NIH Funding: A Roller Coaster Ride?
Priorities If NIH Funding Increases

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Just a few months ago, the American Heart Association (AHA), National Institutes of Health (NIH), and others in the biomedical research community were celebrating the historically large 15% increase in NIH funding for fiscal year (FY) 1999 that the US Congress had proposed and the President had signed into law. The FY 1999 increase was a very positive step on the road to doubling NIH funding by the year 2003, which is why the Administration’s recent announcement that it would request only a 2.4% increase for NIH in FY 2000 is such a shock and disappointment. It is likely that Congress will react this October with a more substantial increase—for FY 1999, the Administration had requested only an 8.4% increase. However, we cannot avoid being concerned and about the message that is being sent to scientists, particularly young researchers, by such a low budget request from the Administration.

The confusing signals from the Administration—the historic 15% increase for NIH in FY 1999 and the proposed 2.4% increase for FY 2000—suggests to young scientists that if they want a career in research, they should get ready for a roller coaster ride. Society needs young scientists for the future, but will they be there—studying the molecular biology of the HIV of 2020, developing a drug to prevent the earliest pathologic changes of Alzheimer’s, or conducting phase 3 clinical trials of another neuroprotectant against stroke? Or, will many of them have left research for more stable career paths?

If we are to stay on course for doubling NIH funding by 2003, another 15% increase for FY 2000 is essential. The FY 1999 NIH funding increase was a $2 billion down payment on the future of our nation’s—and indeed the world’s—health. It is now in Congress’ hands to follow through on the investment.

The research community must also be aware that new research dollars beg important questions. How should NIH, and specifically the National Heart, Lung, and Blood Institute (NHLBI), invest this added money in research? And, how should the AHA work with the NHLBI to ensure that the new influx of dollars means more dollars for promising cardiovascular research?

The AHA’s President has been privileged to represent the organization—and indeed, cardiovascular science—on the SPARK Working Group. Its members are scientists who the NHLBI Director enlisted last year to identify—to “spark”—ideas for research opportunities that should be funded as NHLBI’s budget improves (as it will next fiscal year). On September 19, 1998, in Bethesda, Md, the SPARK group held a conference that included representatives from the American Thoracic Society, the American Hematology Society, and the AHA. Our goal, however, was not for the organization’s representatives to advocate for their respective interests but to step back and look at the whole picture, the whole body, the whole effect of disease, and the whole scope of our research community and what it needs to accomplish to solve the human health problems that are the focus of the NHLBI.

The research theme, or schema, “From Genes to Health and Health to Genes” (Figure), identified 3 areas of opportunity and 5 “enabling” approaches that would be needed for these opportunities to be fulfilled. The areas of opportunity are: tissuegenesis/organogenesis; vascular immunobiology; and gene–gene interactions, functional genomics, and gene–environment interactions. The conference participants divided into working groups on these subjects. Each group developed a list of recommendations for research for the NHLBI. Some overlap exists among the groups’ recommendations; however, almost complete consensus about enabling approaches existed among the groups.

The following sections provide some of my comments about the recommendations on areas of opportunity and enabling approaches.

Areas of Opportunity
Tissuegenesis/Organogenesis
Two main themes emerged in the discussion on tissuegenesis and organogenesis: (1) replacement biology and (2) genes and environment in tissue and organ injury and healing. The group distinguished between tissuegenesis, which was seen as relating to stem cells that lead to definitive parenchymal cells, and organogenesis, which was viewed as being related to the development of whole organs. All organ development was seen as beginning from the stem cell, followed by interaction of the definitive parenchymal stem cell with the extracellular...

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matrix and establishment of blood vessels and blood flow to the developing organ. Research on the fundamental underpinnings of these processes is essential for finding new ways of repairing or replacing diseased or injured tissues and organs.

Studies on the role of genes and the environment in injury and healing would encompass a broad array of diseases, including infection/inflammation/rejection in heart disease (e.g., myocarditis, rheumatic fever, pericarditis, Kawasaki disease, and transplant rejection), atherosclerosis, vasculitis, and reperfusion injury.

Vascular Immunobiology

The explosion of new fundamental knowledge in immunobiology has begun to yield dividends in new approaches to infectious diseases and malignancies, but the opportunities in cardiovascular diseases are unlimited. Thus, disease and thrombosis have many links with the immune system that are just beginning to be uncovered. Understanding the “cross talk” between immunocytes, in particular T cells and macrophages, and target cells in the heart will open up new therapeutic targets.

