

Fiscal Year 2012 Budget Request

Open TECHNOLOGIES TO ACCELERATE DISCOVERY configuration options

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Witness appearing before the Senate Subcommittee on Labor-HHS-Education
Appropriations

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May 11, 2011

Mr. Chairman and Members of the Committee:

I am pleased to present the Fiscal Year (FY) 2012 President's budget request for the National Institute of General Medical Sciences (NIGMS). The FY 2012 budget request includes \$2,102,300,000, an increase of \$70,263,000 above the FY 2011 appropriation of \$2,032,037,000, which has been adjusted comparably to reflect NIH proposed transfers. This statement is submitted with the recognition of the Department's notification to the Congress of an NIH reorganization that would establish a new National Center for Advancing Translational Sciences and reallocate the remaining portions of the National Center for Research Resources to other parts of NIH.

Since the mid-20th century, NIGMS has played a leading role as NIH's "basic research institute." Spanning a broad spectrum, the Institute's mission supports discovery ranging from how cells work to how diseases affect communities across towns, nations, and countries. NIGMS-supported scientists probe the unknown to solve mysteries about fundamental life processes. This effort goes well beyond the need to satisfy innate curiosity; answering basic research questions such as how bacterial and human cells divide, move, and communicate has increased our knowledge about infections, cancer, birth defects, and heart disease in ways that would have been difficult to achieve with more directed studies. Other ongoing NIGMS research investments, such as in chemistry, continue to provide tangible benefits to society and our economy. This past year, an NIGMS-supported scientist shared a Nobel Prize for his discovery of a ground-breaking chemistry method that is used routinely in the pharmaceutical, electronic and agricultural industries.

Continued investment in basic research is vital because many of today's therapies, although effective, nevertheless have significant limitations. Treatments that are applied after the onset of serious illness—kidney transplants and dialysis, bypass surgery for

coronary artery disease, surgical removal of tumors—though often lifesaving, are still not optimal. Treating disease before such interventions are needed would likely improve both outcomes and quality of life. Basic biomedical and behavioral 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.

TECHNOLOGIES TO ACCELERATE DISCOVERY

Basic research on stem cells remains one of the most rapidly advancing areas of biomedicine, in large part because of the knowledge base scientists already have about how cells behave and change. NIGMS-supported research on stem cells continues to provide hope that these multitasked cells will find use in customized therapies for a range of conditions. In the near term, stem cells are providing researchers powerful tools for understanding diseases and developing drugs to treat them. This past year, NIGMS-funded researchers made important progress on several fronts:

- Stem cell research pioneer James Thomson, D.V.M., Ph.D., created a powerful tool to trace the individual steps in a deadly cancer by turning the clock back on blood cells from a person with leukemia.
- Chemist Laura Kiessling, Ph.D., developed an inexpensive and simple synthetic culture system for growing embryonic stem cells in the laboratory.
- NIH Director's New Innovator Awardee Alysson Muotri, Ph.D., used cells from a person with Rett syndrome to create a cellular model of autism.

Another area showing great promise is molecular diagnosis. This past year, NIH Director's Pioneer Awardee Thomas Kodadek, Ph.D., applied a unique and creative strategy that conducts an "immune surveillance" of human blood to look for early signs of disease before symptoms appear. To date, he has obtained exciting evidence that Alzheimer's disease may be detectable by this approach, and he has licensed the technology to further its development and application.

The study of systems—of cells, organs, and diseases—is an important area of basic discovery within the NIGMS mission. In 2010, the Institute grew its support of systems biology by adding two new National Centers for Systems Biology. All 12 centers integrate approaches from engineering, genomics, and systems- and synthetic biology to identify principles and architectural features involved in common cellular behaviors, including the response to disease-causing microorganisms, poisons, and metabolic imbalances.

Computer modeling is a key element of all systems biology, and a central aspect of the NIGMS-led Models of Infectious Disease Agent Study (MIDAS). This international effort continues to add new research expertise to increase its capacity to simulate disease spread, evaluate different intervention strategies, and help inform public health officials and policymakers. This past year, two MIDAS findings are worth highlighting:

- One MIDAS study used computer modeling to analyze the spread of H1N1 flu in a Pennsylvania elementary school. The researchers collected extensive data from seating charts, school timetables, bus schedules, nurse logs, attendance records and questionnaires. The findings indicated that transmission occurs mostly through girl-to-girl and boy-to-boy interactions and that sitting directly next to a child with the flu does not raise a child's risk of getting it.
- In another MIDAS study, researchers learned that the Haiti cholera outbreak that followed that nation's colossal earthquake in 2010 could have been blunted with the use of a mobile stockpile of oral cholera vaccine.

TRANSLATIONAL SCIENCES AND THERAPEUTICS DEVELOPMENT

Since the landmark discovery of the structure of DNA in the 1950s, our increasing knowledge of how all living things share a basic set of working parts has catalyzed progress in biomedicine. Large-scale efforts to scan and compare genomes are teaching scientists about individual differences in DNA scripts that predispose us to disease. However, such sequence information is only useful if it can be properly interpreted. NIGMS has been at the forefront of supporting research that facilitates this interpretation, leading to numerous discoveries that have revealed new, unforeseen mechanisms by which DNA information is made operational.

As one example, the NIGMS Protein Structure Initiative (PSI) has been creating knowledge and providing tools to researchers for more than 10 years. This past year, NIGMS enhanced this signature effort by launching PSI:Biology, a new program that supports research partnerships between groups of biologists and high-throughput structure determination centers to solve medically important problems. Already this investment is bearing fruit, yielding new structures that show how the largest class of drug receptors functions.

