

# William E. Paul

## (1936–2015)

A leading force in immunology.

William Erwin Paul was a major contributor to the development of modern immunology. He helped to transform cytokine biology, the study of small proteins involved in cell signalling, from crude assessments of uncharacterized cellular 'factors' into a science involving precise quantitative molecular analyses. He also elucidated the mechanisms controlling the production of antibodies — proteins that recognize and bind to specific antigens such as bacteria and viruses — and provided insights into how antigens are recognized by T cells, a type of white blood cell.

Paul, who died on 18 September, was born in 1936 in Brooklyn, New York. He prided himself on the fact that his higher education was at public rather than private institutions. He obtained his undergraduate degree in 1956 from Brooklyn College and his medical degree in 1960 from the State University of New York's Downstate Medical Center, also in Brooklyn. While at medical school, he married Marilyn Heller.

During a two-year medical residency at Massachusetts Memorial Hospitals (now Boston Medical Center), Paul worked on amyloidosis, a rare disease that occurs when a protein called amyloid builds up in tissues. This led to his first paper, in *Nature*. More than 600 publications would follow.

Paul joined the US National Institutes of Health (NIH) in 1962. While working in the endocrinology branch of the National Cancer Institute in Bethesda, Maryland, he helped to establish that a chemotherapy drug called methotrexate was extremely effective in treating women with choriocarcinoma, a cancer that usually occurs in the placenta. He also helped to develop radioimmunoassays for hormones — *in vitro* techniques used to measure hormone levels in the blood. These studies were just a prelude to the real blossoming of Paul's research career.

Paul had developed a strong interest in immunology as a student. He recounted in a memoir that he was smitten by "a slender volume of essays by Michael Heidelberger, the father of quantitative immunochemistry", which he had read while riding a tram in Brooklyn. Paul sought advice from colleagues on the best places to train in immunology, and in 1964 joined Baruj Benacerraf's group at New York University in New York City.



(Benacerraf later won the 1980 Nobel Prize in Physiology or Medicine for his work on the genetics of the immune response.)

Paul moved with Benacerraf to the NIH in 1968. When Benacerraf left to become chair of pathology at Harvard Medical School in Boston in 1970, he encouraged the appointment of Paul as his successor. Paul remained chief of the Laboratory of Immunology at the National Institute of Allergy and Infectious Diseases until his death.

Under his leadership, the lab emerged as a premier centre of immunology research. This was a result of both Paul's remarkable scientific accomplishments and his astute guidance of the department. He gave both support and independence to those he recruited to faculty positions (myself included).

Paul is best known for his research on the cytokine interleukin-4 (IL-4), which he discovered with Maureen Howard, a post-doctoral fellow in his laboratory. He went on to show how the cytokine both helped to mobilize the body's defence mechanisms against parasitic worms and played a part in the production of allergic symptoms. He also mapped out the IL-4-dependent signalling pathway, the genetic control of the cytokine's expression and the factors that prompted certain types of T cell to produce

it. This all-encompassing and rigorous approach became the prototype for studies on immune-system cytokines.

Paul's impact on science and health went further. As the first director of the NIH Office of AIDS Research from 1994 to 1997, he set the agenda for research on HIV/AIDS in the United States. As Mark Harrington, executive director of an advocacy group called the Treatment Action Group, noted, Paul's work led to "the emergence of highly active antiretroviral therapy, which is now being taken by over 15 million people around the world and is responsible for saving millions of lives and preventing millions of infections".

Paul headed up several societies and served on innumerable advisory panels, prize committees and editorial boards. For 31 years, he served as editor of the *Annual Review of Immunology*; for much of that time, it was the most cited publication in biomedicine. He was also widely known for his textbook *Fundamental Immunology*, first published in 1984.

Bill was highly respected for being both a scholar and a gentleman. He could find flaws in any seminar he attended, but when asking questions, he made the speaker feel as if they were being praised, not skewered.

He remained his optimistic, ebullient, engaged self to the end. Only weeks before his death, he was calling colleagues to discuss ongoing research; attending to his roles as mentor, colleague and administrator; and completing his book *Immunity* (Johns Hopkins Univ. Press; 2015), in which he explains to a lay audience how the same system that defends the body can also cause autoimmune diseases.

His intellectual strength, encyclopaedic knowledge and laser-like focus on science — rather than on scientific politics — were unique. Friends, colleagues and immunologists around the globe mourn his passing. ■

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