Appropriations Subcommittee Statement on the Fiscal Year 1997 Budget

Open configuration options

April 26, 1996

Mr. Chairman and Members of the Committee, good morning. I am pleased to present to you the programs, progress, and plans of the National Institute of General Medical Sciences (NIGMS).

I listen with admiration and envy to the testimony of my colleagues from the other Institutes. The envy arises from their ability to describe the research which they support in terms that are understandable and of direct meaning to the public--such as heart disease, stroke, and cancer. The research supported by NIGMS ranges from the most fundamental chemistry to pharmacology and physiology and impinges on many different areas of health and disease, but rarely is it immediately related to these areas. Much of the research is done on model organisms, such as yeast or worms, which are unappetizing, or involves isolated molecular systems, that are, to many, incomprehensible. In order to illustrate the widespread influence of this research I would like to provide two examples, one qualitative and one quantitative. The qualitative example is a short story, presented as a case study of the way basic research supported by NIGMS progresses to application.

From Basic Research to Applications

For 28 years, beginning in the early 1960's, NIGMS supported an investigator at Ohio State University who did research on the way metals interacted with chemical compounds. He had no specific interest in biology at all, but we supported him because metals are omnipresent in biological systems, and it was, and is, important to understand their chemistry. In the 1980's, an NIGMS-supported investigator at Johns Hopkins University who was looking at proteins that interact with DNA found a pattern that suggested that zinc was bound to the protein in a specific structural form, called a "zinc finger." In the late 1980's and early 1990's, three groups supported by NIGMS independently determined the three-dimensional structures of some of these zinc-binding proteins, showed that they corresponded to the model earlier proposed, and further showed how the zinc fingers participated in binding to the DNA. About three years later, an NIGMS grantee demonstrated that these zinc fingers occurred in a protein that was found in the human immunodeficiency virus. Within two years, in 1995 (notice how the pace accelerates), a group at the National Cancer Institute in Frederick, Maryland, showed that a class of compounds that bind to zinc could inactivate HIV, and just a few months ago a research team at Parke-Davis Pharmaceuticals demonstrated that removal of zinc was indeed the mechanism for inactivation of the virus. Preclinical studies of a family of related drugs are

now under way. These applications could not have happened without the fundamental chemical, biochemical, and biophysical studies supported by NIGMS over a period of 30 years and more.

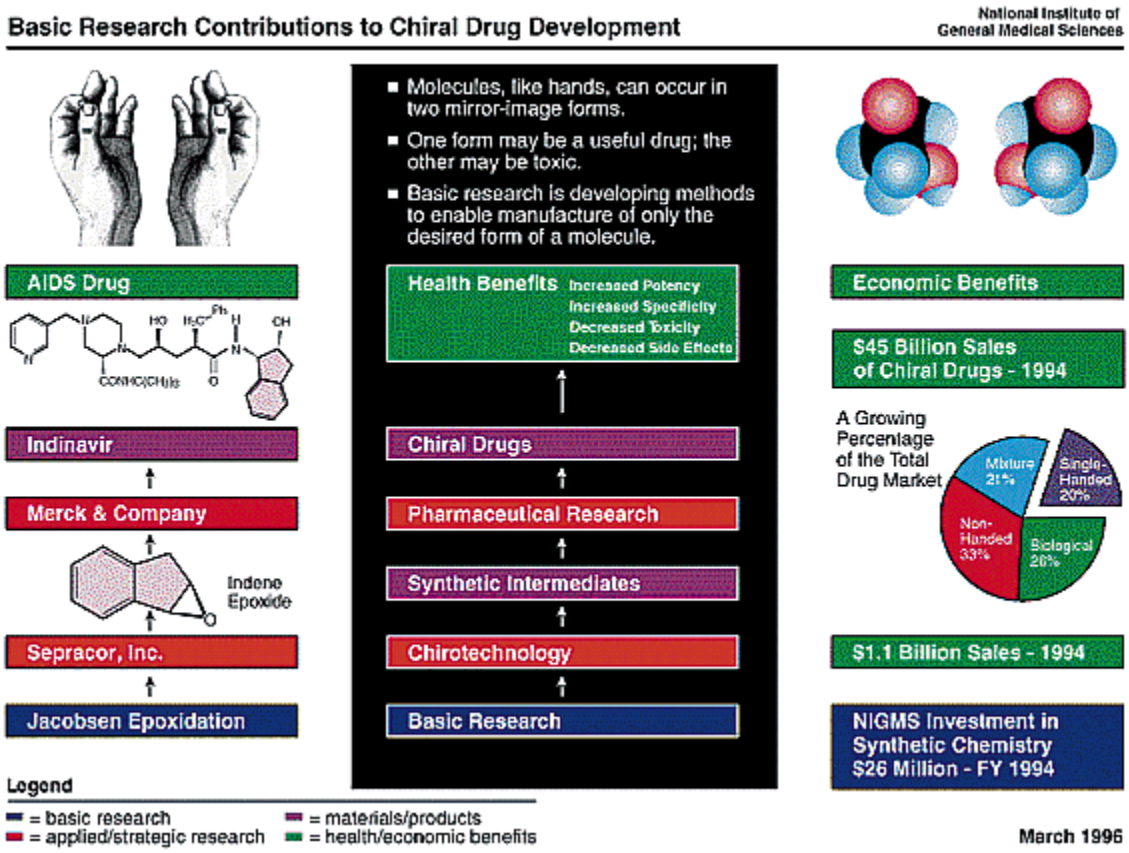
Why has the pace picked up so rapidly in moving the fundamental research to applications? Think of a jigsaw puzzle, with each piece a new discovery. When NIH was just beginning its postwar expansion, most of the jigsaw puzzle was blank, and although each new piece linked up to a few others, the picture was barely visible. The area covered by basic research had very few connections to the applied fields of biology and medicine. Now, 50 years later, we still have many empty areas that need to be filled in, but the expansion of knowledge ensures that each new piece of basic research makes many connections, including connections with medicine and with industrial applications.

