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## 2000

### Gerald Fischbach

As Director of the NIH National Institute of Neurological Disorders and Stroke, Gerald Fischbach directs the \$1 billion, 1,000-person federal agency that is responsible for federally funded research on the brain and nervous system. The Institute supports research by investigators in public and private institutions across the country, as well as by scientists working in 23 intramural laboratories and branches at the NINDS.

Born in New Rochelle, New York, Fischbach's family moved to Mt. Vernon, New York when he was five. His parents were first generation immigrants who were "strong, wonderful influences" for him and his older sister, Joan. "They saw academics as both a high ideal and as a road to success. They were relentless in what they expected of us."

Always interested in analyzing situations and solving problems, mathematics and chemistry seemed natural fields of study in college; Fischbach earned his A.B. from Colgate University in 1960. Even though his college years did not provide much hands-on lab experience, his desire to do biomedical research was strong.

In the early 1960's, Fischbach recalls, medical school was the common route for someone interested in biomedical research, so he followed that course, earning his M.D. in 1965 from Cornell University Medical School. He took a year off during medical school to do lab research on steroids and steroid binding proteins in the blood, laying the groundwork for his focus on laboratory research.

After an internship at the University of Washington, Fischbach began his research career at the National Institutes of Health in 1966. "The NIH was wonderful in those years. It had great science, was very interactive, and had a wonderful peer group. I thought I would stay for two years and then go into neurology, but I stayed for almost eight. It was here that I really began what turned out to be a lifelong interest in synapse formation and synaptic plasticity," reflects Fischbach.

The NIH was followed by nearly a decade on the faculty of Harvard Medical School. In 1981, Fischbach and his family moved to St. Louis where he served as Head of the Department of Anatomy and Neurobiology at Washington University School of Medicine. Of his time at Washington University, Fischbach says, "we spent ten wonderful years in St. Louis. They had a great tradition in neurological sciences. It was a very interactive environment."

In 1990, the Fischbachs left St. Louis to return to Harvard Medical School where he became Chairman of the Neurobiology Departments at Harvard Medical School (the first department of neurobiology in the country) and Massachusetts General Hospital before returning to the NIH as NINDS Director in 1998.

Comparing the NIH of the 1960's with the NIH of the new millennium, Fischbach characterizes frankly the earlier iteration as more impressive, more of a "mecca for biomedical researchers." He reflects that "there is great potential for unfettered research here [at the NIH], but I think it's time for renewal of the intramural program. There are real islands of excellence that everyone will agree on, by any criteria, but my own view is that it's not uniformly excellent and really could be... more focused and mission oriented. In the '60's, it was a very uniformly excellent environment, very interactive, and there were very fundamental discoveries being made."

Of course much of the challenge of the NIH's diminished profile is of its own making: the NIH has seeded so much outstanding research in universities and elsewhere across the country that the consequent explosion of growth in research-intensive academic programs and development of biotechnology firms has attracted much of the Nation's best talent elsewhere. This wealth of alternatives for outstanding training and work environments for scientists was not nearly as available for researchers in the 1960's as it is today.

Fischbach sees effective biomedical research as a partnership among government, the biotech industry and academics. "Research funded by the NIH and performed at the NIH is the engine that is driving all of biotechnology and industry. NIH investigators need the expertise in industry to develop and really focus on the implications and the applications of some of their discoveries. I'd like to see that facilitated," comments Fischbach.

ASCB President Richard Hynes says of Fischbach, "Gerry Fischbach has an outstanding reputation, both as a leading scientist and as an academic and administrative leader — he has built first-rate departments in several places. He has breadth, insight, good taste and an ability to deal well with people."

Throughout his career, Fischbach has studied the formation and maintenance of synapses, the junctions between nerve cells and their targets through which information is transferred. He has been particularly interested in the neuromuscular junction, a synapse that is easily accessible to experimental manipulation. He pioneered the use of cultured neurons and muscle cells to characterize the biochemical, cellular and electrophysiological mechanisms underlying development and function of the neuromuscular junction.

Beginning in the 1970's, Fischbach embarked on a search for molecules released by motor neurons that regulate the number of acetylcholine receptors on muscle cells. This work culminated in 1993 with the purification and cloning of the ARIA (acetylcholine receptor-inducing activity) protein that stimulates synthesis of acetylcholine receptors by skeletal muscle cells. This molecule is now known to be a member of a family of trophic factors called neuregulins that are thought to be involved in a variety of important developmental processes in the nervous system. Because ARIA and other neuregulins act by binding to tyrosine kinase receptors on target cells, Fischbach's work was key to demonstrating that synaptic development relies upon biochemical mechanisms that are broadly similar to those that underlie the action of nerve growth factor and other well known trophic molecules. Even now, Fischbach's NIH lab remains active; its current focus is on trophic factors that influence synaptic efficacy and nerve cell survival.

Fischbach met his wife, Ruth, while they were students at Cornell: Ruth was at the Nursing School while he was a student at the Medical School. After they were married and raised their four children, Ruth returned to school where she earned a Masters degree, and later a Ph.D., in medical sociology. Her work has focused on the doctor/patient relationship and end of life issues, including pain management, advance directives and privacy. Today, Ruth Fischbach is building on her work at Harvard in the early 1990's by serving as Senior Advisor to the NIH Director on biomedical ethics.

The next generation Fischbachs are spread across the country: daughter Elisa Grayer is a mother of two living in Manhattan; son Peter Fischbach is a pediatric cardiologist doing clinical and disease-oriented research at the University of Michigan; son Mark Fischbach is an architect who is starting his career in Philadelphia, and Mark's twin, Neil Fischbach, is a physician-researcher currently serving an oncology fellowship at UCSF. Free time for the senior Fischbachs, such as it is, is spent visiting their children, reading, playing tennis, and relaxing at their vacation house in Woods Hole, Massachusetts.