Michael Frank, MD, passed away with his family at his side on Thursday, August 1, 2019. Dr Frank was born in Brooklyn, New York, in 1937. In one of his recollections, he pointed out that his interest in immunology began before he was 10 years old when he read Paul de Kraif’s Microbe Hunters. This early fascination set the stage for his lifelong interest in how antibody and complement control microorganisms and contribute to tissue damage. Mike’s brilliance and potential were recognized early on when he received a Ford Foundation Scholarship to attend the University of Wisconsin–Madison at age 15 years. There he met the microbial biologist and future Nobel Laureate Joshua Lederberg. Lederberg suggested that Mike get a PhD in microbiology; however, Mike decided to go to medical school. He graduated from Harvard Medical School in 1960 and did an internship in medicine at Boston City Hospital and later an internship in pediatrics at Johns Hopkins. Mike came to the National Institutes of Health (NIH) for 2 years, working in the laboratories of Herb Rapp and Tibor Borsos in the National Institute of Mental Health, where he discovered the dependence of complement components on divalent cations and their sensitivity to reducing agents.1 Mike then spent a year at the Mill Hill Medical Research Laboratories in London, England, where he worked with Dr J. H. Humphrey, studying the distribution of antigens in draining lymph nodes, the structure of IgM, and electron microscopic imaging of complement lysis of red cells.

Mike returned to the NIH as a senior investigator and quickly became Head of the Clinical Immunology Section in the Laboratory of Clinical Investigation at the National Institute of Allergy and Infectious Diseases (NIAID). In 1977, he was appointed Clinical Director of the NIAID and Chief of the NIAID’s Laboratory of Clinical Investigation, positions he held for 13 years. It was during this time that Mike began the groundbreaking work for which he is best known. He collected a cohort of patients with hereditary angioedema (HAE), which at the time had a mortality rate of 20%. In a series of landmark articles, he identified multiple strategies to treat HAE caused by C1 esterase inhibitor deficiency using epsilon-aminocaproic acid,2 fresh frozen plasma, the androgen derivative danazol,3 and C1 inhibitor concentrates.4-6 Said John Atkinson, “Mike was largely responsible for the development of two successful therapies for HAE at a time when we had no treatment.” His approach became used worldwide for prophylaxis and for treatment of acute HAE attacks.

Working with Baruch Benacerraf, Ira Green, and Lenny Ellman, Mike’s laboratory identified C4 deficiency in the guinea pig, a model in which there was no detectable classical complement pathway function. John Atkinson noted, “I joined Mike Frank’s laboratory at a great time.” Mike’s model provided many insights into the role of alternative versus classical complement pathways in immunopathologic settings. These insights delineated the function of complement and Fcγ receptors in human subjects; Mike showed in animals and then in human subjects that IgG-sensitized red blood cells are removed by Fc receptors in the spleen. In another landmark study he demonstrated impaired Fc receptor–mediated clearance in patients with systemic lupus erythematosus and dermatitis herpetiformis7,8 and performed a prospective study of serum sickness in patients treated with antithymocyte globulin9; the latter provided an in-depth immunologic analysis of a disease identified in the early 20th century. Reflecting on his experience, Tom Lawley said, “Mike was a wonderful person and a great mentor.” Mike also identified impaired immune responses of splenectomized patients to pneumococcal vaccination.10 Tony Fauci summed up Mike’s years at the NIH, saying, “It was such a pleasure to have Mike as a...
colleague for so many years at NIAID. He was an extraordinarily creative basic and clinical investigator and a devoted mentor to so many future stars in biomedical research.” An NIAID colleague, Warren Strober concluded, “Straightforward, sturdy and serious; you know where you stood with Mike Frank. The perfect complement to NIAID.”

Mike was recruited to be Chair of the Department of Pediatrics at Duke, where he served from 1990 to 2004. Rebecca Buckley noted, “In the 14 years he was Chairman, Mike accomplished an amazing number of things, including doubling the number of faculty, building a new Children’s Health Center (for which he had to raise all of the money through his Pediatric Development office), improving enormously the fiscal situation in the department, and advancing the level of NIH research funding in the Department so that we were ranked 10th in the nation among pediatric departments in that regard.” Duke Children’s Health Center is widely regarded as a top children’s hospital and remains a legacy to his perseverance and drive.

Mike was a consummate physician-scientist. He followed his childhood dream spurred by de Kraif’s book and substantially advanced our basic understanding of the biology of the complement system. Equally important, he contributed substantially to treating HAE and understanding complement and Fc receptors in human subjects. Throughout his career, Mike was a wonderful mentor to many young investigators who have gone on to major leadership roles in academia. John O’Shea pointed out how fortunate he was to be in Mike’s laboratory, learning serious biochemistry with a group of dedicated rigorous scientists. Notably, the American Academy of Allergy, Asthma & Immunology Foundation recently honored his life’s work with the creation of the Michael M. Frank, MD, FAAAAI, Lectureship.

Another NIH colleague, Dean Metcalfe, summed it up as follows: “Mike was a true gentleman with unrivaled sincerity and compassion for medical education and research and will be greatly missed.” John Gallin echoed these sentiments: “Mike set a very high bar for excellence in science for everyone around him. Those of us who collaborated with Mike benefited tremendously from his extraordinary insight and talent. It was a privilege to work with him.”

John O. Atkinson, MD
Thomas Lawley, MD
Dean D. Metcalf, MD
Warren Strober, MD
Rebecca H. Buckley, MD
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