

Appropriations Subcommittee Statement on the Fiscal Year 2007 Budget

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April 6, 2006

Mr. Chairman and Members of the Committee:

I am pleased to present the Fiscal Year (FY) 2007 President's budget request for the National Institute of General Medical Sciences (NIGMS). The FY 2007 budget includes \$1,923,481,000, a decrease of \$12,137,000 from the FY 2006 enacted level of \$1,935,618,000 comparable for transfers proposed in the President's request.

NIGMS supports a broad spectrum of research central to the National Institutes of Health's mission of improving the nation's health. Over the years, this foundational work has led to important breakthroughs and treatments. Biophysical studies sparked the development of life-saving drugs for AIDS. Inventive burn and trauma research yielded the first artificial skin to treat severely burned patients. Most recently, research in pharmacogenetics led the Food and Drug Administration (FDA) to change the label of irinotecan, a drug approved in 1996 for colorectal, lung, and other cancers. The label now indicates that people with a certain genetic variation are at a greater risk for life-threatening reactions to the drug and encourages doctors to use a lower starting dose for those patients.

In other areas, such as chemistry, groundbreaking basic research helped support drug development by the pharmaceutical industry. NIGMS' investment in this area was recognized with the 2005 Nobel Prize in chemistry, bringing the number of laureates whose research we have funded to 57. Long-time grantees Robert H. Grubbs, Ph.D., of the California Institute of Technology and Richard R. Schrock, Ph.D., of the Massachusetts Institute of Technology were honored for developing a revolutionary way of synthesizing new molecules. Their discoveries transformed a seemingly esoteric process into a practical tool that is now routinely used in the pharmaceutical industry and in other areas of the economy, including the plastics industry.

Strengthening the Pipeline

In addition to providing stable research support to these chemists, NIGMS provided funds to support their transition from trainees to independent researchers. The Institute has a number of structured programs that offer thousands of trainees access to state-of-the-art resources, rigorous curricula, and high-quality ethics training. Each year, many scientists receiving NIGMS support launch independent careers and join the ranks of top-notch researchers in a wide range of scientific disciplines.

Many creative contributions like the few I have highlighted above are the work of individual bright minds. However, as biomedical research converges and scientific fields meld together in new ways, researchers working in different areas need to combine their talent and expertise. Recognizing the dual need for teamwork and individual intellectual contribution, NIGMS has invested its resources wisely. In addition to funding a substantial number of individual investigators, we have broadened our investment by funding large, multidisciplinary scientific teams. These programs have served a truly catalytic role in tackling issues of great importance to public health, and I would like to describe some of their recent advances.

The Dawn of Personalized Medicine

The NIGMS-led Pharmacogenetics Research Network (PGRN), a trans-NIH project consisting of 12 scientific teams, has just completed its first 5 years of work with an impressive track record. For example, the treatment of childhood leukemia is improving due to the discovery that variations in two genes can predict which patients with the most common form of the disease have a higher risk of relapse. On the horizon is safer dosing of the widely used blood-thinning medicine Coumadin® (also known as warfarin) due to the discovery that normal variation in two genes can put some patients at risk for excessive bleeding or for heart attacks and strokes. PGRN researchers have also made important strides in unraveling disparities in response to treatments for asthma, a disease that affects roughly 20 million Americans, according to the American Lung Association. Recent findings show that variation in just a few genes affects responses to two mainstay asthma therapies, inhaled steroids and beta-agonists. Genetic tests to detect these variations may be available within a year.

Other payoffs from NIGMS investments in pharmacogenetics extend beyond implications for individual drug dosing. PGRN research has unexpectedly uncovered knowledge that can predict disease risk in subsets of patients, including those taking tamoxifen for breast cancer and beta-blockers for heart disease. Finally, NIGMS-sponsored research in pharmacogenetics is having an impact on policy. PGRN studies have played a role in the FDA's recent decision to develop new guidelines for personalized medicines. For example, an FDA program that allows manufacturers to submit pharmacogenetic data for review has seen a jump from six submissions to 25 in the space of 1 year.

