IN MEMORIUM

WOLFGANG K. JOKLIK (1926 - 2019)

Dr. Wolfgang Karl (Bill) Joklik, noted virologist, teacher and mentor, who pioneered the application of biochemical, molecular and genetic techniques to studies of how viruses replicate, interact with their hosts and cause disease, died in Durham, NC, on July 7, 2019.

Bill was born in Vienna, Austria. When he was eleven, his family moved to Sydney, Australia, where his father, an engineer, was General Manager of the Australian branch of Styrian Steelworks, a manufacturer of fine steels. He graduated from Sydney University with a First Class Honors Bachelor of Science degree in Biochemistry in 1948 and a Master of Science degree in 1949, and obtained a D. Phil. Degree from the University of Oxford, England, in 1952, working on the mode of replication of bacteriophage T1 in the laboratory of Sir Paul Fildes, the "Father of English Microbiology," at the Sir William Dunn School of Pathology, the head of which was Sir Howard Florey, the Australian who was awarded the Nobel Prize for his work on the development of penicillin. After a year's postdoctoral work at the Institue of Cytophysiology of the University of Copenhagen, where he teamed with Paul berg to isolate and characterize nucleoside diphosphokinase, the enzyme that exchanges the γP between nucleoside triphosphates, he joined the staff of the Department of Microbiology, headed by Prof. Frank Fenner, at the Australian National University in Canberra. It was there that he started work on animal viruses, more specifically, on vaccinia virus. It was a highly propitious time for a biochemist to start working with animal viruses. Techniques for growing viruses in cultured mammalian cells, as well as powerful techniques for purifying and isolating proteins and nucleic acids had just been developed, which together generated the new fields of molecular cell biology, molecular genetics, and molecular virology. Bill pioneered studies on the nature of the genome of poxviruses (he was the first to isolate intact vaccinia virus DNA) and on the nature of the mechanisms that enable poxviruses to enter cells (the "uncoating process"). It was while he was engaged in these studies that he accepted, in 1962, an invitation from Dr. Harry Eagle, of tissue culture fame, in whose laboratory at the National Institutes of Health he had spent a sabbatical in 1959, to join him in the Department of Cell Biology at the Albert Einstein College of Medicine in New York, the Chair of which Dr. Eagle had assumed in 1961. It was there that Bill began working on the nature of "early" and "late" poxvirus mRNAs and their association with ribosomes to form polyribosomes, the identification of poxvirus "early enzymes" like thymidine kinase, and DNA-dependent RNA polymerase and poly(A) polymerase, and the nature of the structural proteins of a variety of subviral poxvirus particles components and their synthesis and assembly during morphogenesis. It was also at this time that he started work on an aspect of virology that always interested him, namely how to inhibit virus infections. Among the agents capable of inhibiting virus multiplication on which he worked were interferon, for which he established its primary mode of action; isatin-β-thiosemicarbazone (IBT), a derivative of which played an important role in eradicating smallpox virus from human populations in the late seventies; and ribavirin, currently used to control infections in humans of viruses like respiratory syncytial virus and hepatitis C virus. It was also in 1967, while he was still at the Albert Einstein, that Bill started working on the double-stranded RNA-containing reovirus, a research interest that lasted three decades.

In 1968 Bill was offered the Chair of the Department of Microbiology and Immunology at Duke University Medical Center in Durham, NC, a position he held for 25 years, guiding the growth of the

Department from an initial six faculty members to thirty-three when he retired, and to a ranking as one of the top three Medical School Microbiology Departments in the country. As for his work with reovirus, he demonstrated the segmented nature of its genome, isolated, characterized, and identified the functions of the proteins encoded by its genome segments, sequenced most of them, and by elaborating a system in which these genome segments are infectious, developed a "reverse genetics" system for reovirus that permits the introduction of foreign genes into its genome, thereby transforming it into a carrier virus, which has great potential for engineering highly efficient nonpathogenic vaccine strains for members of the Reoviridae family like the human rotavirus, the virus that causes human infantile enteritis and that kills more than one million infants annually worldwide.

