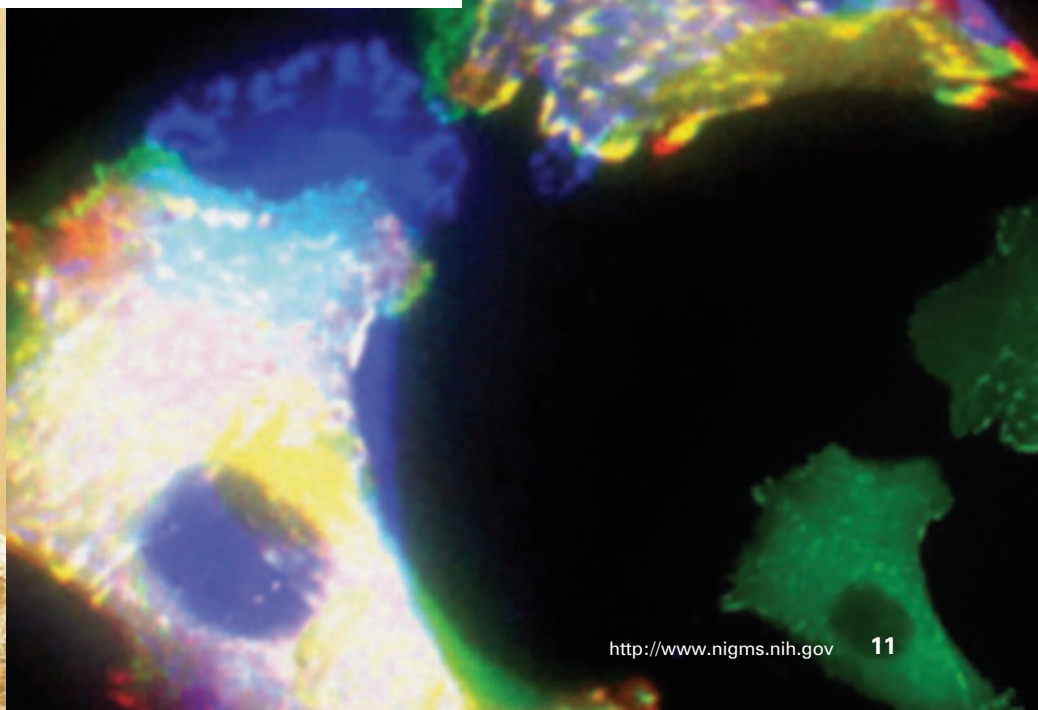
Cell movement, revealed here using fluorescent dyes (corner), is the focus of one of the glue grants. *Courtesy of K. Donais and Donna Webb, University of Virginia School of Medicine.*

GOAL II: Address selected scientific needs and opportunities through coordinated research programs.

The Institute recognizes that multiple approaches are needed to solve complex research problems. Modern biomedical research is a collaborative enterprise that may involve one or a few laboratories or a large group of researchers.

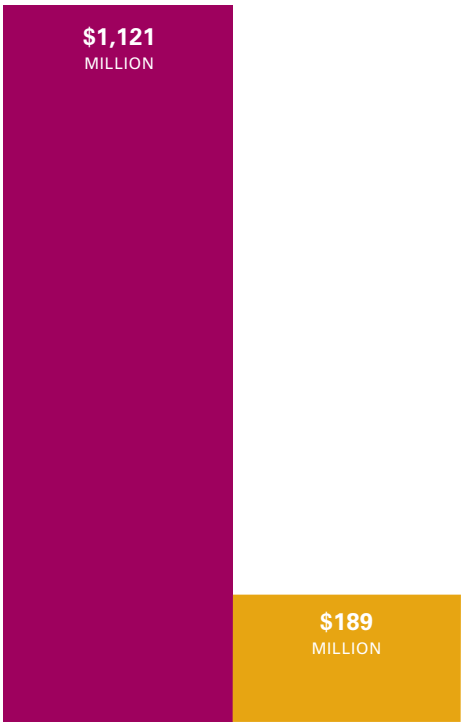
NIGMS will pursue this strategic goal through the following objectives:

