



William E. Paul

1936–2015

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William E. Paul, the ‘immunologist’s immunologist’, whose research career spanned almost 50 years, witnessing and contributing to the development and maturation of immunology from a descriptive and empirical field to a modern rigorous cellular and molecular discipline, passed away after a brief illness on 18 September 2015. Bill received his MD from the State University of New York, Downstate Medical Center, in 1960; obtained postgraduate training at Boston Medical Center; and was a Clinical Associate at the Endocrinology Branch of the National Cancer Institute during his first stint at the US National Institutes of Health (NIH). He then was a research fellow and instructor in the Department of Pathology at New York University School of Medicine from 1964 to 1968, where he first engaged in immunological research under the tutelage of Baruj Benacerraf. Bill then accompanied Benacerraf to the Laboratory of Immunology of the National Institute of Allergy and Infectious Diseases, in Bethesda, Maryland. Following Benacerraf’s departure in 1970, he was appointed the laboratory chief at age 34, the youngest such chief at the NIH, a position that he held without interruption (occupying the same office) until his death. In addition to guiding the laboratory, which had been established by Jules Freund in 1960, Bill simultaneously served as Director of the Office of AIDS Research and Associate NIH Director for AIDS Research from 1994 to 1997.

Throughout his tenure at the NIH, Bill maintained a highly productive research program and played a major role in training an extraordinary number of post-doctoral fellows who assumed leadership roles worldwide. He served as president of the American Society for Clinical Investigation (1980–1981) and of the American Association of Immunologists (1986–1987), was elected a member of the National Academy of Sciences, USA, in 1982, was on numerous editorial and advisory boards, including the board of the *Annual Review of Immunology* (1982–2001), and shepherded a major advanced textbook, *Fundamental Immunology*, through seven editions from 1984 to 2012.

His research contributions highlight the diversity of his interests and include the mechanism of immune-response gene function and major histocompatibility complex restriction, the definition of type 1 and type

2 thymus-independent antigens, the role of membrane immunoglobulin D and immunoglobulin M, the identification of cytokines that regulate B cell and T cell differentiation (in particular interleukin 4), the regulation of immunoglobulin class switching by cytokines, and the production of cytokines by basophils and mast cells. A central theme of his latest work was the characterization of the transcriptional control of helper T cell differentiation and the definition of the feedback mechanisms that function in T cell homeostasis, relating those functions to autoimmunity and immunodeficiency. He demonstrated the central role of interleukin 1 in the population expansion of primed CD4⁺ and CD8⁺ T cells and addressed questions of innate inactivation of the adaptive immune system. He had a long-standing interest in how immunological responsiveness is modulated at the cellular level by a ‘tuning’ phenomenon. The breadth of these accomplishments reflects not only his ability to sense the developing directions of contemporary immunology research but also his facility in synthesizing disparate aspects of immunological molecular and cellular function.

To those who worked closely with him, through interactions during hundreds of laboratory meetings and seminars, Bill would always direct the probing question, frequently pointing out a critical flaw in the work or the presentation. Despite such sharp focus, his queries were invariably delivered gently and were aimed at the science, not the person. Despite working in a field dominated by descriptive and qualitative assays and interpretation, he always strove to develop and encourage quantitative understanding of complex biology. His scientific advice and guidance were frequently sought by colleagues within the NIH and elsewhere. His contributions were often not just supportive but also critical to improving the science involved and never required co-authorship.

Given his broad grasp of not only immunology but also biology, medicine and history, it is indeed ironic that he succumbed to acute myelogenous leukemia, a disease whose cellular and molecular underpinnings he understood very well. He will be sorely missed by those who worked with him on a regular basis, as well as all those who benefitted from his academic and administrative gifts, but his teaching and example will continue to inspire.

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