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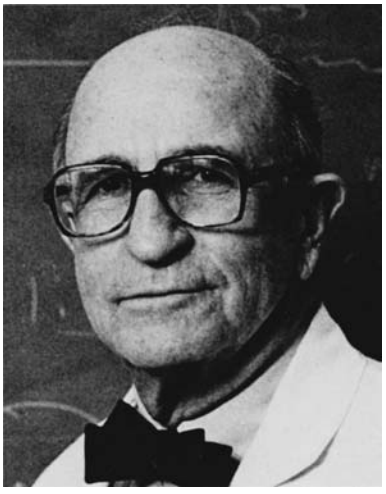
Virology Division News

Obituary

In Memoriam
Harold S. Ginsberg (1917–2003)



Harold S. Ginsberg, a pioneer in the field of infectious diseases and molecular virology, died on February 2nd, in Woods Hole, Massachusetts. Harold (or Harry as he was almost universally known in the virology community) was born on May 27, 1917 in Daytona Beach, Florida. He was an undergraduate at Duke University, graduating with an AB in 1937. He then attended Tulane University and earned his MD in 1941. Following his Internship and Residency training, he served in the military and was posted to the United Kingdom at the time of the Normandy landings. During this period, he noticed a high occurrence of hepatitis in soldiers who had received blood transfusions. His investigations led to the discovery that the pooled plasma that was being used to treat the wounded was causing hepatitis. This work led to changes in medical treatments that saved the lives of many servicemen in World War II. It also stimulated research efforts that eventually led to the discovery and isolation of *Hepatitis B virus*. For his efforts, Harry was awarded the Legion of Merit Award by the US Army in 1945.

Harry began his career in academia as an Associate at the Rockefeller Institute for Medical Research, now the Rockefeller University, in New York. In 1951, he joined the faculty at Case Western Reserve, in Cleveland. Shortly after joining the faculty, he began his groundbreaking exploration of the *Adenoviridae*, his initial interest sparked by the epidemiology and pathology of Acute Respiratory Disease (ARD) among new recruits in the armed forces. He demonstrated that certain adenovirus serotypes were the causative agents of atypical pneumonia, pharyngitis, and ARD, and he also demonstrated that in asymptomatic children, the virus was latent in the adenoids, prior to becoming infectious. These early investigations sparked a life-long interest in adenoviruses and the relationship between viral infection and pathology.

In 1961, Harry was named Chairman of the Department of Microbiology at the University of Pennsylvania. During this phase of his scientific career, his laboratory began to focus on the viral structural proteins. His lab was among the first to isolate temperature sensitive mutants of type 5 adenovirus and this allowed the functional characterization of the viral capsid proteins. In parallel, biochemical approaches were applied to isolate the individual late viral gene products. Collectively, these efforts laid the foundation for understanding viral DNA packaging, capsid maturation in host cells, and changes in host cell transcription and translation during the course of a virus infection. As with many pioneers, Harry was closely associated with the development of an agreed upon terminology for a new field and a short paper in Virology established the universally accepted terms “hexon, penton, and fiber” for the major external capsid proteins.

From 1973 to 1985, Harry was the Chairman of the Department of Microbiology at Columbia University Hospital of Physicians and Surgeons. During this period, he assumed many responsibilities. First and foremost under his leadership, he built a first class department, consisting of faculty members with balanced interests in classical microbiology and who were thought leaders in the emerging fields of molecular immunology, bacteriology and virology. In addition, he was for several years the editor of the Journal of Virology, among the premier journals for virologists, and co-authored several key books and textbooks on the subjects of microbiology and virology. If you attended medical school or studied microbiology in graduate school in the seventies and eighties, you were likely to have a well-thumbed copy of Davis, Dulbecco, Eisen, Ginsberg and Wood's Microbiology. His many academic contributions to the field of microbiology led to his election to the National Academy of Sciences in 1982.