Another theme common to both immunobiology and organ replacement relates to the realization that the cellular and humoral immune systems are intimately involved in the short- and long-term allograft transplantation of bone marrow, the heart, and the lungs. Specific directives to define more clearly the unique problems involved in heart, lung, and bone marrow transplantation, such as graft versus host disease and bronchiolitis, should result in new therapies and improved survival of transplanted organs.

Gene-Gene Interactions, Functional Genomics, and Gene-Environment Interactions

Gene-gene interactions (functional genomics) were viewed as a way both to combine the sequence information, tools, reagents, and technologies developed and stimulated by the Human Genome Project and combine these items with the rich array of research approaches that define pathways and mechanisms to develop a better understanding of the complex processes of abnormal and normal function.

The special challenge of genetic and environmental interactions responsible for complex diseases requires special investment. Funding should be devoted to recruit, ascertain, and characterize appropriate pedigrees or populations to map and characterize disease genes (and modifier and susceptibility genes) and to understand the influences of environmental factors responsible for phenotypic variability. The working group cited sudden cardiac death as an example of a cardiovascular disease that could benefit from this research because recent population studies indicate that familial inheritance plays a larger-than-realized role in the incidence of lethal ventricular arrhythmias and that underlying susceptibility factors remain unexplained by conventional risk factors.

Enabling Approaches

Progress depends heavily on a blend of diverse enabling approaches. These include genomics with automation-processing technology, computational biology, and other emerging technologies (including a variety of imaging tools), as well as access to population resources and the expanded use of large-scale clinical trials by the NHLBI. However, I would like to emphasize the enormous importance of training and of the development of clinical research networks and “virtual centers” of research.

Training and Securing Careers

An increase in pay-lines could significantly increase the numbers of scientists and, thereby, alleviate existing concerns about the adequacy of the future pool of research personnel. The NHLBI could make more long-term commitments while ensuring more accountability by monitoring the progress of each scientist. In addition to supporting training programs that are multidisciplinary, involve multiple mentors, emphasize translational research, and perhaps lead to an additional degree, NIH should develop a new grant mechanism for promising young scientists. The new mechanism could emphasize the investigator over the project and be reviewed by multidisciplinary teams so that innovative multidisciplinary research would be recognized. Conference participants also suggested that research and training needs should be combined to provide opportunities for retraining some scientists and ensure exposure to both basic and clinical research areas. It could also be structured to allow trainees to move from one site to another and, again, encourage development of a multidisciplinary approach to biomedical research.

Clinical Research Networks and “Virtual Centers”

Whether local or national, clinical research networks would promote integration of all active work in a particular area of science and be an effective way to gather adequate numbers of patients with rare diseases and participants for gene mapping and population-based studies. Use of the Internet to assist with the operation of the networks should be encouraged; it could not only assist in training but also provide remote access to expertise, such as image analysis.

Virtual, multidisciplinary centers without walls, defined by research areas and expertise, would be cooperative and established by having the NIH pick the goals for the center
and then allowing scientists to compete for funding. Such a concept could readily accommodate new scientists and pilot projects on new ideas. One way of developing such centers would be to permit individual applications for infrastructure grants that could be used to support the development of resources. As a result, the center may have gene array technology accessible in one geographic location and population studies coordinated at another. A major advantage of this approach is that the various infrastructure components developed for the center could be used for other purposes as well. Scientists could be permitted to apply for individual research project grants so that they could become a member of an ongoing team linked through computers, not geography. Large resource cores that could be offered through the center approach include repositories, animal models, informatics, sampling, differential displays, and a central database for gene expression. Suggested themes for the centers include chemical biology, vascular biology, and functional genomics.

Within the context of clinical research networks and virtual centers, a national registry of acceptable animal models, especially transgenic and gene knockout mice for heart, lung, and blood disease, and centers to develop and distribute them, should be established by the NIH. Experts on developing animal models could be attracted to heart, lung, and blood diseases by encouraging efforts to generate mutations in new animal models.

In conclusion, cardiovascular scientists and the many members of the public who support the research advocacy efforts of the AHA have had reason to celebrate last year’s historic increase. This October, with Congress’ help, perhaps we’ll be able to celebrate again and take another step toward doubling the NIH’s budget.
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