

Appropriations Subcommittee Statement on the Fiscal Year 1999 Budget

Open configuration options

March 27, 1998

Mr. Chairman and Members of the Committee: The President in his FY 1999 budget has proposed that the National Institute of General Medical Sciences (NIGMS) receive \$1.115 billion, an increase of \$77.6 million over the comparable FY 1998 appropriation. Including the estimated allocation for AIDS in both years, the total support proposed for NIGMS is \$1.145 billion, an increase of \$79.5 million over the FY 1998 appropriation. Funds for NIGMS efforts in AIDS research are included within the Office of AIDS Research budget request.

I am pleased to present to you the programs of the NIGMS. The goal of NIGMS is to ensure the continuing productivity of basic biomedical research, which has provided the foundation for the astonishing developments we witness daily in the understanding and treatment of disease. In its 35-year existence, NIGMS has supported some of the most significant advances in biomedical science. One reflection of the success of NIGMS-funded research is the number of Nobel Prizes awarded to our grantees. Since 1962, we have supported almost 60 percent of all the American Nobel laureates in chemistry and physiology or medicine. Among these was the award in 1978 for understanding the way bacteria cope with foreign invaders, an esoteric study that would seem to have little practical value. Yet this work formed the basis for recombinant DNA technology, which underlies the biotechnology industry.

From Basic Research to Disease Applications

But we do not have to go back 20 years to trace the contributions of basic research. A number of striking developments have emerged in the past year alone, of which I have time to describe only a few. The examples I have selected all have in common that they began with the examination of a fundamental biological process in an organism other than humans, but quickly revealed applications to human disease. Indeed, the studies were not even done in mammalian organisms, but in much simpler systems such as bacteria, yeast, and the common fruit fly. There are obvious reasons why many biological processes cannot be studied in humans, and the use of these models is based on the repeated observation that many fundamental processes are common to a variety of species. Examining these phenomena in model organisms provides a detailed understanding that can lead to general principles with broad applications. The examples I will give show how studies in bacteria, yeast, and the fruit fly have generated knowledge that can be applied to Lyme disease, neurodegenerative disorders, and cocaine addiction.

The first example is a [study in an unusual bacterium](#) that may lead to a therapy for Lyme disease. The bacterium is part of an esoteric class called archaeobacteria, which are found in a variety of inhospitable locations such as ocean bottoms, hot acid springs, and high-salt environments. One of our investigators was interested in the very fundamental question of how this bacterium carries out protein synthesis, a universal requirement of all living organisms. It appeared that one essential component of protein synthesis was missing in the bacterium, and he was curious to see how the organism survived without it. It turns out that the component is present, but in a form unrelated to that found in all other bacteria and higher organisms. Or almost all. Careful examination of the genomic sequence of the organisms that cause Lyme disease and syphilis showed that in these pathogens there exist compounds with strong similarity to the material found in the archaeobacterium, but these compounds are quite different from those with analogous functions in humans. Scientists could exploit this fundamental difference between a pathogen and its human host to develop new antibiotics to treat Lyme disease. Such antibiotics would attack the compound involved in protein synthesis in the bacterium without damaging this essential process in the human host. Parenthetically, this is but one illustration of the enormous value of having complete genomic sequences of organisms other than humans.

A second example is a discovery in yeast that sheds light on certain kinds of neurodegenerative diseases in humans. This sounds inherently unlikely, and certainly could not have been predicted. After all, even if a yeast cell did have a form of dementia, how would we know? But this relationship between humans and yeast is in the apparent existence of prion-like particles in both organisms. Prions are thought to be infectious protein particles that are implicated in the initiation of so-called "mad cow" disease and other disorders. The 1997 Nobel Prize in physiology or medicine was awarded to the scientist who championed the role of prions in disease. An NIGMS investigator has recently shown that there is a protein in yeast that has many of the same characteristics as the prions found in mammalian brains. For example, the yeast protein generates the same fibers formed by mammalian prions, which are comparable to those found in the autopsies of humans and animals that have died of diseases where prions were implicated. Furthermore, critical interactions with other materials in the cell are exactly the same for the yeast protein and mammalian prions. These studies now provide a model system to investigate an immensely complex problem in a comparatively simple organism, yeast. They even begin to suggest a new target for potential therapies.

