

Joshua Lederberg – In Memoriam

The foundations of the young science of molecular biology were laid towards the middle of the last century, primarily resting on a series of outstanding discoveries where microorganisms played a significant role. The exploitation of bacteria to address fundamental questions related to the nature of genes and how they function unleashed a steady stream of path-breaking discoveries during the 1940s and 50s. This was rather ironic since the term bacterial genetics would have been considered an oxymoron only a few years ago as the idea of bacteria possessing genes was alien to most geneticists who were busy working with plants, flies, and fungi. Joshua Lederberg, who passed away in February 2008, was one of the undisputed leaders of this molecular biology revolution. Lederberg's work led to the discovery of two forms of genetic exchange in bacteria – conjugation and transduction. These discoveries had an enormous impact in opening up the genetic analysis of bacteria that resulted in other major breakthroughs such as the elucidation of the mechanism of gene regulation. For his contributions to microbial genetics, Lederberg shared the 1958 Nobel Prize for Physiology or Medicine with Edward Tatum and George Beadle. Lederberg's contributions however did not confine only to the field of bacterial genetics. He was keenly interested in exotic areas such as artificial intelligence, extra-terrestrial life (exobiology) and space exploration and made significant contributions to these fields too. He also championed the cause of disarmament and elimination of biological weapons. In a sense, he was also a science journalist as he regularly contributed articles dealing with science and public issues in the *Washington Post* and *The Chronicle*. With his passing away, the world lost one of its pioneer microbial geneticists and a great statesman of science.

Joshua Lederberg was born in New Jersey in 1925. His father was a Rabbi who had recently immigrated to the US from the erstwhile Palestine. Lederberg's early education was in New York City. Right from school days, his ambition was "to be like Einstein and discover a few theories in science". In 1944, he graduated with honours in Zoology from Columbia University. Even as an undergraduate, he carried out experiments in the laboratory of Prof. Francis J. Ryan at the university. Ryan had a significant influence in guiding Lederberg during the formative years of his research career. Though he joined Columbia University's College of Physicians and Surgeons to pursue a medical degree, Lederberg's main interest was medical research. His interest was further "ignited" by the discovery of Avery and colleagues at Rockefeller University that DNA is the genetic material (for more details, see *Resonance*, Vol.12, No.9, 2007). Deriving inspiration from the work of Avery, Lederberg decided to pursue bacterial genetics further and collaborated with Edward Tatum at Yale University. It was while working in the laboratory of Tatum during a one-year leave from medical school that Lederberg made the



important discovery of bacterial sexuality in 1946 (see article by Jayaraman in this issue). This work was later submitted as his doctoral thesis and he received his PhD from Yale in 1947.

Lederberg never completed his medical degree. Immediately on receiving his doctorate, he was offered a faculty position at the University of Wisconsin at Madison. His work on replica plating (with his wife Esther) and the discovery of phage mediated transduction (with his student Zinder) were carried out while he was at Madison. His successes earned him the chair of the newly established Department of Genetics at Stanford University Medical School in 1959. His move to Stanford was preceded by the announcement of the award of the Nobel Prize. Lederberg's association with Stanford continued for the next two decades during which he explored different areas of research, primarily focusing on health and medicine. It was while at Stanford that he explored the areas of artificial intelligence, robotics and exobiology.

In 1978, nearly after two decades of research at Stanford, Lederberg moved to his home town of Manhattan, New York, to take up the Presidency of Rockefeller University, which he served till 1990. Lederberg could redefine the focus of research at Rockefeller to molecular medicine. After his retirement, he continued as Professor Emeritus and Raymond and Beverly Sackler Foundation Scholar at Rockefeller University.

Lederberg pursued active research as well as his advisory activities to different governmental bodies till his death. He maintained a dignified silence throughout the 1990's, when the spontaneous nature of mutations in bacteria that he helped to establish, was challenged by several investigators led by John Cairns. His stand was vindicated by more recent findings that confirmed that mutations are selection-independent. Lederberg was honoured with several national and international awards, the most recent one being the US Presidential Medal of Freedom in 2006.

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When we pursue our passion to master what was once unknowable, we move from a plodding struggle with nature to an ongoing, enlightening conversation.

– Joshua Lederberg