■ **Facilitate team science along a continuum of scales to advance multidisciplinary and interdisciplinary inquiry.** NIGMS endorses the scientific community's recognition of the value of team science for some challenges in modern biomedical research. Novel combinations of researchers often self-assemble to broaden the canvas of biomedical inquiry and encourage diversity in thinking. NIGMS will continue to fund cross-cutting research in the basic biomedical, behavioral, and clinical sciences through collaborative programs among researchers from a wide range of disciplines, including the clinical, social, and quantitative sciences. One example is the Models of Infectious Disease Agent Study (MIDAS), which is using computational tools to simulate how infectious diseases emerge and spread through communities, countries, and even continents. NIGMS will encourage use of the recently established NIH multiple-principal investigator mechanism as a method to extend the scope of the Institute's funded research. A key NIGMS strategy will be to accommodate the evolution of new fields that emerge at the interfaces of existing disciplines. The Institute will nurture the talent pipeline in emerging fields through its support of cutting-edge, rigorous training environments that accompany basic research pursuits.



Large Grants Working Group

The Large Grants Working Group, a subgroup of the National Advisory General Medical Sciences Council, and the NIGMS Office of Program Analysis and Evaluation lead evaluation teams to monitor the progress of NIGMS large grant programs.[8]



Budget for NIGMS R01s Fiscal Year 2007

Budget for All NIGMS Large-Grant Programs Fiscal Year 2007

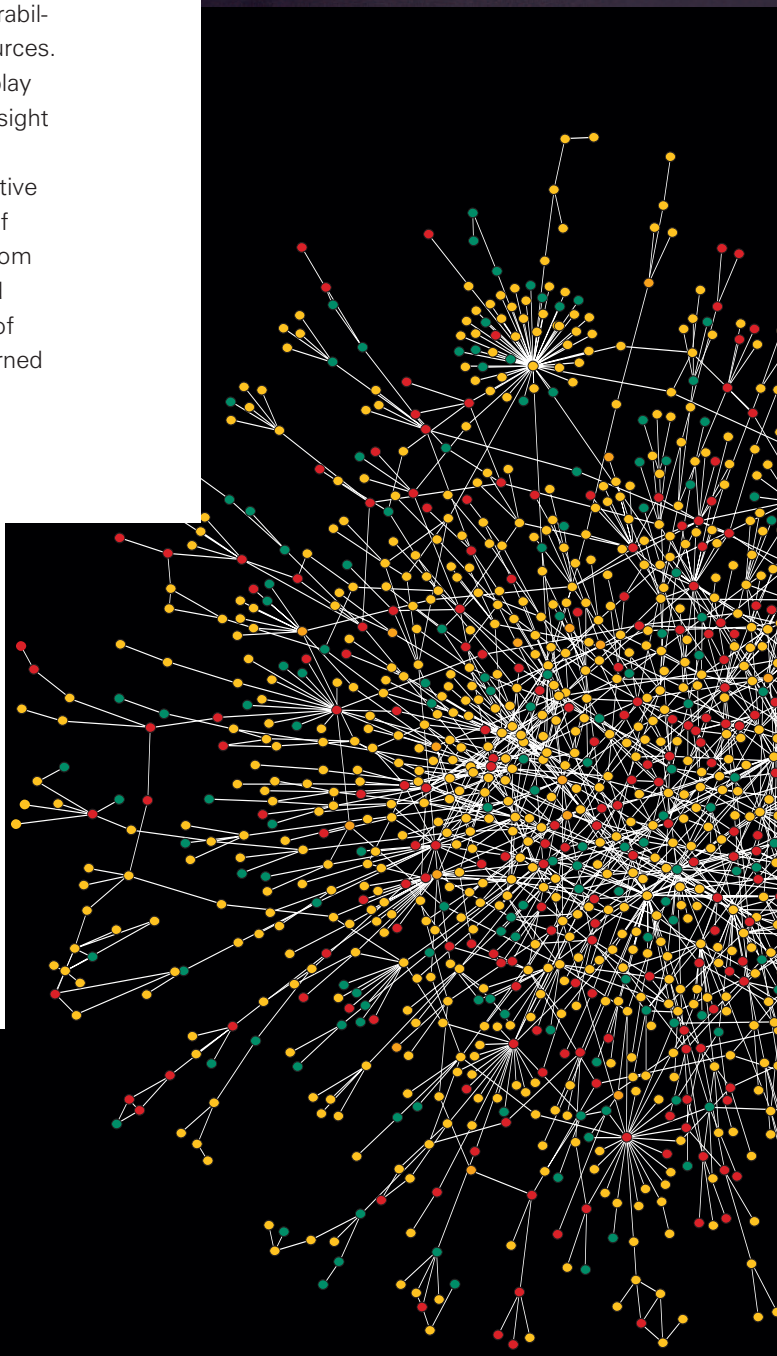
■ **Identify and develop large-scale research programs that offer value, insight, and the broadest applicability to the scientific community.** The NIGMS portfolio currently includes the Large-Scale Collaborative Award program, the National Centers for Systems Biology, the Pharmacogenetics Research Network, the Protein Structure Initiative, and MIDAS. These endeavors conjoin the efforts of multiple institutions working in a common area of major biomedical significance. Advantages of large-scale science initiatives include their economies of scale and synergy, as well as the capacity to build new communities. NIGMS will continue to fund these efforts while assuring the proper evaluation of their outcomes. For Institute-directed large-scale efforts, NIGMS will determine whether project goals have been met in a timely fashion and assess the projects' impact on the broader scientific community. The Institute will strive to ensure that instrumentation, data, and resources developed at NIGMS-funded large-scale science facilities are made broadly available to all scientists.

