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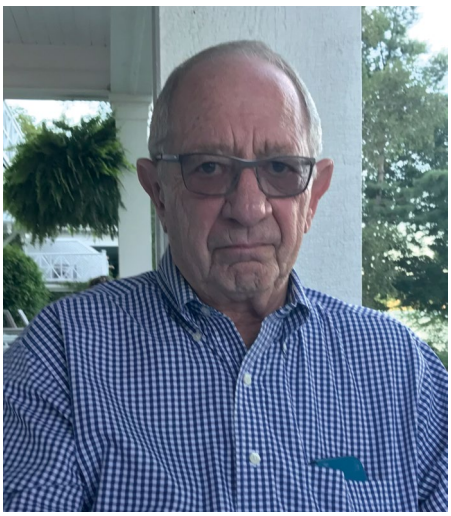
Stuart Schlossman (1935–2023)

By Christopher E. Rudd

We mourn the loss of Stuart Schlossman, the outstanding and impactful pioneer of human T cell immunology. Born in Brooklyn, New York, Stuart peacefully passed away on 13 August 2023, in Palm Beach Gardens, Florida. During his productive career, Stuart made many seminal contributions to basic science and translational medicine, revolutionizing the landscape of human immunology. He completed his medical degree at NYU College of Medicine in 1958 followed by formative training in Elvin Kabat's laboratory at Columbia University and then fellowships at Washington University and the National Institutes of Health (NIH), before joining Harvard Medical School in 1966. His initial independent work defined the diversity of immune responses to antigens in guinea pigs. In 1973, Stuart became the chief of tumor immunology at the Dana-Farber Cancer Institute, and in 1990 he became the inaugural Baruj Benacerraf Professor of Medicine at Harvard until his retirement in 2006. He played a pivotal part in formulating fundamental principles in T cell immunology and laid the foundation for ground-breaking immunotherapies.

Monoclonal antibodies were first produced by George Kohler and Cesar Milstein in 1975, and provided Stuart with the tools to unleash his subsequent research. The discovery led to a 'gold rush' of antibody research worldwide. However, Stuart had the special insights that identified key receptors such as CD2, CD3, CD4, CD5 and CD8, which are central to T cell immunity today. His antibodies were assigned identical CD numbers by the Human Leukocyte Differentiation Antigen Workshops, an international collaboration that he co-founded. Furthermore, his pioneering work catalyzed flow cytometry into a sophisticated investigative and diagnostic tool for immune pathologies.

Together with Ellis Reinherz, his laboratory described the first anti-human CD3 monoclonal antibody as well as clonotypic antibodies that defined clonal diversity among human T cells. Importantly, together with Cox Terhorst's lab, they then characterized the multimeric human T cell receptor (TCR) complex. In addition, his lab developed the first anti-human CD4 monoclonal antibodies that were crucial



in identifying the loss of this subset in individuals living with HIV. Then, with Reinherz and Stefan Meuer, Stuart outlined the human CD4 and CD8 link to helper and cytolytic functions, as well as restriction to HLA class II and I molecules, respectively. These concepts stand as fundamental cornerstones of immunology. He received numerous accolades, including induction into the National Academy of Sciences and the Robert Koch Award.

As a leader, Stuart created an international epicenter of immunology in Boston, which molded generations of aspiring immunologists. His first mentees were translational physicians, including Reinherz, Jerry Ritz, Jim Griffin, Lee Nadler and Ken Anderson, leading to the first antibodies to common acute lymphocytic leukemia antigen (CALLA, now known as CD10), and CD19 and CD20 on B cells. They further pioneered the use of monoclonal antibodies in treating refractory immune cell disorders that heralded rituximab and biosimilars for treating conditions such as non-Hodgkin lymphomas, acute lymphocytic leukemia and other cancers.

Subsequent generations included more fundamental immunologists such as Tom Tedder, Chikao Morimoto, Paul Anderson, Eric Vivier and myself. Tedder became a world leader on B cells, Morimoto on T cell subsets, Anderson on mRNA translation, while Vivier was first introduced to innate receptors in Stuart's division. My own group defined how tyrosine kinases and adaptors are regulated by the TCR and coreceptors to stimulate T cells. Attendance at Stuart's weekly divisional meetings was de rigueur, and included trusted collaborators such as Norman Letvin and David Hafler who used Stuart's antibodies to interrogate AIDS and multiple sclerosis, respectively. Stuart had initial quandaries about PhDs, at one point declaring that 'there was nothing a PhD could do that an MD could not'. However, within a decade, his division was recruiting mostly high-level, specialized science PhD graduates as faculty. He eventually became concerned about the ability of the clinical community to compete with in-depth science in modern medicine. Stuart also pioneered academic collaborations with pharmaceutical companies such as Coulter Corp and helped to conduct some of the earliest human immunotherapy trials using ricin-modified monoclonal antibodies.

Stuart had a colorful personality, was instinctually insightful, often outspoken with an ironic sense of humor and proudly identified as a libertarian with a touch of eccentricity. With Stuart, one embarked on a rollercoaster ride, not always for the faint-hearted, but thrilling for others, a ride that shaped many careers. He also had several mysterious fixations, such as an ongoing concern about human versus mouse immunology. Without fail, our one-to-one 'scientific meetings' would lead to a spirited parley about one political event or another. I appreciated his shared love for debate and witnessed Stuart's 65th birthday celebration with hundreds of former mentee professors and institute heads in attendance. He was also keenly loyal to his staff, including Herb Levine in flow cytometry, and Felice Coral, an oncology nurse managing immunotherapy trials, while his passion for wines led to his proud induction into the Confrérie des Chevaliers du Tastevin.

With the retirement of long-term colleague Baruq Benacerraf, Stuart showed a growing interest in a more balanced life. He once sadly remarked to me, 'In 5 years, everyone will have forgotten our names and contributions'. Despite a shift at the Dana-Farber Cancer Institute from immunology to molecular oncology, in the 2000s, in a remarkable twist of irony, cancer research was again impacted by immunology with groundbreaking clinical results of immune checkpoint blockade against inhibitory receptors on T cells that changed the face

of cancer therapy. Gordon Freeman's seminal work on the inhibitory ligand PD-L1 began in Stuart's division, and our signaling motifs are used today in chimeric antigen receptor (CAR) T cell therapy. Stuart's lifelong work as a giant of human immunology continues to revolutionize cancer therapy worldwide and will not be forgotten.

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