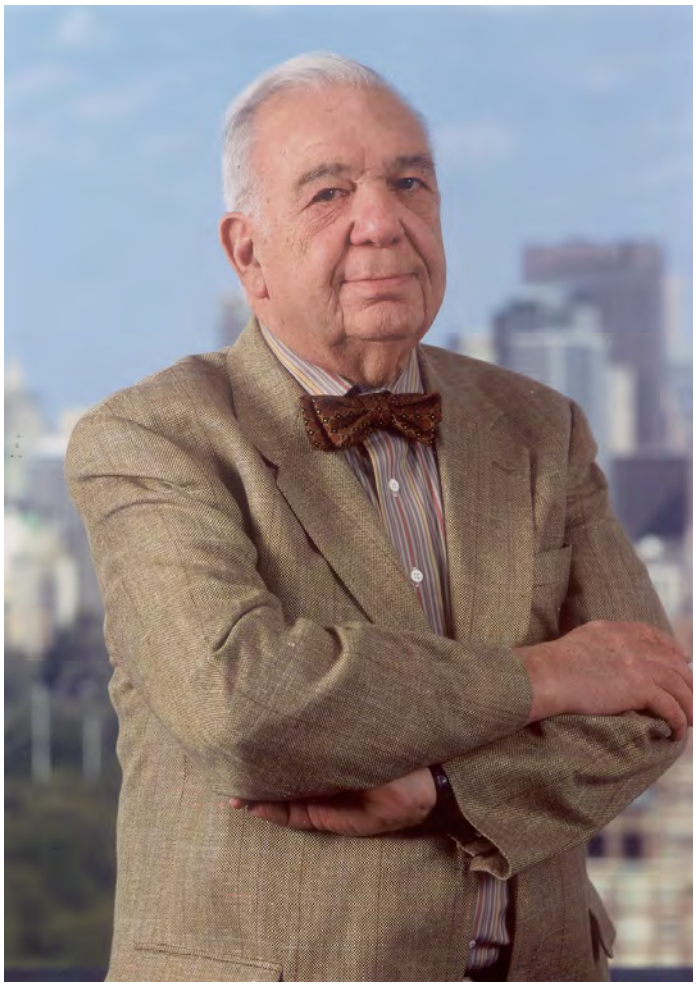
THE FACULTY OF MEDICINE
Harvard University

Fred Saul Rosen



Fred S. Rosen, M.D., a world leader in pediatric immunology and the first James L. Gamble Professor of Pediatrics, died on May 21, 2005, a few days short of his 75th birthday. His career was marked by his devotion to his patients, by his talent for converging seemingly disparate scientific and clinical information in developing novel therapeutic approaches to their diseases, and by his unwavering dedication to supporting the careers of young colleagues. His life's work is measured not just by his remarkable intellectual contributions and service to his patients, but by the multitude of medical and graduate students, pediatric residents and fellows, and clinical and scientific colleagues whom he inspired. Indeed, his death occurred a day after an international symposium was held in Boston in his honor. Scores of his colleagues from around the world attended and many of them came to his bedside to bid him farewell. He knew they were there and why they had come. They knew it, also.

Fred was born in Newark, New Jersey, the only child of Phillip and Amelia (Feld) Rosen. He received his college education at Lafayette College, which later awarded him an honorary degree, and his medical school training at Case Western Reserve University Medical School, where he developed his lifelong interest in the mechanisms of defense against infections.

After medical school, Fred undertook an internship in pathology and then a residency in pediatrics at Children's Hospital in Boston. There he met Charles A. Janeway, then the Chief of the Department of Medicine, who was equally interested in susceptibility to infectious diseases. The two established a collaboration that resulted in deep explorations of the inherited disorders that cause severe susceptibility of children to infections. Except for a two-year period of service at the National Institutes of Health in the midst of his residency, Fred spent the entire 50 years of his academic life at the Children's Hospital and later at the Center for Blood Research Institute for Biomedical Research (CBRI) and Harvard Medical School. The immunology laboratory at Children's Hospital, led by Fred from the mid 1960's to the mid

1980's, soon became a lodestone for trainees from around the world, and Fred ultimately became a leading figure in the World Health Organization's efforts to define the complex "immunodeficiencies" that illuminate the mechanisms by which humans and animals ward off infectious organisms. After 30 years at the helm of this endeavor, his decision to move from his role as Chief of the Division of Immunology at the Children's Hospital to assume the Presidency of the CBRI was, in many ways, another example of his devotion to and respect for Charles A Janeway. Dr. Janeway had always hoped that Fred would assume a position of responsibility at the CBRI, an organization that Dr. Janeway had fostered out of respect for his own mentor, Edwin J.Cohn, the founder of the Protein Foundation that became the CBRI.

The author of more than 300 scientific papers, Rosen focused his research on the pathogenesis of primary immune deficiencies that afflict children, such as Wiskott-Aldrich syndrome, Bruton's agammaglobulinemia, the multiple severe combined immunodeficiency syndromes and the various complement deficiencies. He also developed bone marrow transplantation as a treatment for these congenital defects. He was instrumental in defining and understanding the molecular basis of several of the primary immunodeficiency diseases and pioneered methods of treating them, including the use of intravenous gamma globulin therapy. A tireless and totally committed investigator, he had, at the time of his death, two ongoing National Institutes of Health–funded grants for the study of cytoskeletal organization in blood cells and the signaling pathways that regulate the development and function of lymphocytes.

Thus Fred was a quintessential translational clinical investigator with one foot firmly planted in the laboratory and the other by the bedside. He often threw himself into areas beyond his own expertise if he thought he could make a contribution. His work on the Kawasaki Syndrome is a perfect example. He inspired a team of clinicians and basic scientists to work assiduously on that still arcane disease and promoted studies of its treatment with immune gamma globulin that proved extremely valuable.