■ **Create programmatic linkages in support of NIH-wide translational initiatives.** The NIH Roadmap has begun to address translational gaps through the Clinical and Translational Sciences Award (CTSA) program. NIGMS will consider possible linkages to CTSA institutions through NIGMS efforts such as the Medical Scientist Training Program. In concert with other NIH institutes and centers, NIGMS will also seek opportunities for enhancing workforce diversity through the nationwide CTSA network of clinical and translational investigators.

■ **Seek collaborative and shared research opportunities with other agencies and NIH institutes and centers in areas that show particular promise.** NIGMS will continue to communicate regularly, and to partner when appropriate, with other Federal components that fund basic research, such as the National Science Foundation and the Department of Energy Office of Science. NIGMS will also join with the NIH community in several ways to achieve its mission of funding outstanding basic biomedical research. A key partnership includes the NIH Roadmap. NIGMS grantees already benefit significantly from this shared, trans-NIH investment. Current NIH Roadmap initiatives that fund a substantial number of NIGMS grantees include chemistry, computational biology/bioinformatics, imaging, nanomedicine, proteomics, and structural biology. In addition, several new NIH Roadmap initiatives will benefit the Institute's grantee pool, providing funding and collaborative opportunities in epigenetics, microbial ecology, and other areas of science relevant to the NIGMS mission.

■ **Expand support for resources and database developn biomedical research advances.** Advances in genomics an science have created incredible opportunities to systemati biomedical problems related to human health. NIGMS will a key role in supporting the creation of research resources repositories, databases, and interoperable software and ha that enhance data exchange among diverse groups of part of this involvement, NIGMS will develop policies to ensure the broad availability and interoperability of publicly developed resources. The Institute will continue to play a leadership role through oversight of the Biomedical Information Science and Technology Initiative Consortium, which consists of senior-level representatives from each of the NIH institutes and centers plus representatives of other Federal agencies concerned with biocomputing.

The Institute will strive to ensure that instrumentation, data, and resources developed at NIGMS-funded large-scale science facilities are made broadly available to all scientists.



Andrzej Joachimiak (above) leads a structural genomics center supported by the Protein Structure Initiative, which aims to make the detailed structures of most proteins obtainable from their DNA sequence. *Courtesy of Argonne National Laboratory.*

Mary Relling (top) is a member of the NIH Pharmacogenetics Research Network and seeks to understand how a person's genetic make-up influences his or her response to anticancer medications. *Courtesy of St. Jude Children's Research Hospital.*

This network diagram (corner) shows all of a yeast cell's protein-protein interactions, which mirror many of those in humans. *Courtesy of Albert-László Barabási, University of Notre Dame, and Hawoong Jeong, Korea Advanced Institute of Science and Technology.*

Fostering diversity cannot be separated from the broader challenges of future workforce development.

