

Robert W. Mahley, M.D., Ph.D.



BIOGRAPHICAL SKETCH

Robert W. Mahley, M.D., Ph.D., an internationally known expert on heart disease, cholesterol metabolism and, more recently, Alzheimer's disease, is president of the J. David Gladstone Institutes, director of the Gladstone Institute of Cardiovascular Disease, and professor of pathology and medicine at the University of California, San Francisco (UCSF). He is a member of the prestigious National Academy of Sciences, the Institute of Medicine, and the American Academy of Arts & Sciences.

After receiving his B.S. from Maryville College (Maryville, Tennessee) in 1963, he went on to complete his medical and doctorate degrees at Vanderbilt University in 1970 and a pathology internship in 1971. Following his training at Vanderbilt, he joined the staff of the National Heart, Lung, and Blood Institute at the National Institutes of Health, and in 1975, he became head of the Comparative Atherosclerosis and Arterial Metabolism Section, Laboratory of Experimental Atherosclerosis. In 1979 Dr. Mahley was recruited by the Gladstone Trustees to San Francisco to create the Gladstone Institutes, and he founded the Gladstone Institute of Cardiovascular Disease.

As president of the J. David Gladstone Institutes, Dr. Mahley has been instrumental in guiding the growth of the institutes with the addition of the Gladstone Institute of Virology and Immunology in 1992 and the Gladstone Institute of Neurological Disease in 1998. Most recently, he has worked with the Gladstone Trustees to build a new laboratory facility that now houses all three institutes and allows for future expansion and scientific growth at the Mission Bay campus of UCSF.

Dr. Mahley is a member of many scientific and professional societies, including the American Heart Association, the American Society for Biochemistry and Molecular Biology, the Society for Neuroscience, the American Society for Clinical Investigation, the Association of American Physicians, the International Academy of Pathology, and the American Association for the Advancement of Science. In addition, he serves on the editorial boards of several scientific journals.

RESEARCH ACCOMPLISHMENTS

For 25 years, his research has focused on the structure and function of apolipoprotein (apo) E, specifically its critical role in cholesterol homeostasis and atherosclerosis and, more recently, in Alzheimer's disease and neurodegeneration. ApoE regulates the clearance of plasma lipoproteins by mediating their binding to lipoprotein receptors. His laboratory described apoE's ligand function, determined its protein and gene sequences, mapped the amino acid residues involved in receptor binding, defined the three-dimensional structure of the ligand-binding domain, and identified mutations that established its role in the pathogenesis of type III hyperlipoproteinemia. Along with others, his studies contributed to understanding the mechanisms through which the new class of drugs, called statins, can lower blood cholesterol levels.

Understanding the structure and function of apoE laid the groundwork for the recent explosion of studies concerning apoE4 and Alzheimer's disease. Dr. Mahley's laboratory was involved in describing the role of apoE in peripheral nerve regeneration, lipid transport in the nervous system, and cytoskeletal stability and neurite extension and remodeling. By establishing brain-specific apoE transgenic mice, he demonstrated detrimental effects of apoE4 on the central nervous system in vivo. A goal of his research is to develop a drug that will block the detrimental effects of apoE4 in neurodegenerative disorders.

For the past 15 years, he has directed an epidemiological study that has defined the major risk factor for heart disease in Turkey—genetically determined low levels of plasma high-density lipoproteins. The discovery has served as an impetus for developing guidelines for a national cholesterol education program in Turkey and has wide implications for healthcare in the United States and worldwide. The genetic nature of this disorder is under investigation.