Obituary

Elvin A. Kabat (1914–2000)

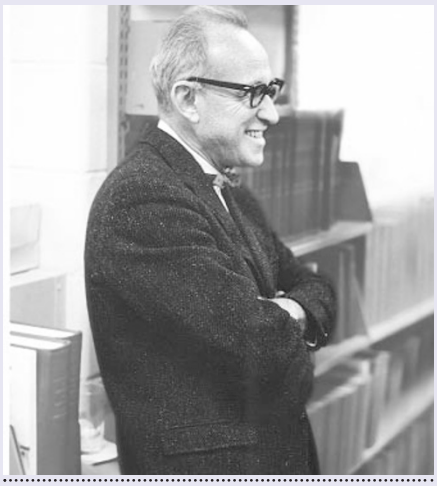
Elvin A. Kabat, who died on 16 June 2000, was a founder of modern immunochemistry. A man of great forthrightness and acerbic wit, he set the standard for immunological science for more than three decades.

Starting with his predoctoral work with Michael Heidelberger at Columbia University in New York, from 1933 to 1937, Kabat was a student of carbohydrate chemistry. He had a career-long interest in the structure and immunochemistry of blood-group substances, and determined the chemical basis of the ABO blood groups. This work, along with that of Walter Morgan and Winifred Watkins in Britain, laid the foundations for our current understanding of carbohydrate 'differentiation' antigens (cell-surface structures that vary according to developmental stage or tissue type) and their roles in cellular interactions.

Carbohydrate chemistry later allowed Kabat to analyse the binding properties of antibodies. Dextran — a polysaccharide found in yeast and bacteria, but not humans — was being used as a blood plasma substitute at the time. In 1951, after showing that dextran produces an immune response in humans, Kabat and his students started to use a series of oligosaccharides, containing different numbers of sugar subunits, to inhibit the interaction between dextran and the antibodies that recognize it. They found that the size and shape of the antibodies' dextran-binding sites varied; at most, they could accommodate six or seven single sugar units. This provided the first reliable estimate of the effective size of an antibody's antigen-binding site. These conclusions, as well as Kabat's later predictions that the shapes of antigen-binding sites can vary from shallow grooves to deep cavities, were eventually confirmed by X-ray crystallographers.

On moving to Uppsala in Sweden in 1937, Kabat worked for a year as a postdoctoral fellow with Arne Tiselius. While in Uppsala, Kabat provided the first physicochemical characterization of the antibodies known now as immunoglobulin G when he showed that they migrate electrophoretically in the gamma-globulin fraction of serum. Kabat's work led the way to all further studies of the chemical nature of immunoglobulins.

Kabat always had a keen interest in medicine. On returning to Columbia



GEOFFREY KABAT

Founder of modern immunochemistry

University in 1941, he developed an immunodiagnostic test for multiple sclerosis, and was among the first to develop an animal model of this autoimmune disease. These studies opened the way to modern experimental autoimmunity, with its promise of major benefit to patients with autoimmune diseases.

In 1970, Kabat recognized that the amino-acid sequences of immunoglobulins appearing in the literature provided an opportunity to determine the likely locations of their antigen-binding sites. He and Tai Te Wu developed the Wu–Kabat plot, which measures the distribution of variability along the immunoglobulin sequence. Their variability plots clearly identified the 'hypervariable' or 'complementarity-determining' regions, which vary the most from protein to protein, and the 'framework' regions, which vary the least. The hypervariable regions are those that contribute to the antigen-binding sites, and their variability means that different antibodies can recognize a huge range of antigens. From their plots, Wu and Kabat correctly predicted the locations of the antigen-binding regions in antibodies.

Following a year as a Fogarty scholar at the US National Institutes of Health (NIH) in 1974–75, Kabat divided his time between Columbia and the NIH for the rest of his career. We saw him often as he visited our laboratories or used our library. As protein and, later, DNA sequences became available, Kabat and his collaborators met at the NIH to collect together the amino-acid and DNA sequences of immunoglobulins and other proteins of immunological importance. They produced a remarkable resource, *Sequences of Proteins of Immunological Interest*, which went through five printed editions. The book had an enormous impact on scientists who studied the relationships between the sequences and the antigen specificity of immunoglobulins, T-cell antigen receptors and molecules of the major histocompatibility complex. The Kabat database is now available on the Internet (http://immuno.bme.nwu.edu/), a living memorial to this great scientist.

Kabat received the National Medal of Science in 1991. He valued this honour greatly, particularly because of the difficulties he had in the 1950s when the NIH cravenly terminated his grants as a fallout of the politics of the McCarthy era. Fortunately, the Office of Naval Research and National Science Foundation continued to support him. Kabat saw the medal as recognition of a career-long record of accomplishment, and as a personal vindication.

But Kabat's influence went beyond his research. Among his published books was the landmark *Kabat and Mayer's Experimental Immunochemistry*, written with Manfred Mayer. This book was a bible for young immunologists in the 1960s. He also enthusiastically and uncompromisingly taught generations of medical and dental students in the laboratory and in lectures. His graduate students and postdoctoral fellows became leading lights in the immunological community. One, Baruj Benacerraf, became a Nobel laureate — an honour that eluded both Kabat and his mentor, Heidelberger, although many believed that their contributions amply merited this recognition.

Kabat was known for his devotion to science and for his view that scientists, as opposed to administrators, should determine how their field is organized. He was often the bane of university and government administrators in his complete commitment to science above all else. To fellow scientists, he was intellectually challenging, unsparing in his standards but always anxious to support them in their pursuit of scientific goals.

He is survived by his wife of 57 years, Sally (Linnick), three sons — Jon Kabat-Zinn, Geoffrey and David — and six grandchildren.

William E. Paul and Rose G. Mage

William E. Paul and Rose G. Mage are in the Laboratory of Immunology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892, USA.
e-mail: wpaul@niaid.nih.gov