

Emil Raphael Unanue 1934–2022

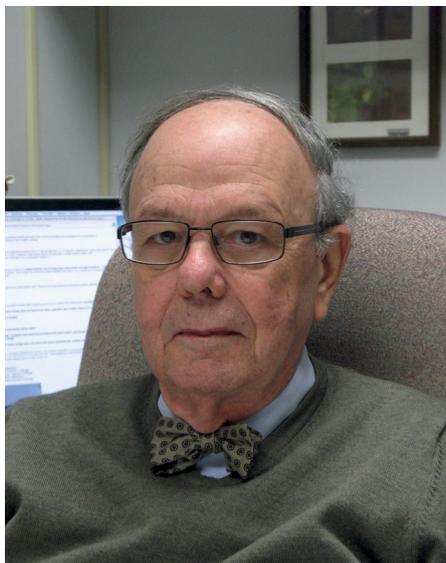
By Robert Schreiber & By Andrey Shaw

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Dr Emil Raphael Unanue, the Paul and Ellen Lacy Professor of Pathology and Immunology at Washington University School of Medicine in St Louis, died on 16 December 2022 from glioblastoma. He was 88 years old. Emil was an extraordinary scientist, whose work reached well beyond his own domain of immunobiology and influenced many other biological fields, including cell biology, microbiology, neurobiology, and genetics. We have lost a giant, whose work ethic and personal philosophy of “excellence in science” have had a profoundly positive influence on countless numbers of today’s successful biologists.

Emil was born in Havana, Cuba, in 1934 and obtained his MD degree in 1960 at the University of Havana School of Medicine. He emigrated to the USA in 1960 to receive residency training in pathology at Presbyterian University Hospital in Pittsburgh, Pennsylvania. In 1962, he joined the group of Dr Frank Dixon, a renowned immunopathologist, and moved with the group to the Scripps Clinic and Research Foundation (now the Scripps Research Institute) in La Jolla, California. There, Emil pioneered animal models of immune complex glomerulonephritis.

In 1966, Emil was awarded a fellowship to join the laboratory of Dr Brigitte (Ita) Askonas in the unit headed by Professor John Humphries at the National Institute for Medical Research at Mill Hill in London. There, he was encouraged to work on macrophages and their role in inducing antibody responses. At the time, the prevailing view was that macrophages ingested proteins and pathogens and digested them completely to their component amino acids (and other monomeric constituents). How this ingestion of pathogens by macrophages could induce an antigen-specific immune response was not known. Emil and Ita first made the important observation that the immune recognition of protein antigens required the lysosomal function of macrophages, and then went on to show that the antigens were only partially digested, suggesting that fragments of the protein antigen were important in promoting adaptive immunity. These observations set the stage for his eventual discovery of antigen processing and presentation.



Emil returned to Scripps in 1968, and in 1970 was recruited by Dr Baruj Benacerraf to the Pathology Department of Harvard Medical School. Emil quickly rose through the ranks to become the Mallinckrodt Professor of Immunopathology in 1974. While at Harvard, he made important observations about the process of receptor capping in B lymphocytes, and on the mechanisms of macrophage activation needed to protect mice and humans against microbial infections. This latter work culminated in the seminal discovery of antigen processing and presentation, whereby protein antigens are partially degraded, and certain protein-derived peptides are presented on the surface of macrophages bound to receptors encoded in the major histocompatibility complex (MHC). His demonstration, together with his colleague Dr Paul Allen, that peptides bind directly to an MHC molecule explained the long-standing conundrum of self-MHC restriction—the requirement of T cell antigen receptors to recognize self in order to recognize foreign.

Upon assuming the position of Mallinckrodt Professor and Chairman of the Department of Pathology (now the Department of Pathology and Immunology) at Washington University Medical School in 1985, Emil proceeded to build what would become a world-class immunology community. At the same time, he continued his efforts to define the mechanisms underlying antigen presentation in greater

detail, with a special focus on type I diabetes. Emil’s work established the molecular basis for key immunological questions such as immunologic specificity, thymic education, transplant rejection and autoimmunity.

This enormous body of work won Emil international recognition and multiple national and international research awards and honors. These included his election into the National Academy of Sciences (1987), the American Academy of Arts and Sciences (1989), and the National Academy of Medicine (1995). Among his most prestigious awards, Emil received the Albert Lasker Basic Medical Research Award in 1995, the Gairdner Foundation International Award (Canada’s highest scientific award) in 2000, and Germany’s Robert Koch Gold Medal in 2005. Other awards included the Marie T. Bonazinga Research Award of the Reticuloendothelial society (now the International Cytokine and Interferon Society) (1986), the William B. Coley Award for Basic Research in Immunology from the Cancer Research Institute (1989), the Rous–Whipple Award from the American Society for Investigative Pathology (1998), the Lifetime Achievement Award from the American Association of Immunology (2014), and the Sanofi–Institut Pasteur Award, International Senior Category (2015). In recognition of Emil’s discoveries in identifying the basic mechanisms underlying the pathogenesis of type I diabetes, he was awarded the Gerold Grodsky Basic Science Award from the Juvenile Diabetes Research Foundation in 2018.

Yet, even as his research successes continued, Emil never lost sight of the importance of teaching and mentoring generations of students, postdocs, and junior faculty. The Graduate Program in Immunology that he created at Washington University has a 35-year legacy of populating both academia and industry with holistically trained immunologists who are thought leaders. Very much hands-on in his style, Emil was often seen demonstrating experimental techniques at the bench. Despite his busy schedule, he showed by example the importance of educating, by carrying a major load in the teaching of graduate students and medical students. He was a frequent visitor to the offices of his junior and senior faculty to provide advice and to hear and critique their scientific work. If asked, he never hesitated to read and make insightful suggestions on their

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research grants. He instilled in the immunology community a commitment to carry out high-level and impactful science, not only through his directness but also by reminding them to always ask whether their scientific queries were “vertical or horizontal research”. Many who trained with, or were mentored by, Emil now hold senior positions at institutions around the world, including Washington University, and would be the first to acknowledge that their interactions with Emil contributed directly to their ultimate successes.

Emil was multidimensional – a true Renaissance man. He was a highly literate individual who read widely in both English and his native Spanish, could quote Marquez and Saramago from memory, and enjoyed exchanging favorite novels with his friends. He loved classical music and particularly opera. He attended

and supported opera globally and frequented performances not only in St Louis but also in New York, Santa Fe and Glyndebourne, UK, making a special effort to visit opera houses in cities that he visited for meetings. He enjoyed taking groups of uninitiated faculty members to the opera. Emil was also unabashedly liberal in his political leanings and was not afraid to express his views, no matter the company.

His love of, and dedication to, science was matched only by his love and dedication to his family and friends. Emil leaves behind his wife of 58 years, Marianne; his three children, Marie, Rachel and David, and their partners; and six grandchildren whom he adored. He also leaves a large community of trainees and colleagues, whom he mentored but also to whom he extended his deep and lasting friendship.

We have lost a titan of science, whose breadth and depth and understanding of life will be hard to replace. Although he is gone, the lessons he taught us will continue to stimulate us to be the best scientists that we can be. We can only hope that those whose lives he has so profoundly influenced can collectively keep driving the field of immunology forward and thereby honor his memory. He will be sorely missed.

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