Fred was a tireless scientific talent seeker. He was particularly skillful in the art of inveigling basic scientists to become deeply interested in clinical disorders and persuading them to lend their considerable skills in the unfolding of basic mechanisms of human disease. Much of the enthusiasm of the basic scientists came from the pleasure of working with Fred and interacting with his critical mind. He also swept talent into the Children's Division of Immunology and the CBRI. It is no accident that one of his trainees, Raif Geha, succeeded him as Division Chief after an exhaustive international search had proven that he was the best person for the job and that Fred Alt succeeded him as Scientific Director of the CBRI. In a recent testimony to Fred, Raif Geha described him as follows: "Fred Rosen was a unique man who connected with people of all backgrounds and races. And Fred Alt stated that "Fred Rosen essentially single-handedly built the institute (CBRI) into one of the premier immunology and inflammation centers in the world."

Fred was an outstanding academic tactician and an effective leader for the Department of Pediatrics at Harvard Medical School. His multi-decade tenure on the Executive Committee was maintained by five Chairs of the Department at Children's Hospital and three Chairs of the Department at the Massachusetts General Hospital. All of them valued Fred's high scholarly standards and his insistence on excellence when promotions were under consideration. He had an uncanny ability to make a shrewd assessment of both the scientific accomplishments, psychological strengths and weaknesses and promise of a candidate, which he would promptly summarize in pithy (and often witty) statements that cut through to the essence of the person. He was unprejudiced and open-minded about people and his assessments

were not ruled by notions of political correctness.

He was a tireless mentor of young investigators, particularly of young women who were struggling to combine a medical career with family life. Many of the present Children's Hospital and CBRI faculty members owe their careers to him.

Fred was also an indefatigable supporter of immunology research at Harvard Medical School. The recent creation of the Jeffrey Modell Immunology Center in the quadrangle is a testimony to his deep commitment to the field at Harvard that was initiated by Baruj Benacerraf, one of Fred's closest friends and admirers. Fred was at the heart of the "Committee on Immunology", the loose association of basic scientists and clinicians that defined the Harvard Medical School "department" of immunology. In the early years of the Committee, the Harvard Medical students had only a handful of role models for the seamless integration of this science in clinical practice. One of the immunology MD, PhD students from that period, Robert Sackstein, commented that "Fred's knowledge was encyclopedic; he knew all that was known and all that needed to be known. The consummate teacher-physician-scientist, he was PUBMED incarnate well before PUBMED existed."

Although Fred was devoted to the science of immunology and received many honors and awards for his own research including membership in the Institute of Medicine of the National Academies and the American Academy of Arts and Sciences and the first Dana/American Association of Immunology prize for career-long accomplishment, his most powerful attachment was to his young patients. He was absolutely committed to the solution of the devastating illnesses that assailed them. The development of intravenous gamma globulin treatment for the management of children born with an inability to make the protein was perhaps his greatest therapeutic contribution. Before this development, those patients usually died in their teens. Now many are enjoying successful careers; at least one, John Girard, has become a physician. Girard stated, "We wouldn't have survived from then until now without Dr. Rosen." John's brother, William, recently stated,"His rapport with his patients was extraordinary. He was so incredibly bright. He could make diagnoses that would stump others just hearing the symptoms on the phone."

Professor Walter Gratzer at the Guy's Center in London was one of Fred's close friends. He eruditely described him. "Albert Szent-Gyorgi viewed the practice of science as 'seeing what everybody else has seen and thinking what nobody else has thought'. This was Fred's supreme gift, and his capacity to discern an interesting, important, and, above all, soluble problem attracted a succession of talented and percipient colleagues, all eager to take up the challenges that he defined, and with all of whom he worked closely."

Fred had countless friends and associates around the world, but among his best friends were his friends' children. He never married, but he solved the problem of family life by borrowing all those children, many of whom at times preferred his company to that of their own parents. He understood children and truly enjoyed them. He loved their games and joined in them with complete abandon. He openly supported their teenage rebellions from their parents and never revealed a secret. They loved him deeply long after they themselves married and had their own children. One such child, Deborah Nathan Charness, a flutist and mother of three, described her relationship with Fred. "When we were growing up, we could go to Fred with our problems. His breadth of knowledge was formidable. He was the original Google."

Fred Rosen was a true polymath. His mind was ever active as he relentlessly pursued knowledge in every sphere. He was a superb physician-scientist; a brilliant writer and conversationalist; a collector of antique furniture and silver; a polylinguist who learned French, Italian Spanish, German and Italian, then additionally taught himself Arabic and Russian; a constant attendee at Chekov plays in English and Russian; an expert needle pointer who presented gifts of elegantly fashioned cushion covers, footstools, vests, wall hangings and piano bench covers to his friends and admirers; an omnivorous reader of literature in seven original languages; a talented producer of Seville orange marmalade; and an inveterate traveler. Though he did not play an instrument himself he was deeply devoted to classical music and was a generous supporter of musical institutions in Boston and New York. His fondness for grand opera, particularly the Ring Cycle, induced him to travel to opera performances around the world.

Above all Fred Rosen was a sparkling character, a wise advisor and a steadfast and generous friend ready to discuss any intellectual issue with a firm opinion and an uproarious sense of humor. All this and a venerated physician, scientist, teacher and mentor. All who had the pleasure of the company of this most unique human being will sorely miss him.

David Nathan, MD, *chair*
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Stephen Harrison, PhD
Judy Lieberman, MD, PhD
Frederick Lovejoy Jr., MD
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