GOAL III: Identify innovative approaches among individuals and institutions to foster training and the development of an inclusive and effective scientific workforce.

A key aspect of the NIGMS mission is nurturing the biomedical research workforce, and achieving a workforce that accurately reflects the U.S. population remains an Institute priority. The NIGMS training investment will continue to set a high standard for students' acquisition of both research skills and important career-related knowledge beyond specific research training. The positive effects of NIGMS-funded training grants and fellowships are extended through collaborative interactions with students and faculty within and across academic departments.

NIGMS will pursue this strategic goal through the following objectives:

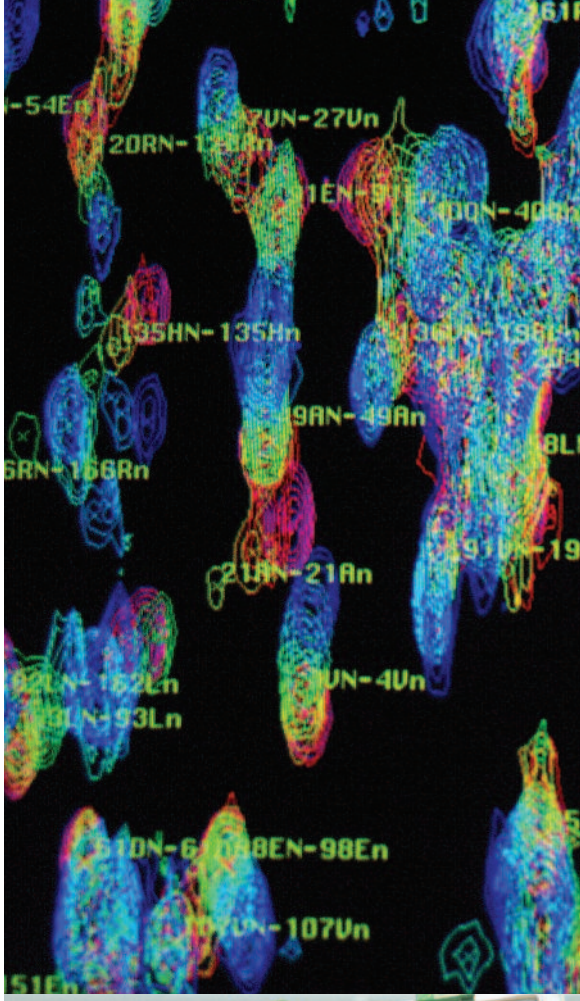
- **Support a broad range of high-quality institutional training programs across the biomedical sciences.** The Institute views a rigorous, yet nurturing, training environment as a key element of a healthy research enterprise. NIGMS recognizes the broader effects of its institutional training grants in that these programs impact many students and faculty beyond those supported by the grants. NIGMS will leverage its training investment by encouraging institutional training grant recipients to continually improve their existing practices while also welcoming new approaches. NIGMS is keenly aware of the need for more personnel in quantitative disciplines as well as the integrative sciences like physiology, pharmacology, and the clinical sciences. The Institute will consider approaches that provide institutional incentives that encourage students to interact with investigators in more than one discipline.

- **Provide funding for graduate students and postdoctoral fellows through investigator-initiated research project grants.** The NIGMS research training investment is multifaceted and tightly linked to the Institute's workforce development efforts. Independent of its institutional training grant activities, the Institute will continue to support the training of students and fellows working in individual-investigator (mostly R01 grant-funded) laboratories. NIGMS considers this an important avenue for research training. The Institute also acknowledges the reality that one size does not fit all, and it will remain open to both distinct training mechanisms and alternative career outcomes that depend on "market-place" influences.

■ **Expand and extend the NIGMS commitment to facilitating the development of a diverse and inclusive biomedical research workforce.** Fostering diversity cannot be separated from the broader challenges of future workforce development. Dimensions of diversity include ethnicity, gender, disability, socioeconomic status, and national origin. The Institute is also aware of the low representation of women in leadership positions in the basic sciences and aims to close these gaps. NIGMS acknowledges the special circumstances faced by various segments of society in accessing career opportunities. The Institute will examine the purpose, intent, and desired outcomes of NIGMS-sponsored training programs as they relate to workforce diversity.