Another example is a pilot study by an individual scientist that searched systematically for environmental factors—nutrients, chemicals and toxins—that may be linked to diabetes. Based conceptually on the Genome-Wide Association Studies approach, Atul Butte, M.D., Ph.D., developed a new technique he calls Environment-Wide Association Studies. In this method, he considered many different factors at once, using health survey data from the U.S. Centers for Disease Control and Prevention, which led him to identify 266

environmental factors linked to type 2 diabetes. This example highlights the tremendous potential benefits of integrating existing data sources and asking the right questions.

ENHANCEMENT OF EVIDENCE BASE FOR HEALTH CARE DECISIONS

Although medicines have been revolutionary in humankind's ability to stay healthy, we now know that people having widely varying responses to the drugs they take to heal their various ills. NIGMS has been a long-time supporter of pharmacogenomics, the study of how our DNA influences the way we respond to medications. This area of research is an especially important focus in our country today, as the baby-boom generation gets older and is more likely to take multiple medicines routinely. NIGMS leads the trans-NIH Pharmacogenomics Research Network (PGRN), a nationwide collaborative of scientists looking for clues to inherited variability in the response to medicines used to treat heart disease, asthma, cancer, depression and addiction.

This past year, two new groups joined the network, adding rheumatoid arthritis and bipolar disorder as new focus areas. Over the next five years, the PGRN plans to expand to pursue cutting-edge DNA sequencing methods and statistical analysis, as well as to perform pilot studies to learn about medication response from de-identified medical records in health care systems. Furthermore, previous PGRN-based discoveries are now moving further into clinical application with evidence accumulating on improved outcomes and lower costs.

NEW INVESTIGATORS, NEW IDEAS

Biomedical and behavioral research is a human endeavor, and NIGMS has a long-standing commitment to supporting and sustaining the people behind the research. Creativity comes from the sparks of individual minds, and thus the Institute has always adhered to the principle that a healthy workforce is an essential ingredient for good science that leads to better health for all.

Science and the conduct of research continue to evolve, though, as do workforce needs. It is our responsibility to stay attuned to these new needs and opportunities. In 2010, NIGMS launched a process to examine its activities and general philosophy of research training—to assure that all of the Institute's activities related to the training of scientists are aligned with our commitment to build an excellent, diverse research workforce to help achieve the NIH mission, now and in the long term.

NIGMS gathered data and input from the scientific community through a series of regional meetings across the country, as well as through other means of electronic communication including a webinar, online postings, and comment submissions via email. The resulting plan, *Investing in the Future, the NIGMS Strategic Plan for Biomedical and Behavioral Research Training*, was released in early 2011.

A key focus of this plan is the importance of putting the needs of trainees first—by focusing on mentoring, career guidance, and diversity. The plan also affirms the Institute's strong assertion that there are multiple avenues in which a well-trained scientist can make meaningful contributions to society. These include research careers in academia, government, or the private sector, as well as careers centered on teaching, science policy, patent law, communicating science to the public, and other areas.

In closing, and on the cusp of my departure from federal service, I want to note how proud I have been to play a role in furthering the basic research that has had such a profound effect on the health and well-being of our nation. I will treasure the time and effort spent leading the fine institution that is NIGMS.

Biographical Sketch

Jeremy M. Berg became director of the National Institute of General Medical Sciences (NIGMS) in November 2003. Prior to his appointment as NIGMS director, Dr. Berg directed the Institute for Basic Biomedical Sciences at the Johns Hopkins University School of Medicine in Baltimore, MD, where he also served as professor and director of the department of biophysics and biophysical chemistry. In addition, he directed the Markey Center for Macromolecular Structure and Function and co-directed the W.M. Keck Center for the Rational Design of Biologically Active Molecules at the university.

Dr. Berg's research focuses on the structural and functional roles that metal ions, especially zinc, have in proteins. He has made major contributions to understanding how zinc-containing proteins bind to the genetic material DNA or RNA and regulate gene activity. His work, and that of others in the field, has led to the design of metal-containing proteins that control the activity of specific genes. These tailored proteins are valuable tools for basic research on gene function, and such proteins could one day have medical applications in regulating genes involved in diseases, as well. Dr. Berg has also made contributions to our understanding of systems that target proteins to specific compartments within cells and to the use of sequence databases for predicting aspects of protein structure and function.

Dr. Berg served on the faculty at Johns Hopkins from 1986-2003. Immediately before his faculty appointment, he was a postdoctoral fellow in biophysics at the university.

Dr. Berg received B.S. and M.S. degrees in chemistry from Stanford University in 1980 and a Ph.D. in chemistry from Harvard University in 1985. He is a coauthor of more than 130 research papers and three textbooks, *Principles of Bioinorganic Chemistry*, *Biochemistry (5th Edition and 6th Edition)* and *A Clinical Companion to Accompany Biochemistry*.

His honors include a Presidential Young Investigator Award (1988-1993), the American Chemical Society Award in Pure Chemistry (1993), the Eli Lilly Award for Fundamental Research in Biological Chemistry (1995), the Maryland Outstanding Young Scientist of the Year (1995), election as an American Association for the Advancement of Science Fellow (2007), the Distinguished Service Award from the Biophysical Society (2009), the Howard K. Schachman Public Service Award from the American Society for Biochemistry and Molecular Biology (2011, presented in 2010), and election to the Institute of Medicine of the National Academies (2010). He also received teaching awards from both medical students and graduate students and served as an advisor to the Johns Hopkins Postdoctoral Association since its founding.

NIGMS supported Dr. Berg's research from 1986-2003.