

THE HOWARD HUGHES MEDICAL INSTITUTE

Purnell W. Choppin, M.D., President

The Howard Hughes Medical Institute (HHMI) is an institution unique in the United States both because of its size, as the nation's largest philanthropy, and because of its organization and mode of operation. HHMI is not a foundation but an operating medical research organization (MRO) governed by different federal regulations than a foundation. As an MRO, HHMI must be principally involved in the direct, active conduct of research by scientists, termed investigators, who are not grantees but employees. HHMI investigators are based at leading medical schools, universities, and research institutes across the country. Though HHMI employees, they are also faculty members of the host institutions with which HHMI enters into collaborative agreements defining the roles and the responsibilities of the partners. In addition to the salary and benefits, HHMI provides investigators with supplies, equipment, and supporting personnel. In many cases, HHMI has provided funds for construction of the laboratories in which the investigators work. Since 1984, it has invested over \$230 million in the construction of new laboratories and over \$30 million in renovation.

HHMI was founded in 1953 by the aviator-industrialist Howard R. Hughes, who had had an interest in medical research since his early twenties. The planning for the establishment of a research institute began in 1949 and culminated in 1953, when Hughes spun the Hughes Aircraft Company off from the Hughes Tool Company and gave it to the newly created research institute. Hughes indicated that he wished HHMI to engage basic research "that probed into the genesis of life processes," and HHMI's charter indicates that the objective was "the promotion of human knowledge within the field of the basic sciences (principally, the field of medical research and education) and the effective application thereof for the benefit of mankind." This remains the primary objective of HHMI.

Initially, HHMI's research operations were guided by a Medical Advisory Board chaired by Dr. Verne R. Mason, a professor at the University of California School of Medicine and Hughes' physician. Dr. Mason was succeeded by Dr. George W. Thorn, a founding member of the board and the first director of research for HHMI. Dr. Thorn has remained associated with HHMI up to the present as a Trustee, serving as chairman of the Trustees until 1990, when he was succeeded by Mr. Irving S. Shapiro.

Although it was founded in 1953, the modern history of HHMI began in 1984 with the appointment of a new group of Trustees who decided to sell Hughes Aircraft Company. The proceeds of the sale concluded in December 1985 created an endowment, which made rapid expansion possible. At the beginning of 1984, HHMI had 54 investigators based in 12 host institutions. Today, there are 278 investigators in 64 institutions. The budget has grown approximately 8-fold since 1984, to \$413 million for this year. The endowment is currently approximately \$8.3 billion.

HHMI investigators conduct research in five areas: cell biology and regulation, genetics, immunology, neuroscience, and structural biology. These areas are broadly interpreted and thus much of basic biomedical research is covered. For example, there is a major effort in developmental biology. Although the focus is on basic biological processes and disease mechanisms, many HHMI investigators are based in clinical departments and carry out disease-oriented research on topics such as AIDS, genetic disease, heart disease, cancer, and neurological disease.

The philosophy of HHMI is to support the careers of investigators, not specific projects. The Institute seeks to identify outstanding scientists, provide them with adequate resources, and give them the freedom to pursue their research goals. Potential investigators are nominated by their

host institutions. They are evaluated for appointment by two levels of review boards, consisting of leading scientists in their fields: a Scientific Review Board, which consists of disciplinary panels in each of the above five programs, and a Medical Advisory Board, which has overall review responsibilities and consists of representatives of each of the program areas. Investigators are appointed for 3- to 7-year terms, depending on their academic ranks. They are evaluated periodically for reappointment, and there is no limit to their length of service as an investigator as long as they are producing outstanding research. HHMI investigators are outstanding scientists: five have been awarded the Nobel prize, and 53 are members of the National Academy of Sciences.

Periodically, HHMI announces a competition in which nominations for investigators are solicited widely from research institutions. The most recent competition, completed in 1994, resulted in 44 new appointments, increasing the number of investigators by about 20%. It is anticipated that such national competitions will be the primary mode by which investigators will be appointed in the future.

The primary activity of HHMI is research carried out by its investigators, and until 1987 that was the only way the HHMI could make expenditures under the existing interpretation of federal regulations. In 1987 HHMI reached an agreement with the Internal Revenue Service that allowed it to make an important expansion in its activities. The items in that agreement included the ability of HHMI, after it has expended in a given year 3.5% of its endowment in the conduct of research by its investigators, to spend above that amount by giving grants, fellowships, or scholarships to individuals or institutions. As mentioned above, the support of education is a stated objective in HHMI's charter. However, educational activities were previously limited by the employer-employee relationship requirement. The new flexibility in the 1987 agreement made possible major initiatives in education. Through a variety of grant programs, HHMI now supports science education at every level, from elementary school through high school, college, graduate school, and postdoctoral fellowships. The grants program budget for this fiscal year is approximately \$81 million.

Thus, in the MRO mode HHMI investigators carry out biomedical research at the cutting edge of their fields, and the grants programs are designed to insure that there are succeeding gen-

erations of well-trained scientists to do the research of tomorrow. In addition, the investment in science education at all levels should help to enhance the level of science literacy in the general population.

The largest single program is support of college undergraduate science education. Since 1988, 213 colleges and universities have received approximately \$290 million in grants, and applicants are now being evaluated for an additional \$43 million. Significantly, about 20% of these grants to colleges and universities are being used for precollege outreach programs. In addition, grants are also provided to medical schools, museums, and related institutions such as aquaria, botanical gardens, and zoos for precollege science education programs. There are major fellowship programs for medical student research, predoctoral fellowship for Ph.D. candidates, and postdoctoral fellowships for physician scientists. HHMI also supports science courses at Cold Spring Harbor Laboratory and the Marine Biological Laboratory at Woods Hole. In addition, it provides funds to the Jackson Laboratory to support its mouse collections, particularly transgenic animals.

This year HHMI announced a new \$80 million, 4-year program for medical schools to provide flexible institutional support for their research programs at a time when these institutions are under increasing constraints with regard to funds from federal sources.

The one component of the grants program that is not devoted to education is an international research scholars program in which research grants are provided through a competitive review of outstanding scientists in selected countries, including Canada, Mexico, Australia, New Zealand, and the United Kingdom. The most recent competition involved 10 countries in Eastern Europe and the Former Soviet Union; 90 scientists have recently received awards in those countries.

The headquarters of HHMI are located on a beautiful 22-acre campus in Chevy Chase, Maryland, which was completed in 1993 (Fig. 1). The headquarters are the seat of all administrative, scientific, financial, and legal activities, including management of the HHMI endowment. The complex includes a conference center that is used extensively for scientific meetings of HHMI investigators, and topical workshops involving HHMI and other scientists from the United States and abroad. The conference center is also used by various review panels that evaluate HHMI investigators or applications for the grant programs, as



FIG. 1. The Howard Hughes Medical Institute, Chevy Chase, Maryland

well as for meetings of program directors of grants projects, for example, the undergraduate education program. The conference center, which includes residential rooms where participants stay during meetings, is in a serene, wooded setting. It is the scene of many exciting

and informative meetings in which new collaborations are constantly being formed. By providing the means to bring together investigators and others associated with HHMI's far-flung operations, the conference center insures that HHMI is greater than the sum of its parts.