Economic Benefits

The quantitative measure of the impact of NIGMS-funded research comes from a look at patents. The primary purpose of NIGMS-funded research is the production of new knowledge, which is very hard to measure. Publications are one index, and patents are another. Both of these measures have limitations, but patents in particular can serve as an indicator of invention and technical change. Intuitively one would expect that an Institute such as the National Institute of General Medical Sciences, which focuses on basic research, would not have a high patent rate. After all, basic research is undertaken "to gain more complete knowledge or understanding of the subject under study, without specific applications in mind," while applied research is considered to be targeted to meeting a specific, recognized need, and it is those specific needs that are reflected in patents.

In fact, NIGMS-supported research has made significant contributions to the practical applications that are reflected in patents. In 1993-1994 alone, 1890 patents cited discoveries made by NIGMS grantees as part of the underpinning of the patent, and this remarkably high number of citations is triple that found only six years before. (This reflects the increased pace of "connectivity" between basic research and applications that I described earlier.) Some 14 percent of all U.S. patents for drugs and medicines in 1994 cited NIGMS-supported papers. Further, the number of NIGMS citations is the second highest of all the Institutes at NIH, and it is the fifth highest when measured against all organizations, including all private organizations. Why have the basic research efforts supported by NIGMS had such a significant effect on practical outcomes as reflected by patents? It is because the effort to understand the fundamental nature of biological systems is closely linked to the desire to find applications for the concepts that emerge. It is important to recognize that basic research and the application of the research are inextricably linked. If the basic research is diminished, so will be the applications.

Increasingly, investigators and their institutions are applying for patents based on their own breakthroughs. I will give one example in the field of organic chemistry. Many chemical compounds exist in two forms, which are mirror images. These are called "chiral" forms. They are analogous to your right and left hands. In nature, only one form usually exists, and drugs are active in only one of the two forms. The other form is either inactive or sometimes can even have deleterious effects. However, when these compounds are synthesized in the laboratory, both forms are usually produced, often in equal quantities. Clearly, it can be of great importance to develop an approach to make only the active form. NIGMS grantees have been working on this for some time, with several recent successes. One such successful approach is now pending issuance of the patent. The fundamental discovery, which we supported, is a chemical reaction named after its discoverer, Dr. Eric Jacobsen, from Harvard University. The process has been licensed to a biotech company, which produced a key molecule that served as an intermediate in the synthesis of a new anti-AIDS drug. This drug is now demonstrating considerable promise in extending survival in individuals with advanced AIDS. This is one specific example of basic research leading to a new industry, chirotechnology, which ultimately leads to a variety of health benefits arising from these new drugs--increased potency of the drug, increased specificity, decreased toxicity, and decreased side effects [see chart].



