

Appropriations Subcommittee Statement on the Fiscal Year 2011 Budget

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April 28, 2010

Mr. Chairman and Members of the Committee:

I am pleased to present the Fiscal Year (FY) 2011 President's budget request for the National Institute of General Medical Sciences (NIGMS). The FY 2011 budget includes \$2,125,090,000; an increase of \$74,118,000 above the FY 2010 enacted level of \$2,050,972,000, which has been adjusted comparably to reflect HHS proposed transfers.

For nearly a half-century, NIGMS-supported science has advanced understanding of human health and disease. This vital public investment has closed specific knowledge gaps, created powerful new technologies, built community-wide resources that leverage research findings throughout the nation and the world, and helped develop safer, more effective medicines. Decades ago, for example, basic inquiries about how muscles use energy led to the discovery of previously unknown molecules known as protein kinases. Scientists later discovered related kinases that help simple cells divide. The pioneering researchers who made these discoveries were recognized with Nobel prizes. But those prizes are only a proxy for the real value of the research: In this case, more than 10 drugs directed against protein kinases are now available to treat various cancers, and more are in development for cancer and for other diseases. These targeted medicines have revolutionized the care of some types of cancer, improving the lives of many Americans and individuals around the world.

Seeing It All

All living things share a basic set of working parts, and focusing on this unity of biology at the molecular level has contributed greatly to our understanding of human health and disease. Large, cataloging, 'omics efforts—genomics, proteomics, lipomics, glycomics and many others—have let us see many of the parts, including the DNA, RNA, proteins, fats and sugars that make up all the body's organs. While NIGMS-funded teams have made impressive progress—developing new methods and producing extensive inventories—having a complete parts list is only a small step toward understanding how complicated biological processes take place. Systems biology approaches, which promote a more thorough grasp of the intricate and dynamic workings of how the parts interact to make the whole, will be the next intellectual and technological leap for biomedical research.

The NIGMS Protein Structure Initiative (PSI), begun in 2000, has dramatically reduced costs and decreased times for three-dimensional protein structure determination, one important

parts-cataloging effort. PSI investigators have now determined thousands of unique structures. In one example of the utility of these structures, scientists constructed the first complete, detailed map of how metabolism works in a living organism, using 120 experimentally determined structures and 358 structures modeled using ever more powerful computer-based methods. This new knowledge will help explain how our organs process nutrients and drugs, providing crucial information about the building blocks of health and disease. In 2009, the PSI entered a new and exciting chapter: PSI:Biography will climb to the next level by linking a wide range of biologists with the high-throughput capabilities of PSI to explore pressing biomedical questions.

Good Science for Better Health

Americans are eager for information that will help them make intelligent, individualized choices about their health. Toward this end, 10 years ago NIGMS partnered with a number of other NIH components, universities and research institutes to launch an effort to determine how genes affect the way people respond to medicines. The payoff from this investment has been impressive: Studies by the NIH Pharmacogenetics Research Network (PGRN) have shown that genetic information can help predict how heart drugs, cancer medicines, nicotine patches, and a range of other treatments will work in a particular person. This research is contributing to personalized approaches to health care.

For example, in early 2009, PGRN researchers merged data sets from around the world to demonstrate that information about certain genetic variations could aid doctors in determining the proper, personalized dose of warfarin, a blood-thinning drug taken by millions of Americans. This work set the stage for a prospective clinical trial that will test if using such genomic information will make it quicker and easier to get the right dose, as well as whether doing so could prevent serious treatment complications like heart attacks, strokes and internal bleeding.

In another arena, NIGMS-funded research aiming to understand how our genetic material—DNA and RNA—is copied and interpreted by cellular machines earned several long-time Institute grantees the 2009 Nobel Prizes in physiology or medicine and in chemistry. This year's installment of awards recognized pioneering work on telomeres—the “shoelace tips” that cap and protect the ends of chromosomes and on the structure of ribosomes, the cellular factories that create proteins from DNA's blueprint. The findings are being translated to the design of new classes of drugs. Rapidly growing cancer cells require highly active telomerase, the enzyme that makes and preserves telomeres. Clinical trials are under way to test molecules that block telomerase and vaccines that train a patient's own immune system to target telomerase. In addition, many antibiotics target bacterial

ribosomes, and the newly identified structures of the ribosome are facilitating the design of novel ribosome blockers, some of which are now in clinical trials.

