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From: Gottesman, Michael (NIH/OD) [E]
Sent: Friday, September 02, 2016 2:41 PM
To: CCR-ALLSTAFF@LIST.NIH.GOV
Subject: Sad news, David Davies, 1927-2016

Dear Colleagues,

I'm saddened to relay the news about the passing of one of our most distinguished NIH scientists, David Davies, a man widely considered to be one of the greatest innovators in the field of X-ray crystallography. David died early Thursday morning, September 1, from medical complications following a recent hospitalization. He was 89 years old.

Among the first to structurally characterize nucleotides and important classes of proteins such as antibodies and toll-like receptors, David was intricately connected with some of the most significant scientific discoveries to arise from the NIH campus. His structural identifications served as a platform for Marshall Nirenberg's cracking of the genetic code and Michael Potter's contributions to the development of monoclonal antibodies, among other great advances. He helped establish numerous structural biology groups across the NIH. And he had rubbed shoulders with many of the scientific greats of the 20th century, first as a postdoc with Linus Pauling at Caltech and then as a visiting scientist with John Kendrew and Francis Crick at the famous MRC Laboratory of Molecular Biology in Cambridge.

David first arrived at the NIH in 1955 and was chief of the Section on Molecular Structure in the NIDDK Laboratory of Molecular Biology from 1961 to 2012, upon which he retired and transitioned into an active scientist emeritus. His earliest days at the NIH were as a visiting scientist at the National Institute of Mental Health, from 1955 to 1961. David was recruited by Alex Rich, who himself was addressing fundamental questions about RNA. One breakthrough discovery during this time came when the two men mixed poly-rA and poly-rU. The solution immediately became viscous, and the X-ray diffraction revealed a pattern comparable to that of DNA. No one could believe that complex biopolymers could combine like this without an enzyme. What the two stumbled upon was the first known hybridization reaction. Together with another NIH great, Gary Felsenfeld, these three would eventually discover the DNA triple helix, colloquially known as the F.D.R. triplex after their initials (Felsenfeld, Davies, Rich). It was during this time, circa 1959, when David had his first formal visit to the MRC Laboratory of Molecular Biology; the engagement culminated in a 1960 Nature paper on the first atomic-resolution, three-dimensional structure of a protein (myoglobin), for which Kendrew won the 1962 Nobel Prize in Chemistry.

In 1961, David became a founding member of the Laboratory of Molecular Biology, then located in the National Institute of Arthritis and Metabolic Diseases, a precursor to both NIDDK and NIAMS. Among his accomplishments during the early 1960s was establishing the structures of guanosine monophosphate (GMP), a nucleotide used as a monomer in RNA, and also the enzyme gamma-chymotrypsin and the structure of a number of polyribonucleotides. His interactions with Marshall Nirenberg during the "code race" reaffirmed his new focus on determining protein structures. At a time when it took years to determine the structure of complex molecules, David's best asset was having the intuition of knowing which proteins to pursue. He was the first to determine the structure for an antibody and an antibody-antigen complex.

Never losing his relevance, David continued to innovate and dominate the field of structural biology through the 1970s, 1980s, and 1990s. He guided the next generation of structural biologists at the NIH as they pioneered protein NMR in the 1980s. In the mid-1990s, his group determined the structure of HIV-1 integrase, the enzyme produced by the AIDS virus that enables its genetic material to be inserted into the DNA of the infected cell. Numerous medicines have been developed based on this critical work. Another fascinating structure he helped to uncover during this period was the tunnel-like enzyme complex tryptophan synthase, another important drug target. David approached his 80s in what could be described as a career resurgence: Published articles on his work on toll-like receptors from the past decade

have garnered hundreds of citations. His group's landmark 2008 paper in *Science*, "Structural Basis of Toll-Like Receptor 3 Signaling with Double-Stranded RNA," explains how innate immunity works in our body.

"I sometimes wonder how a country boy from Wales managed to stumble into such a rich research environment," David wrote in a 2005 memoir published in *Annual Reviews*, titled "A Quiet Life with Proteins." His answer was luck and timing but you'd have to think his keen intelligence and even-handedness factored in equally. He was raised in a small Welsh village called Pontardulais, where the only industries were coal mining and tin plating. He was the first in his family to attend college, and a famous one at that, Magdalen College, Oxford University. He spent exciting post-war years at Oxford, from 1945 to 1952, earning both an M.A. and Ph.D. in Physical Chemistry. David described the following two years at Caltech with Linus Pauling as being in the land of milk and honey, compared to the war-rationing he had left in England. It was here that he established what would be enduring friendships with fellow postdoc Alex Rich and graduate student Gary Felsenfeld, the latter with whom he would travel by train across America in 1954 on their way to a year in England.

David attributed his success to his amazing postdocs and colleagues, of which there are many. A quick review of his hundreds of peer-reviewed papers will reveal the extent of his collaborations, most often with his NIDDK and NIH colleagues. A beloved mentor, David trained dozens of young scientists who have gone on to productive careers, many with their own successful labs; at least three have become members of the National Academy of Sciences. He has recruited to the NIDDK one of the strongest and most productive collections of structural biologists in the world. His many honors include election to the National Academy of Sciences in 1978, the Distinguished Presidential Rank Award in 1987, and the prestigious Stein & Moore Award from the Protein Society in 1998. He also was a member of the American Academy of Arts and Sciences, a Fellow of the Biophysical Society, and a Fellow of the American Association for the Advancement of Science.

David is remembered not just as an insightful scientist but also as a friend, a generous colleague, a dependable NIH citizen, and a true gentleman who touched many with his dignified manner and European charm. I highly recommend David's short memoir, "A Quiet Life with Proteins," parts of which are quite humorous. You can download this at <http://bit.ly/2bGuTs8>.

David is survived by his wife, Monica; his two daughters from a previous marriage, Helen and Sally Davies; and his first wife, Cynthia Davies. Services for David will be held on Thursday, September 8, from 3:00 to 5:00 p.m. at the Pumphrey Funeral Home, 7557 Wisconsin Avenue, Bethesda. A death notice will appear in this Sunday's *Washington Post*.