It is worth mentioning that the industry based on these chiral drugs is growing rapidly. The NIGMS investment of about $26 million a year in all of synthetic organic chemistry helped to generate, in 1994, a chirotechnology industry with about $1.1 billion in sales, and a chiral drug market with $45.2 billion in sales in 1994, an increase of 27 percent over 1993.

I have stressed our contribution through the mechanism of patents because this is an easily measurable and generally accepted indicator of the production and utilization of new knowledge. However, I want to make it clear that patents are only a reflection, and a pale reflection at that, of the contributions that the basic research supported by NIGMS makes to science and society. The broad impact of the research emerging from the laboratories of NIGMS-supported investigators goes far beyond patents, and can be seen in many fields. . .from cancer and genetic disorders to immunology and aging. New ideas have a generative force that can't easily be measured but are widely felt. It is there that the primary contribution of NIGMS exists.

Research Training

As part of our commitment to ensuring the existence of a highly trained workforce, NIGMS has a major involvement in predoctoral research training. This activity is primarily through the means of training grants given to institutions. Our approach was reaffirmed by a recent National Academy of Sciences report as the preferred mode for research training, since "They have been used effectively to meet a variety of national objectives, and they can be tuned to the goal that we [NAS] emphasize: the development and sustenance of locally conceived program innovations that enhance versatility in the graduate population." This describes quite well the intent and practice in the primary mechanism we use to support training. Although we define some quite broad interdisciplinary fields of interest, in other respects we rely on the institutions themselves to define their "locally conceived program innovations" which "enhance versatility." We require of the applicants that the programs be interdisciplinary, that appropriate mentoring is provided, and that the students are permitted to draw from a broad pool of faculty who cross departmental boundaries. We also require a commitment to recruit underrepresented minorities and to insure appropriate training in scientific ethics. Beyond that, we expect, and get, a wide variety of approaches to training.

These programs are limited to a small number of the highest quality institutions, and even at most of those institutions only a small percentage of the graduate population in the biomedical sciences is supported. The intent is to insure the quality of the training, through programmatic requirements and through evaluation of the training faculty and the student populations. The rigorous peer review the applications receive makes them the gold standard for training, and the programs have an effect far beyond the limited numbers of students supported. The success of these programs has been attested to many times, as evaluations have been conducted about once every decade since their initiation and have consistently demonstrated that our predoctoral trainees do better, based on a number of criteria, compared to control groups. A new evaluation of NIH training is now under way, and the first phase is expected to be completed this year.

The commitment that the NIGMS has to training is part of our commitment to maintaining the health of the biomedical research enterprise, as reflected in our concern for bringing a cadre of well-trained new investigators into the research system, both through training and research mechanisms. Our ability to conduct cutting-edge research will not survive for long if new blood is not continually infused into the body of science.

Minority Support

The NIGMS programs that focus on stimulating the involvement of underrepresented minorities in science cover both support for research and for training. Our long-standing training program, and the best known, is the Minority Access to Research Careers, or

MARC, Program. At the request of Congress, we have recently completed an evaluation of this program. We conducted a series of surveys to gather information on the outcomes of the MARC Program. The major conclusions of the report show that students derived significant benefits from participating in this program. For example, the MARC students have pursued and obtained graduate degrees at greater rates than minority bachelor's degree recipients who were not in the program. However, we have not had much effect on increasing the numbers of minority students going on to the Ph.D., either at many of the institutions we support or nationally. It is still a distressing fact that the percentage of minorities receiving the Ph.D. in the biomedical sciences remains at the same low level that it has been for at least the past decade. We are currently expanding our efforts through new initiatives to try and make some headway in increasing the numbers of minority Ph.D.'s by strengthening the capabilities of institutions to recruit and retain qualified students and by enhancing their research and training efforts.

Mr. Chairman, the Fiscal Year 1997 budget request for the National Institute of General Medical Sciences is $936,573,000. I would be pleased to answer any questions that you might have.