■ **Address diversity and workforce development in all programs administered by NIGMS as a matter of both policy and practice.** NIGMS is committed to the regular and rigorous review of all of its training efforts, including special diversity and career development programs, as well as to achieving closer coordination among the Institute's various programs. NIGMS will continue to evaluate its efforts to promote biomedical research workforce diversity, seeking the most productive ways to distribute funding, and will continue to integrate diversity efforts across its programs. The Institute will consider implementing a "broader aims" component of research project grant applications that explicitly evaluates an investigator's training, mentoring, and diversity activities.

■ **Adopt a comprehensive, systems-based approach to address future workforce development issues.** The challenge of scientific workforce diversity is fundamentally a systems problem, and NIGMS will approach it in this fashion. The Institute will investigate the issue of workforce diversity in a data-driven, scientifically rigorous manner. Developing effective approaches will require that NIGMS continually acquire evidentiary data, even if those data do not lead to concrete solutions in the near term. NIGMS will expand its investment in research to understand the efficacy of interventions designed to increase diversity. The Institute will assess the feasibility of developing computer models that reflect key trends in workforce development and related career path issues, incorporating pivotal demographic, societal, and behavioral variables. NIGMS will also continue to identify and use early predictors of longer-term outcomes for enhancing workforce diversity at research institutions.



Opposite: Carlos Gutierrez studies how bacteria acquire and transport iron and leads the Minority Access to Research Careers and Minority Biomedical Research Support programs at his institution. *Courtesy of Public Affairs, California State University, Los Angeles.*

NMR spectrum (top) shows how an enzyme changes shape, which is vital to its function. *Courtesy of Dorothee Kern, Brandeis University.*

Susan Wente and student Kristen Noble (bottom) investigate how molecules travel between the nucleus and cytoplasm of the cell. *Photo by Dana Thomas for Vanderbilt Medical Art Group.*

Nobel Prize-Winning Research

In its 45-year history, NIGMS has funded the Nobel Prize-winning work of 64 scientists (see http://www.nigms.nih.gov/GMNobelists.htm). Recent Nobelists supported by NIGMS include:

- Mario R. Capecchi & Oliver Smithies *Physiology or Medicine 2007*
- Roger D. Kornberg *Chemistry 2006*
- Andrew Z. Fire & Craig C. Mello *Physiology or Medicine 2006*
- Robert H. Grubbs & Richard R. Schrock *Chemistry 2005*
- Avram Hershko & Irwin Rose *Chemistry 2004*
- Paul C. Lauterbur *Physiology or Medicine 2003*
- Roderick MacKinnon *Chemistry 2003*

GOAL IV: Advance awareness and understanding of the basic biomedical research enterprise, including its value, requirements, and potential impact.

NIGMS values transparency and positive relations with the scientific community and the public as critical to carrying out its mission. The Institute also believes that it is important to contribute to improvements in science education at the K-12 and other levels as a distinct diversity and workforce development strategy.

NIGMS will pursue this strategic goal through the following objectives:

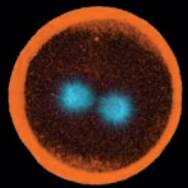
- **Continue to foster an open dialogue with the scientific community about evolving scientific trends, gaps, and opportunities.** NIGMS will communicate with its grantees and other members of the scientific community directly and through partnerships with universities, research institutes, scientific and professional societies, and organizations. The Institute will continue to issue regular programmatic updates to these constituents and seek input and feedback from them. NIGMS will also enhance efforts to empower its approximately 4,000 grantees and its advisory council members to serve as a highly visible group of ambassadors who can effectively and broadly communicate Institute programs and policies to multiple audiences. Additionally, the Institute will explore ways to increase communication among scientists working in diverse fields, potentially leading to new interactions and discoveries.