In his laboratory at Columbia, the direction of his scientific endeavors began to shift towards applying the emerging tools of molecular biology to relate viral and cellular phenotypes with viral genotype(s). Through his direction, the function of many of the adenoviral genes was discerned and correlated to an understanding of viral capsid maturation, viral replication and recombination, modulation of host cell transcription and translation and cellular immortalization. What now might seem to be a subtle shift in focus, was clearly a paradigm shift in his science. Cells were no longer being used as vehicles solely to understand viral functions. Rather, the virus was now being employed as a molecular tool to dissect and gain insights into complex cellular processes. The contributions from his laboratory and many other animal virus groups around the world laid the foundation for the emerging fields of Molecular Biology and Human Genomics.

Following Harry's tenure at Columbia, he remained vigorous in his pursuit of scientific discovery and was named as an Emeritus at the National Institute of Allergy and Infectious Diseases (NIAID). Working with Dr. Gregory Prince, he developed the cottontail rat as an animal model for adenovirus respiratory infection. They also began to investigate the role in pathology of the adenoviral early gene 3 region, and determined that the proteins encoded by the E3 transcripts influenced the host inflammatory response. This observation led the way to the creation of adenoviral gene delivery vectors that could persist in the host cell for long periods of time, thus promoting prolonged transgene expression. He also expanded his interests into the field of AIDS and began working on the simian AIDS virus. He was able to apply his experience from years of work on adenoviruses to understanding the molecular basis for pathogenicity of *Simian immunodeficiency virus* in an attempt to define the viral proteins that drove this process. The ultimate goal was to apply his discoveries to Human immunodeficiency viruses, in the hopes of driving the discovery of novel antiviral therapeutics and vaccines. Harry described this time at NIAID as "being like a second post-doc" and his enthusiasm for science remained steadfast and infectious.

Reflecting on an individual's lifetime achievements never truly captures the spirit of that individual. While Harry had an illustrious scientific career, with highly ranked academic appointments, multiple publications, seminal discoveries and prestigious awards, such recognition only scratches the surface of his true contribution to science. As a graduate student in his laboratory at Columbia in the late 1970's, one of us (LEB) learned a great deal about and from him. First and foremost, he was a superb mentor. His encyclopedic knowledge of science was second to none. He taught me how to read manuscripts critically and apply these criteria to my own studies. He taught me the basics of scientific experimentation. He challenged me to think logically and also creatively. When our hypotheses were not borne out by our studies, he encouraged and challenged me to move forward. When we had those golden moments of scientific discovery, we celebrated, but with respect and the recognition that much more work was to be done. He understood and accepted his own mortality and as such recognized the importance of passing on what he knew to the next generation. This

is the ultimate achievement and recognition for a scientist – to have his or her vision live on through the many he or she has trained. To a young faculty member appointed by Harry in the mid 1970's, the indispensable ingredients of trust and encouragement necessary to succeed in the competitive world of science were there in abundance. He was always ready to listen, criticize constructively, and make suggestions that carried the individual far beyond the narrow confines of his or her parochial interests. He also made it abundantly clear that the Department's students came first, and he led by example. Very rarely did he miss the weekly students and post-doctoral fellows department seminar, and as a consequence all of the faculty made it a point to attend, to everyone's benefit. Also, it is important to emphasize both the importance of his family to Harry's life and the role played by his wife Marion in maintaining a collegiate atmosphere in the Department. In sum, Harry was a man not only of integrity but also of compassion, and one with a good sense of humor. He was a yard-stick by which to measure one's attempts at scientific and human achievement.

Harry's broad aims for the future of Molecular Virology were clear – to define human diseases caused by viruses based upon an understanding of the relationship between viral and cellular gene products. He knew that the only way this future direction could be realized was to pass his knowledge on to his graduate and MD/Ph.D. students, Postdoctoral Fellows and his colleagues. Speaking on behalf of all of those who were trained and/or encouraged by Harry, we can confidently say that the flame of his vision lives on in all of us. He will be sorely missed.

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