Modern molecular genetics has revolutionized medical research by providing approaches to determine the location of genes that cause disease, even in the absence of knowledge about the underlying biological defects. These new approaches, when combined with innovative techniques derived from such traditional disciplines as physiology and biochemistry, will have far-reaching effects. Potential benefits include improved methods for presymptomatic diagnosis, carrier detection, primary prevention, and treatment.

The National Heart, Lung, and Blood Institute (NHLBI) has an established record of encouraging and supporting the development of innovative genetic approaches to study monogenic disorders, including cystic fibrosis, familial hypertrophic cardiomyopathy, hemophilia, and sickle cell disease. While continuing its commitment to stimulate and support such efforts, the institute is placing a major emphasis on the use of existing knowledge to devise effective methods of genetic therapy for these diseases. One manifestation of that emphasis is the Working Group on Gene Therapy Approaches and Resources for Heart, Lung, and Blood Diseases, convened by the institute in 1992. Its charge was to identify new opportunities and chart a course for future research efforts.

The working group recognized that several clinical protocols involving gene transfer were already approved and generating data, but they noted the existence of barriers to the further evolution of human gene therapy. Although genetic interventions for heart, lung, and blood diseases may differ in the specifics of the approach, the working group identified common themes in scientific issues and resources fundamental to facilitating development of gene therapy for these diseases.

Two planned NHLBI programs already reflect the influence of the working group's report. Gene Therapy Approaches for Cystic Fibrosis and Other Heart, Lung, and Blood Diseases will promote collaboration within and between research institutions, develop infrastructural resources, and foster the entry of both young and established investigators into the field of gene therapy research. The other, Gene Therapy for Sickle Cell Disease, is directed toward developing strategies to correct or replace the endogenous, defective gene in sickle cell anemia.

The institute also recognizes that many gaps presently exist in our understanding of the more prevalent multifactorial disorders, such as hypertension and asthma, that impose a substantial economic and social burden. These diseases of complex inheritance and phenotype represent a new frontier because they do not follow the classic laws of genetics and because they involve special challenges that make progress difficult. Nonetheless, the remarkable scientific advances of recent years suggest that molecular genetics offers a timely approach that can realistically be expected to pay off within the foreseeable future.

To identify scientific priorities related to the genetic factors involved in the pathogenesis of cardiovascular, pulmonary, and hematologic diseases, the NHLBI convened an Expert Panel on Genetic Strategies for Heart, Lung, and Blood Diseases in 1992. The report of the expert panel provides a master plan that describes major research opportunities and operational strategies for their implementation. It reflects the collective judgment of an eminent group of researchers and critical, independent review by other scientists in the community. Successful implementation of this plan relies on a wide range of scientific disciplines, including genetics, biostatistics, epidemiology, molecular biology, genomics, physiology, clinical medicine, and biochemistry. It is a balanced approach that offers the brightest prospect for the future.

The NHLBI and its advisory council are planning new research initiatives based on the expert panel's report. An institute-wide program, The Mammalian Genotyping Service, is a shared support facility that will enable efficient, rapid genotyping for projects that use genetic linkage analyses, association studies, and mutational analyses to identify genetic determinants of disease. Two other new programs will establish networks that focus on the role of specific genetic mechanisms in the development of disease. For example, the Genetic Determinants of High Blood Pressure program will support collaborative investigators who share technology, data, skills, and biological materials as they delineate the major genetic determinants of high blood pressure. Another program, Specialized Centers of Research on the Molecular Genetics of Hypertension, will engage in mapping and identification of genes responsible for hypertension or its complications, pursue mechanistic studies on the biological consequences of variations in genes linked to hypertension or its complications, and encourage research utilizing molecular genetic tech-

From the National Heart, Lung, and Blood Institute, Bethesda, Md.
niques to elucidate basic mechanisms of normal and altered regulation of blood pressure.