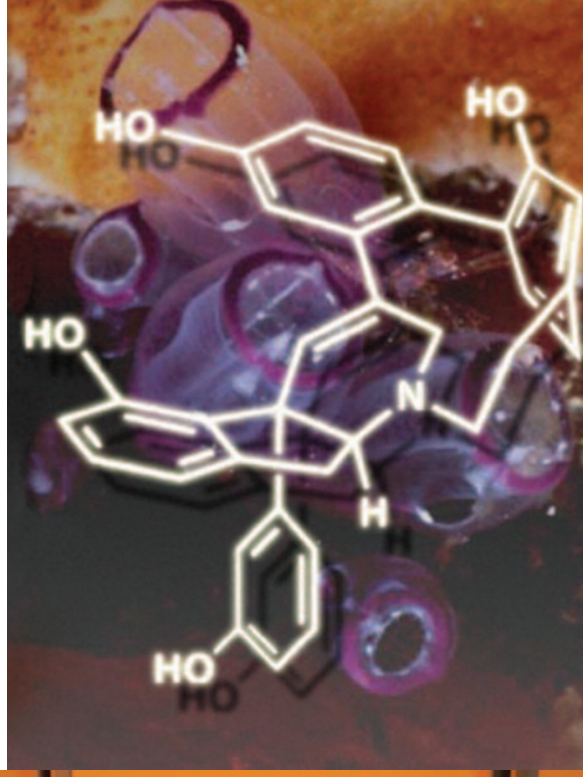
Surgeon J. Perren Cobb (left) leads a multidisciplinary group of scientists who seek to identify gene activity patterns that signal sepsis, a dangerous response to severe injury. *Courtesy of J. Perren Cobb, Washington University in St. Louis School of Medicine.*

Sea urchin embryos (right) in different stages of cell division. *Courtesy of George von Dassow, University of Washington.*

Opposite: Haouamine A (top), a promising anticancer candidate, is one of many organic molecules synthesized in the laboratory of Phil Baran. *Courtesy of Paul Krawczuk, Scripps Research Institute.*

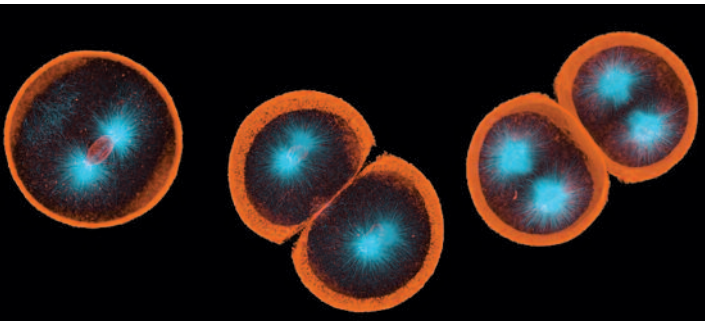
Molecular biologist Marion Sewer and student Houman Khalili (corner) investigate the regulation of steroid hormone biosynthesis. *Photo at the Georgia Institute of Technology by Gary Meek.*





■ **Raise public awareness and understanding about the value and impact of basic biomedical research.** NIGMS will continue its efforts to communicate with the public about its goals and research results, as well as about NIH and its contributions to the nation's health. In our increasingly technology-driven society, knowledge of science—as well as how science is done—is important for making personal health and community decisions as well as for succeeding in a wide variety of careers. Toward this end, NIGMS will team with NIH institutes and centers and/or other organizations to increase scientific literacy. The Institute will also work to diminish misperceptions about biomedical science and scientists that stem from outdated stereotypes and lack of information. NIGMS will continue to provide students, teachers, and the general public with educational materials tha value of basic research and encourage the pursuit of scientific careers. In support of its efforts to foster workforce diversity, the Institute will partner with organizations and institutions to target the distribution of NIGMS educational and career-focused resources to students who belong to groups that are underrepresented in the biomedical research workforce.

NIGMS values transparency and positive relations with the scientific community and the public as critical to carrying out its mission.



Inside NIGMS

In addition to periodic discussions with the scientific community to identify broad research themes, NIGMS routinely sponsors scientific workshops to focus on particular areas of opportunity and develop plans for specific initiatives.

Strategic planning at NIGMS has always focused on identifying broad research themes and opportunities in the biomedical sciences that are either currently available or are likely to emerge in the coming years. In addition to periodic discussions with the scientific community to identify broad research themes, NIGMS routinely sponsors scientific workshops to focus on particular areas of opportunity and develop plans for specific initiatives. The results of these workshops are documented in reports presented to the National Advisory General Medical Sciences Council, which must give approval for Institute-proposed initiatives.