Translating Discoveries Into Treatments

NIGMS-supported studies on stem cells continue to unlock secrets about these remarkable cells, having already revealed dozens of factors that appear to play important roles in their ability to be converted into so many cell types. In a surprising and powerful experiment just a few years ago, researchers learned that adding just four of these factors to ordinary skin cells led to the formation of induced pluripotent stem cells, or iPS cells. This discovery has caused a frenzy of interest and excitement in the research and medical worlds. These iPS cells appear to look and act like embryonic stem cells, although further studies are under way to probe these similarities in depth to fully appreciate any differences and their consequences.

Customized cells derived from iPS cells and other types of stem cells could eventually generate replacements for injured or diseased tissues. In the near term, they will be powerful tools to study diseases and drugs in the laboratory, potentially shaving time from clinical trials by allowing more targeted studies of various disease states. In 2010, NIGMS created an important resource for the scientific community by expanding its Human Genetic Cell Repository at the Coriell Institute for Medical Research in Camden, New Jersey, by adding a collection of iPS cells that carry specific mutations.

In a remarkable convergence of knowledge from the study of stem cells and telomerase, NIH Director's Pioneer Awardee George Daley, M.D., Ph.D., recently created iPS cells from people with a rare blood disease called dyskeratosis congenital (DC) known to be caused by problem telomeres. His research shows that reprogramming DC blood cells fixed their ability to maintain healthy telomeres, a first step toward helping these people who typically die of bone-marrow failure. The discovery also highlights the value of supporting highly creative scientists to do cutting-edge research through the NIH Director's Pioneer Award and related NIH programs specifically dedicated to encourage highly innovative and potentially risky research.

The People Behind the Science

We believe that a strong biomedical research workforce is essential for the tandem goals of improving health and maintaining global competitiveness. NIGMS supports about half of all Ph.D.s supported by NIH training grants, and this investment is leveraged by institutions to improve the educational and research environments for all students, not just those supported on training grants. Knowing that science, the conduct of research, and workforce needs continually evolve, NIGMS strives to be sure that its training activities are

effective and up-to-date. By year's end, NIGMS will issue a strategic plan for research training that will guide our future efforts in this arena and will likely inform the activities of other NIH components. Currently, the Institute is gathering extensive input from stakeholders toward creating a strong plan that is responsive to community needs and charts an effective course toward the future.

A strong workforce is a diverse workforce, and NIGMS continually pushes the envelope toward finding effective strategies to boost the numbers of underrepresented groups in biomedical research. Earlier this year, the Institute led an NIH-wide effort that funded 14 grants that will investigate factors that influence the careers of women in biomedical and behavioral sciences and engineering. The new grants will examine many influences on women's careers, such as family and economic factors, institutional environments, and broader social and cultural issues.

We also recognize that another vulnerable population includes researchers relatively early in their careers, who often face daunting challenges to achieving scientific independence and a healthy career trajectory. For several years, NIGMS has co-funded mentoring workshops for new investigators in chemistry. The workshops provide early-stage scientists with practical knowledge on how to write effective grant applications, how to manage people, and how to find and keep mentors. We hope to emulate this successful endeavor for the benefit of other research communities.

Science Without Borders

The biomedical research universe extends well beyond U.S. borders. One way NIGMS improves global health is through the leverage of scientific resources and knowledge. For example, scientists in every country routinely use biotechnology tools that have emerged from NIGMS-funded basic research.

NIGMS also addresses global health in other ways. In recent years, a number of new diseases have emerged and infected people around the world. To help the nation and the world understand and prepare for contagious outbreaks, NIGMS funds the 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. The MIDAS research network remains at the forefront of infectious disease-modeling efforts, and it continues to serve an important role in preparing for possible outbreaks, including various versions of flu. One newly funded project is currently studying resistance to MRSA, the highly drug-resistant version of the bacterium *Staphylococcus aureus*.

In closing, I want to offer thanks for the extraordinary opportunities provided by the American Recovery and Reinvestment Act of 2009. This injection of support has catalyzed progress in many areas of biomedical research that promise economic and health gains in the near term. The Recovery Act has been a show of confidence in the strength of one of our nation's biggest assets—the intellectual capital that generates new knowledge for the nation and the world.

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