The third group of viruses with which Bill worked are the retroviruses. Using the avian sarcoma viruses Rous sarcoma virus and B77 avian sarcoma virus as models, he worked on aspects of the maturation of retrovirus particles following budding, the nature of their reverse transcriptase and protein kinase, and the effect of interferon on their ability to replicate.

All these studies, extending over a period of almost five decades, involved almost one hundred graduate students and postdoctoral fellows, and it was always his interaction with them that provided him with the greatest pleasure. Nothing pleased him more than launching them into solid scientific careers. He maintained cordial relations with many of them for many years, advising them, nominating them for promotions, writing letters of recommendation for them, visiting them worldwide, greatly enjoying return visits from them, and hearing of their often very significant successes.

Bill published more than 250 scientific papers. He was elected to the National Academy of Sciences in 1981 and to its Institute of Medicine in 1982. He was awarded a Humboldt Senior Investigator prize in 1986 and the ICN International Prize in Virology in 1991. For 25 years he was Editor-in-Chief of and a major contributor to seven editions of Zinsser Microbiology, one of the two leading texts for medical students. He was Editor-in-Chief of Virology for eighteen years, from 1975 to 1993; and Editor-in-Chief of Microbiological Reviews for five years. He was Founder and first President of the American Society for Virology in 1982, and President of the American Medical School Microbiology Department's Chairmen's Association in 1979.

Bill's career at Duke was similarly distinguished. He was elected to a James B. Duke Professorship within four years of his arrival, was a member of the Academic Council and of the Duke University Press Board, and, in 1971 played a leading role in founding the Duke Comprehensive Cancer Center. He was the first Chairman of the Cancer Center Planning Committee.

One of Bill's most important contributions was made in the early nineties. Following the eradication of smallpox virus in human populations by 1980, the World Health Organization set up a Smallpox Eradication Committee to effect and oversee the destruction of smallpox virus stocks in scientific laboratories worldwide. Bill was the US delegate to that Committee. All countries agreed to destroy their smallpox virus stocks except the Soviet Union. As a result it was agreed that all smallpox virus stocks would be destroyed except stocks in the Research Institute for Viral Preparations in Moscow, and in the Centers for Disease Control (CDC) in Atlanta. In the late eighties, however, scientists who had been active in the smallpox eradication program in the seventies began to lobby for the destruction of smallpox virus stocks in the Soviet Union and the United States also. This did not seem advisable to Dr. Joklik since one could not possibly be certain that no smallpox virus stocks whatsoever had escaped destruction either by chance or by design. Clearly the existence of smallpox virus in the

hands of terrorists in the absence of smallpox virus in the possession of manufacturers of smallpox vaccine would present a tremendous problem because it would then be impossible to measure the effectiveness/potency of any such vaccine. Bill therefore initiated a campaign against the destruction of smallpox virus stocks in CDC laboratories by writing and publishing a series of article and papers in in the early nineties. After intensive debate, his views were adopted and the smallpox virus stocks in the CDC and the Soviet Union were not destroyed. In 2002, the US government, fearing the existence of smallpox virus stocks in unauthorized hostile hands, ordered the manufacture of hundreds of millions of doses of smallpox vaccine. The effectiveness of this vaccine could not have been tested and established if the smallpox virus stocks in Atlanta had been destroyed.

Bill was an outstanding scientist, administrator, mentor, and teacher. Strongly rooted in two cultures, the Austrian/German and the British/American, Dr. Joklik will be remembered as a true world citizen, greatly interested in international affairs, a devoted husband, father, and grandfather, a life-long traveler, a lover of classical music, and a golfer and tennis player when time permitted.

Bill married Judith Vivien Nicholas in 1955 in Canberra, Australia. Judith succumbed to breast cancer in 1975 after a most courageous eight year fight. In 1977 he married Patricia Hunter Downey, whose first husband had died of lung cancer in 1974. He is survived by Pat, his son Richard of Columbia, MD and his family; his daughter Vivien of Cary, NC and her daughters; his brother Frank of Salt Lake City, UT, and his family.; and a son and three daughters of Pat's first marriage and their families.