Teaming Science for Public Health Gains

NIGMS' innovative "glue grant" program is a novel approach that brings together scientists from different disciplines to attack problems beyond the scope of an individual investigator but crucial to the future of the public health enterprise. One example of a recent glue grant

advance is the discovery that genes can help explain why patients can have dramatically different reactions to traumatic injury. The NIGMS-funded Inflammation and the Host Response to Injury research group, which performed this study, will also release this year a set of standard operating procedures for the care of critically injured patients. This work, while still in the early stages, is moving ahead rapidly and will likely improve standards for treatment across the nation as well as facilitate the conduct of high-quality research in this important field.

Many areas of basic biomedical research require an incubation period before results emerge and new knowledge is translated into the clinic. Both pharmacogenetics and much of the complex biology being investigated with glue grants are good examples, and the recent achievements I've described offer evidence that the wait has been worth it. However, in other circumstances NIGMS has invested basic research expertise in areas quite ripe for practical development. A case in point is the Models of Infectious Disease Agent Study (MIDAS), not yet 2 years old, which has already made an important mark on the public health policy landscape. Several key papers have emerged from this highly interdisciplinary effort, and the program continues to be fluid, evolving to match public health needs. The MIDAS network is focusing on modeling the spread of influenza, and its models are providing key inputs to policy makers and health officials engaged in preparing for possible influenza pandemics.

Value of a Systems Approach

The ready application of MIDAS research to current flu preparedness efforts is apparent, but I'd like to point out that this research is a shining example of what may seem a more esoteric concept: systems biology. In fact, systems biology is a powerful and promising approach for investigating how to control the progression of diseases worldwide.

Systems biology addresses how the parts of a complex network work together to produce the behavior of the overall system. The threads of systems biology are apparent in pharmacogenetics, which goes beyond the consideration of a drug and its target to examine other molecules that affect drug action and determine how apparently subtle variations in these molecules can affect drug efficacy and safety. In infectious disease modeling, the properties of an infectious agent are superimposed on the structure of society, from transportation networks to human behavior. Systems biological approaches require interdisciplinary teams of scientists working together toward a common goal that is often closer to practical applications than are the powerful, "one component at a time" approaches that have driven biomedical research so successfully over the past decades.

Power of the Mind

Let me finish by returning to the contributions of individual minds. I'll highlight two relatively young scientists who have been recognized by the NIH Director's Pioneer Award program for their exceptional potential to make major breakthroughs.

The first is Sunney Xie, Ph.D., of Harvard University. He is a pioneer in the development of methods that can see single biological molecules in action. Most biomedical experiments examine millions or more molecules, revealing the average behavior of all of them. While this information can be highly useful, many details are lost. Dr. Xie's methods, developed through an inspired application of techniques from physics and chemistry, look at the behavior of one molecule at a time. This is like being able to hear one conversation clearly rather than hearing the din of a room full of people all talking at once. As these methods mature, they have the potential to transform our understanding of how gene expression is controlled in normal and diseased cells.

The second NIH Director's Pioneer Award winner I will mention is neurobiologist Erich Jarvis, Ph.D., of Duke University. Dr. Jarvis, an African American who grew up amid poverty, drugs, and violence in Harlem, seeks to unravel the mysteries of vocal learning. He is investigating this question using songbirds as a model system, and he has already made important strides in unlocking some of the complexity of one of biology's unexplored frontiers: the brain. Although his research falls outside the realm of the NIGMS mission and Dr. Jarvis is not currently an Institute grantee, I tell you his story for a different, very important reason. He is a terrific example of what we stand to lose if we do not continue to invest in the creative individual sparks of young scientists in our diverse society. At least part of Dr. Jarvis's rise to success can be attributed to chances he got in school. He participated in the NIGMS Minority Biomedical Research Support and Minority Access to Research Careers programs as an undergraduate at the City University of New York, Hunter College, where he received a bachelor's degree in biology and mathematics. He later earned a Ph.D. in molecular neurobiology and animal behavior from the Rockefeller University and today works at the forefront of an exciting discipline at the intersection of biomedical and behavioral research.

The creative energies of potential biomedical researchers—not just those in fields traditionally related to biomedicine but also those in associated fields in the physical, mathematical, behavioral, and social sciences—will drive advances leading to improvements in human health for many years to come. Nurturing a diverse scientific workforce will enhance the vitality of our nation and improve the health of our children and their children.

Thank you, Mr. Chairman. I would be pleased to answer any questions that the Committee may have.