Finally, we arrive at the common fruit fly, an organism that has provided us with the opportunity to study many fundamental biological phenomena, particularly in the areas of development and gene regulation. One of our investigators has spent many years studying

fruit fly genes that are involved in the nervous system and in behavior. Comparable genes in humans are involved in depression and other mental disorders, as well as in Parkinson's disease and drug addiction. In the course of his work, the scientist used volatile--or "crack"--cocaine as a tool to stimulate neurological responses in the flies, which led him to observe that flies and mammals respond to cocaine in strikingly similar ways. This time-lapse image shows one such similarity--the circling movement of a single fly following exposure to cocaine. Rodents and primates display similar movement patterns in response to the drug. This, along with other behaviors, suggests that both the fundamental neural pathways involved in cocaine response and the linkage to behavior are retained across species. As a result of this work, the fruit fly now appears to be a very promising model system to examine the genetic and molecular pathways leading to cocaine sensitization, as well as to investigate the pathways involved in a variety of neurological disorders.

It is striking that in all of these examples, health-related applications emerged almost immediately from basic research studies. This is, of course, not the norm for most of the fundamental research studies that we support. And yet, it is not so far from the reality of modern biology. The mosaic of scientific research has expanded to the point at which basic research and its applications follow very closely. It is appropriate to remember a comment made by Louis Pasteur in 1871: "...there does not exist a category of science to which one can give the name applied science. There are science and the applications of science, bound together as the fruit to the tree which bears it." The examples I have given today describe a few such trees and their early fruits.

Tackling Biological Complexity

If the past and the present provided such a bounty of important outcomes from basic research that can be applied to the problems of health and disease, the future promises even more. The incredible volume of detailed knowledge about fundamental biological processes suggests that we may soon be in a position to understand the design principles of living systems. NIGMS has recently held two workshops (New Approaches to the Study of Complex Biological Processes and The Genetic Architecture of Complex Traits) to identify how we can facilitate progress in this difficult research area. Participants in both workshops were unanimous in their opinion that progress will require interdisciplinary approaches. However, a major barrier is the shortage of biological scientists who also have the quantitative and computational expertise that is needed for progress to be made. We are pursuing several approaches to address this shortage. We have already created a program to support [mathematicians, physicists, and engineers in collaborative research projects with NIGMS grantees](#) that are intended to develop new approaches to the study of complex systems.

We are also planning two new training efforts in this area. One will provide individual postdoctoral fellowships to scientists with doctoral degrees in physics, mathematics, engineering, computer sciences, and related areas to allow them to be trained in basic biomedical research. The second will support courses and workshops designed to train biologists in computational and statistical methods.

Another important goal is understanding individual variability in drug responses, a field sometimes described as pharmacogenetics. NIGMS, in collaboration with several NIH institutes, will soon convene a working group of scientists to help us define new research directions in this area. In the meantime, we are collaborating in the initiation of training efforts in clinical pharmacology, a discipline that is critically linked to pharmacogenetics and that has significant shortages of trained personnel.

Training for the Future

We continue our efforts to train tomorrow's scientists and to bring more underrepresented minorities into careers in biomedical research. A new initiative that we are planning for the coming year is to enhance traditional postdoctoral training by promoting the development of teaching skills through innovative programs that involve assignments at minority-serving institutions. We feel that this initiative will provide several benefits. It will be of particular value to the many scientists who during their graduate careers become interested in teaching, but have little or no opportunity to develop those skills. At the same time, it will provide minority-serving institutions with access to individuals who are on the cutting edge of their disciplines, while relieving scientists at those institutions from some of their teaching burden and allowing them time for research and collaborations.

The activities of NIGMS are covered within the NIH-wide Annual Performance Plan required under the Government Performance and Results Act (GPRA). The FY 1999 performance goals and measures for NIH are detailed in this performance plan and are linked to both the budget and the HHS GPRA Strategic Plan, which was transmitted to Congress on September 30, 1997. NIH's performance targets in the plan are partially a function of resource levels requested in the President's Budget and could change based upon final Congressional Appropriations action. NIH looks forward to Congress' feedback on the usefulness of its performance plan, as well as to working with Congress on achieving the NIH goals laid out in this plan.

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