The Journal of Immunology

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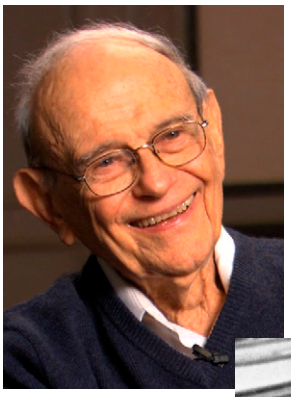
Herman N. Eisen, M.D. (1918–2014) Scholar, Gentleman, and AAI President (1968–1969)

Herman N. Eisen passed away on November 2, 2014, at the age of 96. Herman's contributions to immunology spanned the period from the 1940s to the present—he was working on two manuscripts at the time of his death. He made seminal contributions to our understanding of affinity maturation, specificity of immunological responses, and T cell recognition of peptide–MHC complexes.



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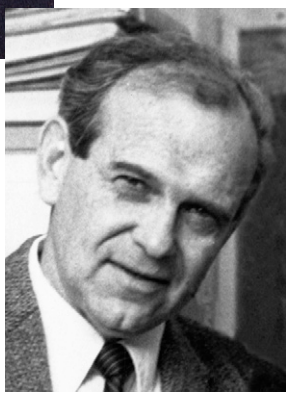

The American Association of Immunologists records, Center for Biological Sciences Archives, UMBC. Photo modified by AAI.

Herman N. Eisen

In the late 1940s, not much was understood about Ab–Ag reactions. Herman made major advances in the field by studying the interactions of Abs with simple molecules such as the hapten benzene arsonate. This approach enabled him to avoid the difficulties in interpreting the experimental findings with complex protein Ags. In 1949, Herman and Fred Karush showed that Ab molecules had two binding sites for Ag—a major finding that led Linus Pauling to write a congratulatory note. During this time, Herman was at New York University, where he continued to make advances such as the contact sensitivity to dinitrofluorobenzene compounds due to T cell–dependent delayed hypersensitivity.

Herman was recruited to the Dermatology Department at Washington University in St. Louis in 1955. He was sought perhaps for his work on contact sensitivity. He ultimately joined the Department of Microbiology and Immunology and became the chair of that department in 1961. Herman's work on immune cell reactions with hapten–protein conjugates while at Washington University led to a very important discovery with Gregory Siskind. By precisely measuring Ab affinity for Ag using fluorescence quenching methods, they were able to show that the affinity of Ab responses to Ag increases with time by several hundred-fold. With Lisa Steiner, Herman subsequently showed that this phenomenon occurred at the cellular level. These experiments demonstrated the process of affinity maturation. Affinity maturation has since been the subject of extensive studies, and we now understand it as a Darwinian evolutionary process that occurs in a short time. Repeated rounds of mutation and selection of B cells in germinal centers results in Abs that bind increasingly more strongly to the selecting pathogen. Vaccines that protect us against a variety of diseases induce affinity maturation processes resulting in potent Abs. Affinity maturation is also mimicked in academic and industrial laboratories for the discovery of Ab-based therapies and protein engineering by directed evolution.

Herman studied myeloma tumors developed by others and found that some, like MOPC-315, produced an Ab that bound DNP and could potentially be a source for mAbs. This work preceded the discovery of hybridomas by Georges J.F. Kohler and César Milstein by about ten years. Herman's work on Abs also revealed two features that captured his interest again in the last decade of his career: the heterogeneity of Ab affinities generated by affinity maturation and the specificity and degeneracy (polyspecificity) of Ab–Ag reactions.

In 1973, Herman was recruited by Salvador E. Luria to be a founding member of the Cancer Center at the Massachusetts Institute of Technology (MIT). At MIT, Herman focused on the T cell arm of the immune system and proceeded to make major contributions. Herman's laboratory isolated a CD8 T cell clone called 2C. 2C recognized an allogeneic class I MHC molecule as well as a syngeneic MHC molecule. Work done with the 2C system allowed Herman to shed light on the plasticity of the recognition of peptide–MHC complexes. His group also reported that activated CD8 T cells could kill a target cell bearing a single peptide–MHC complex. Other scientists used the 2C system to understand thymic development as well as to crystallize the first TCR–pMHC complex.

Herman served the field of immunology in many ways. He wrote the immunology chapter in *Microbiology,* edited by Bernard Davis, which was the standard textbook for microbiology and immunology students for many years. He also served as president of the The American Association of Immunologists (AAI) from 1968–1969, after having served as a councilor (1963–1968). He continued his service to AAI following his term as president, serving on numerous committees between 1969 and 1998, and as an Associate Editor (1968–1974) and Section Editor (1987–1989) for *The Journal of Immunology.*

In 1989, university rules for mandatory retirement at age 70 required Herman to retire from MIT faculty. For several years, however, as emeritus, he maintained an active laboratory that continued to make important discoveries. Even after closing his laboratory around 2005, he continued to

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work closely with several MIT colleagues on scientific problems and publish papers.

Herman was deeply respected by his scientific colleagues. His integrity was legendary. If one were to paraphrase many comments received from immunologists upon hearing of Herman's passing, the dominant sentiment was that a giant of a man and a giant in immunology was no longer in our midst. David Baltimore noted "Herman was a pioneer immunologist who never lost his joy of discovery. His calm and generous exterior cloaked a deep passion to understand immunity."

Herman's scientific accomplishments led to many honors, including his election to the National Academy of Science, the Institute of Medicine of the National Academies, the American Academy of Arts and Science, and the AAI Lifetime Achievement Award in 1997.

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