Proposed new NIGMS research and training programs are made public at the open session of advisory council meetings. Council approval of new initiatives (and major changes to existing initiatives) is called "concept clearance." Concept clearance authorizes NIGMS staff to develop plans, publish funding opportunity announcements in the *NIH Guide for Grants and Contracts,* and award grants. During the initiative planning stages that follow concept clearance, NIGMS welcomes comments and suggestions from the community.

The research priorities identified by scientific experts in planning meetings such as those convened by NIGMS influence future research activities in several ways. The reports of these meetings are widely disseminated among the community of biomedical scientists who are keenly aware of and attentive to emerging opportunities and the stated priorities of funding agencies. The mere communication of these research opportunities can be a major influence on the direction of investigator-initiated research, as scientists seek to develop successful proposals for research funding.

These stated priorities also influence the Institute's grant funding decisions. While the results of peer review are always a major consideration in the funding of research proposals, the peer review score is not the only factor considered when Institute staff and advisory council members recommend specific grant applications for funding. Among the other factors taken into account is scientific program need. Meritorious proposals, but with somewhat poorer peer review scores, may still be funded if they are designated as being of high program priority. Investigators who have not received prior NIH funding are also given special consideration.

Discussion among scientific experts can also identify areas of research in which a more active role of the Institute is required to stimulate the submission of research proposals. In some cases, NIGMS issues a program announcement or request for applications when needed to extend or enhance the Institute's research portfolio.

Strategic Planning Process

The NIGMS Strategic Plan 2008–2012 is the result of a comprehensive consultation process that began in the fall of 2006 and solicited perspectives, opinions, and other input from scientists, policymakers, scientific and professional societies, the general public, and Institute staff. NIGMS Director Jeremy M. Berg appointed a strategic planning committee, composed of NIGMS staff and broadly representing the Institute, to develop the procedures, format, and timetable for the overall strategic planning process and to define some of the key issues. Following an announcement in the *Federal Register,* NIGMS posted questions on its Web site between February 20 and March 20, 2007. These included:

- What factors should NIGMS consider in deciding how to set its priorities with respect to new and existing areas of support?
- What factors should NIGMS consider in deciding how to set its priorities with respect to research training?
- What new and emerging areas, approaches, or technologies in basic biomedical research should NIGMS pursue?
- As part of its efforts to maintain a balanced research portfolio, how can NIGMS best encourage and support research that is highly innovative and/or risky?
- Are there areas of current NIGMS research activity that should receive less emphasis?
- How can NIGMS enhance its communications with the scientific community and the public?
- How can NIGMS more effectively promote and encourage greater diversity in the biomedical research workforce?

Following the Internet comment period, NIGMS convened a 2-day conference in April 2007. About 50 participants were invited to represent all the dimensions of the NIGMS extramural scientific community. The participants met in both breakout and plenary sessions to discuss Institute plans and priorities. Discussion was framed around the same set of questions and issues presented in the Internet comment period.

NIGMS staff worked at length to distill input from both the posted questions and the conference, and this information was used to formulate a draft plan, which was posted on the NIGMS Web site for public comment in September 2007.

NIGMS staff work in the Natcher Building on the NIH campus in Bethesda, Maryland. *Courtesy of Alisa Zapp Machalek, NIGMS.*

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[5] Pharmaceutical Research and Manufacturers of America, Pharmaceutical Industry Profile 2007. Washington, DC: *PhRMA;* 2007.

[6] R01: NIH Research Project Grant; R37: Method to Extend Research in Time (MERIT) Award; R21: Exploratory/Developmental Grant (currently being phased out at NIGMS); R15: Academic Research Enhancement Award (AREA); P01: Research Program Project; R41-44: Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) Grants; U01: Research Project - Cooperative Agreement.

[7] http://enhancing-peer-review.nih.gov

[8] Large-Scale Collaborative Award program, National Centers for Systems Biology, Pharmacogenetics Research Network, Protein Structure Initiative, and Models of Infectious Disease Agent Study.

NIGMS staff and contractors, October 2006. *Courtesy of Bill Branson, National Institutes of Health.*

ACCESSIBILITY

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