OBITUARY

Joshua Lederberg 1925–2008

James F Crow

Joshua Lederberg died on February 2, 2008. Although the immediate cause was pneumonia, he had been troubled by a bad back for some time. With his originality and breadth and depth of knowledge, he was one of the greatest scientists of the century.

His precocious intelligence was apparent at an early age, as was his interest in science. The work that made him famous was begun while he was a medical student at Columbia University, still in his teens. He was inspired by Oswald Avery's argument for the genetic significance of DNA and by his own observation that antigenic types in *Salmonella* seemed to be permutational. Having become convinced that bacteria undergo genetic recombination and deciding that the best laboratory in which to further investigate this phenomenon was that of E.L. Tatum at Yale, he took leave from medical school and moved to Yale. By using selectable mutations, he contrived a situation in which only recombinant types would survive. Remarkably, the first experiments worked. In view of later results showing the rarity of fertile combinations, he was lucky. This discovery immediately opened the opportunity for gene mapping, which he pursued avidly, and his first paper was published when he was 21.

Lederberg's work in the lab led to his decision to change direction, away from medicine and into genetics. He received his PhD in 1947 and immediately accepted a position as Assistant Professor of Genetics at the University of Wisconsin. The next decade was a heady time. With his students and colleagues, he discovered transduction, the carrying of genetic material from cell to cell by a virus. Another discovery was that of the phage lambda, which quickly became a research favorite. Meanwhile, he found that the sex of a bacterium was determined by an episome, termed the Fertility factor, or 'F'. Strains with a very high rate of recombination, called Hfr, resulted from the insertion of an F particle into a chromosome. He also invented a very clever technique, replica plating, to demonstrate that the rapid evolution of traits—such as drug resistance—was the result of selection of pre-existing mutations rather than mutation induction. Recognition came soon. Lederberg was elected to the National Academy of Sciences in 1957, and in 1958, he received the Nobel Prize, both while he was in his early thirties.

Along with his amazing intellect, he had a restless mind and a determination to apply his gifts to things of scientific and social importance. He was an early advocate for the selective, rather than instructive, theory of antibody specificity. A second interest was the origin of life. With the coming of space exploration, he became fearful of the possibility that space vessels could bring back extraterrestrial microbes or contaminate the moon with our own bugs. A third interest was computers. He and I took a course in computer programming back in the days when programming consisted of physically manipulating wires, in the manner of an old-fashioned telephone switchboard. He took to this immediately and started to gear his life around the computer. Meanwhile, he founded a Medical Genetics Department at Wisconsin, with the then-novel idea that the subject involves the genetics of our parasites as well as of ourselves. Another indication of his breadth is the active role he played in developing the Genetics Citation Index.

In the late 1950s, it was becoming apparent that he was considering broader horizons, and in 1959, he moved to found a genetics department at Stanford. Although he continued research in bacterial genetics, the novelty was wearing off. He became more and more interested in broader issues and in world problems. He enlisted Carl Sagan, whom he had met in Wisconsin, to consider space exploration and the search for extraterrestrial signs of life. He coined the word 'exobiology'.

Stanford provided the hardware and the computer expertise that he was looking for. He immediately became interested in expert systems and artificial intelligence. My own favorite among the various results is the program Dendral. Among other things, it provided an unambiguous system for naming organic compounds. For reasons that were never clear to me, it seemed to have had essentially no impact on the community of organic chemists, who seemed content to live with nomenclatural ambiguity.

As his scientific interests broadened, so did his social conscience. From 1966 to 1971, he wrote a weekly column, "Science and Man," for the *Washington Post* and its syndicate. He soon became sought after as a confidential advisor to various government agencies. He was a person with informed judgment who could be trusted to maintain confidentiality. Somehow, he managed to serve on countless advisory boards on a variety of subjects and keep them straight. Among his concerns were nuclear proliferation and biological warfare. He was an early proponent of being alert to possible epidemics, noting that the airplane provided a made-to-order way of spreading a local agent around the globe.

After serving as professor and chairman of genetics at Stanford from 1959 to 1978, he accepted the presidency of Rockefeller University, which he held until his retirement in 1990. Until his health became a problem, his activity remained undiminished.

Joshua Lederberg was born in Montclair, New Jersey, where his father was an orthodox rabbi. He attended New York public schools, where his precocious knowledge was sometimes a problem for teachers. He graduated from Columbia University in 1944. He was married to Esther Zimmer Lederberg, with whom he collaborated extensively. Their marriage ended in divorce, and in 1968 he married Marguerite Stein Kirsch, a psychiatrist. He is survived by Marguerite, a daughter, Anne Lederberg, and a son, David Kirsch.

Among Lederberg's myriad interests was a concern that we are not leaving enough detailed information for future historians. And, true to his custom, he did something about it. He deposited a vast amount of material—notes, papers, correspondences—from an incredibly busy life. Browsing through his papers at the Profiles in Science site of the National Library of Medicine (http://profiles.nlm.nih.gov/BB/) is a great way to gain an appreciation for the tremendous breadth of his interests. ■

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