

Renato Dulbecco

(1914–2012)

Molecular biologist who proved that virus-derived genes can trigger cancer.

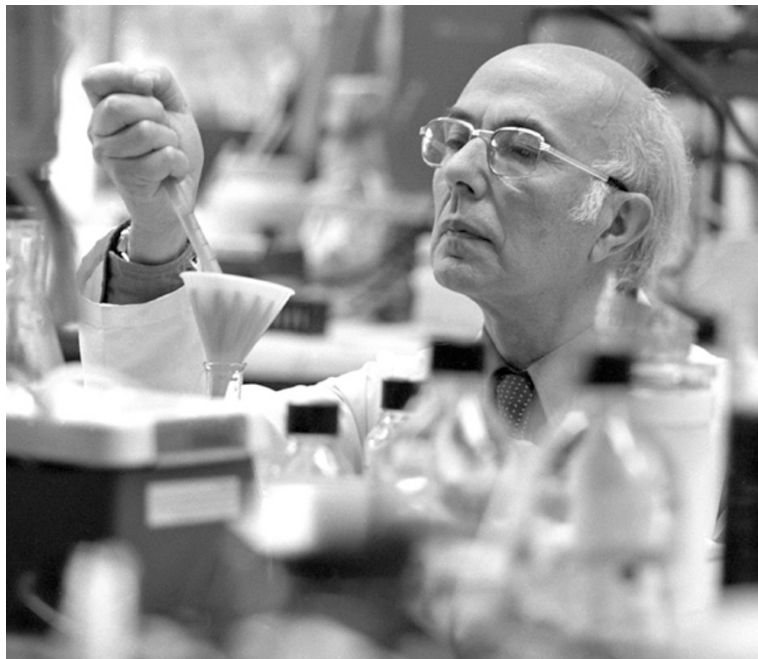
Renato Dulbecco, a giant of cancer biology, passed away peacefully on 19 February, just three days shy of his 98th birthday. Through a decade-long series of experiments that began in the late 1950s — first at the California Institute of Technology (Caltech) in Pasadena and then at the Salk Institute in La Jolla, California — he and his co-workers demonstrated that the behaviour of cancer cells could be traced directly to acquired genes. Some viruses can integrate their genomes into host cell DNA, inducing uncontrolled cell growth — the hallmark of a cancer cell. For these early clues to the genetic origins of cancer, Dulbecco shared the 1975 Nobel prize with the late Howard Temin, his former student, and with David Baltimore, my former mentor.

Born in Catanzaro, Italy, on 22 February 1914, Dulbecco grew up during the First World War and its aftermath with his mother and siblings. He entered the University of Turin in 1930 at the age of 16 to study medicine. His interests quickly shifted to biology and he became a laboratory assistant for Giuseppe Levi, learning from him the cell-culture techniques that had a dominant role in Dulbecco's later scientific work. His fellow students included two other future Nobel laureates — microbiologist Salvador Luria and neurobiologist Rita Levi-Montalcini.

After obtaining his doctorate in 1936, Dulbecco was drafted into the Italian army as a physician. He was called to action in 1939, at the outset of the Second World War, to serve first in France and then in Russia. Disaffected by the war and its consequences, he deserted the army and hid in a small village near Turin, becoming physician to the local partisan units resisting the German occupation. After the end of the war, following a short stint as an elected city councillor in Turin in 1945, he returned to scientific research at the University of Turin.

In 1946, Luria invited Dulbecco to join his research group at the University of Indiana in Bloomington to work on bacteriophages

— the viruses of bacteria. Dulbecco shared his laboratory with a graduate student, James Watson, who was later to determine the structure of DNA with Francis Crick. Dulbecco's finding that visible light can reactivate phages previously rendered inactive by exposure to ultraviolet light — with repercussions for experimental methods



at the time — brought him to wider attention. Phage geneticist Max Delbrück invited Dulbecco to join him at Caltech in 1949 as a research fellow.

Dulbecco felt that research into animal viruses would benefit hugely from improved quantitative techniques. In 1952, he developed the plaque assay for Western equine encephalomyelitis virus: a system that allowed researchers to determine the number of biologically active viral particles in a sample by counting the number of discrete plaques, or clear spots, where a single virus and its progeny had killed host cells. Soon Dulbecco was joined by Marguerite Vogt, a German émigré. Their fruitful collaborations led to quantitative assays for the poliomyelitis virus, a scourge at the time, and later for the polyoma virus — a DNA virus that causes many different types of tumours.

In 1963, Dulbecco left Caltech to become one of the first fellows of the Salk Institute, founded by Jonas Salk of polio vaccine

fame. He and Vogt continued their research collaborations on tumour viruses, definitively proving the essential role of the viral genes in transforming cells into cancer cells. During this highly productive period, Dulbecco trained some of the top virologists in the world. In 1972, he moved to the Imperial Cancer Research Fund (now Cancer

Research UK) in London, where he initiated studies of breast cancer — a subject he continued to pursue after moving back to California in 1977. His last scientific paper, published in 2004, identified tumour-initiating cells in rat mammary cancers. In 1988, Dulbecco assumed the presidency of the Salk Institute, following the illness of long-term president Frederic de Hoffmann, and brought stability during a difficult time.

An experimentalist at heart, Dulbecco loved to work in the laboratory. He was a quiet man, yet did not shy away from making bold visionary statements: in a classic 1986 perspective in *Science* (R. Dulbecco *Science* **231**, 1055–1056; 1986), he argued that the best way to understand cancer would be

to sequence the human cancer genome. In 1992, Dulbecco stepped down from the Salk presidency to organize the Italian contribution to the Human Genome Project. He spent a good part of his time in Italy, where he was much revered and helped the careers of many young scientists.

Dulbecco was an elegant man: a dapper dresser, soft spoken, with an ever-present smile. He was comfortable among the nobility, yet adept at changing the oil in his car; at once distant yet approachable. He was a charming host at dinners organized by his wife Maureen, which my wife and I often had the pleasure of attending. In short, he was always the perfect gentleman. ■

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