Hugh O. McDevitt 1930–2022

On 28 April of this year, the immunology community lost one of its pillars. Hugh O. McDevitt, MD, Professor Emeritus of Microbiology and Immunology at Stanford University's School of Medicine, passed away at the age of 91, depriving us of one of our foundational scholars, researchers and educators.

Hugh was born in 1930 in the small town of Wyoming, Ohio, the youngest of five children. His father was a prominent urologic surgeon who introduced him to the medical world at a young age, encouraged him to pursue medicine as a career and had an important influence on his trajectorial choices. Hugh was an undergraduate student at Stanford University, where he obtained a bachelor's degree in biology in 1952. It was during this time that he was introduced to experimental research in a serious way, performing genetic studies on fungal recombination. This early imprinting of a genetic mindset was to color his studies on immune responsiveness in the years to come. Hugh went on to earn a medical degree from Harvard University Medical School in 1955. Choosing to specialize in internal medicine, he did residencies at Peter Brent Brigham Hospital in Boston and Bellevue Hospital in New York. A subsequent two-year stint in the army, as a military physician stationed in Japan, solidified his desire to pursue medical research. He performed postdoctoral work with Albert Coons at Harvard Medical School and subsequently with John Humphrey at Mill Hill in London, where his interest in immunology became irresistible.

In 1966, Hugh was hired as an assistant professor at Stanford, where he spent the remainder of his career. In addition to running a world-class research program and teaching graduate students, he served as chief of the Division of Immunology and Rheumatology, director of the Clinical Immunology Laboratory, and chair of the Department of Microbiology and Immunology, at various junctures. He retired, to become an emeritus professor, in 2008.

Reflective of the importance of his scientific contributions, Hugh was accorded a number of accolades, including election to the US National Academy of Sciences, the US National Academy of Medicine and the Royal Society of London. He received the Paul Ehrlich and Ludwig Darmstaedter Prize, the Jessie Stevenson Kovalenko Medal, and the Lita Annenberg Hazen Award for Excellence in Clinical Research.

Credit: Stanford Medicine

Much of Hugh's scientific trajectory was aligned to major histocompatibility complex class-II (MHC-II) molecules, from their first identification as genetic traits of mysterious nature to fine mapping of the amino-acid sequences that confer susceptibility to autoimmune diseases. He was one of the giants of the 1960s who demonstrated the importance of MHC molecules, not merely as beacons of graft rejection but, more fundamentally, as anchors of immune responses. These studies were the foundations of several Nobel prizes. While a fellow with John Humphrey, and collaborating with Michael Sela, Hugh discovered that an '*Ir*' genetic locus conditioned the antibody response of inbred mouse strains to (TG)-A-L and similar synthetic polypeptides. Then, at Stanford, he tried in vain to map the trait to immunoglobulin or other loci, in particular by transferring splenocytes between high-responder strains and low-responder strains. These transfers were frustrated by rejection or by graft-versus-host disease; Lee Herzenberg suggested that he use MHC congenic strains to sidestep these issues. But the experimental controls proved to be the answer, showing that responsiveness mapped to the MHC congenic intervals. This discovery established the fundamental importance of variation in MHC-II molecules in epitope selection and the control of immune responses. (In hindsight, it was fortunate that Sela's branched copolymers included anchor residues distinguishable by allelically variant mouse MHC-II molecules.) The purview of MHC molecules was then extended to the control of autoimmune disease with his work on systemic lupus erythematosus in collaboration with Julia and Walter Bodmer. In experiments that foretold antigen presentation by dendritic cells by a couple of decades, Hugh also showed, in parallel with Gus Nossal, that labeled antigen localized mainly to phagocytic cells in naive mice and to germinal center B cells in primed animals. The McDevitt lab was a leading player in the molecular identification of the Ia molecules and delineation of the cells expressing them, using exotic antisera raised by cross-immunization between various congenic mouse strains. One hypothesis was that *Ir* genes encoded the T cell antigen receptor, not an illogical idea, but one that was refuted when Ia antigens were found predominantly on B cells. Molecular cloning, in hot competition with the labs of Lee Hood, Jack Strominger, Bernard Mach and others, clarified some of the hypothetical MHC-II molecules that had been suggested by serology (e.g., I-B and I-J) and established the patterns of allelic variability, perhaps culminating in the identification of key positions in the peptide-binding groove that condition risk for autoimmune diabetes.

Hugh's lab routinely hosted an eclectic cast of international characters, a number of whom went on to be scientific and science policy leaders in their home countries, notably Germany, Japan, France and England. He kept up with his past trainees (now friends), often hosting them at his home in Palo Alto. He fostered a worldwide network that communed at scientific meetings, with one life-changing outcome being an introduction by one of his ex-trainees to his future wife and scientific collaborator, Grete Sønderstrup.

Hugh was a gregarious and down-to-earth individual. He loved to tell Irish jokes, travel, attend the opera and read (including all of the 21 novels in Patrick O'Brian's Aubrey–Maturin series). Hugh is already sorely missed by his family, friends and colleagues, and the sense of loss will only deepen. ❐

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