We fully anticipate that a host of new research initiatives on molecular genetics will emerge in the coming years. The institute will continue to call upon its constituents in the scientific community and its advisory council to provide valuable insight and direction as it prepares for the challenges of the future.

NHLBI Programs for Minority Researchers
A Life in Science

Claude Lenfant, MD

The National Heart, Lung, and Blood Institute's (NHLBI) commitment to enhancing participation of minority investigators in the scientific enterprise is clearly demonstrated in the breadth of its training, career development, and related research programs. Increasing the numbers of well-trained minority biomedical and behavioral researchers is an integral part of the mission of the NHLBI. The Institute continues to develop and support innovative approaches to accomplishing this objective.

One such NHLBI effort is the Research Supplements for Underrepresented Minorities (RSUM) program. The program encourages individuals from minority groups that are underrepresented in biomedical research to pursue careers in cardiovascular, lung, and blood research by adding supplemental funds to ongoing research grants to support their research experience. Minorities at all academic levels, ranging from high school students to established investigators, are eligible for the program.

The NHLBI leads the entire National Institutes of Health (NIH) in funding for the RSUM program. It also supports the greatest number of Minority Investigator Research Supplements, the component of the RSUM program that targets individuals who have completed their research training and are capable of conducting independent research projects. Of the 98 minority investigators supported by the NHLBI since we began this program in 1988, 61 had completed their supplement research experience as of March 1993. The limited data currently available to us indicate that the participants have received regular grant support, assumed academic appointments, and published and presented their research results.

As encouraging as these results are, we are concerned that they reflect less than a third of the investigators who completed their research experience under this program. In order to establish a more complete picture of the program, we need the cooperation and assistance of the principal investigators whose reports are missing or incomplete. NHLBI staff are presently contacting those principal investigators to obtain the missing reports and data. Progress reports are important to the institute in that they enable us to evaluate and document the achievements of our programs and, thus, guide their future directions.

A prime example of the utility of program evaluations is the assessment conducted by the Institute of its Minority School Faculty Development Award (MSFDA). The MSFDA was designed to provide faculty members at minority institutions (academic institutions with predominantly minority enrollments) with an opportunity to manage research projects of their own design in collaboration with established investigators. An important finding of the assessment was that a number of MSFDA recipients were subsequently able to obtain additional support to continue their research.

During consideration of the study results the NHLBI, in conjunction with its advisory council, identified the need for a parallel program directed toward minority faculty at nonminority institutions. As a result, the NHLBI issued a 1993 announcement of its new Research Development Award for Minority Faculty (RDAMF) program. Response from the community has been encouraging. It is particularly noteworthy that a significant percentage of the applicants for the RDAMF were participants in the RSUM program.

Since 1988, the institute has regularly reviewed all training grant applications to assess the adequacy of plans for recruitment of minority trainees. Unfortunately, in some cases we have had to defer applications from further consideration because such plans were unsatisfactory. Over the years, we have provided a number of resources to assist the community in achieving recruitment plan goals. To expand these resources and identify additional opportunities, the Institute recently convened a Working Group on Recruitment of Minorities into NHLBI Training Grants. The working group is developing more effective strategies to improve recruitment of minorities into predoctoral and postdoctoral positions supported by our training grants. Its report will be shared with NHLBI-supported training directors and with others upon request.

The institute focuses considerable effort on attracting young people to careers in biomedical research through activities that provide minority students with individual research experiences. One such effort is the NHLBI Minority Access to Research Careers (MARC) Summer Research Training Program. It allows undergraduate students the opportunity to work in the laboratories of intramural NHLBI researchers. Since 1989, the institute has supported a total of 32 participants, most of whom subsequently entered graduate programs in biomedicine. The NHLBI also provides opportunities for similar research experiences in academic institutions.

It should be clear that the success of our efforts with respect to minority investigators hinges on the participation of the entire research community, minority and nonminority. The diversity of the American population is a strength that we must rely on as we prepare for the future.
Molecular genetics of heart, lung, and blood diseases. The shape of things to come.
C Lenfant

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