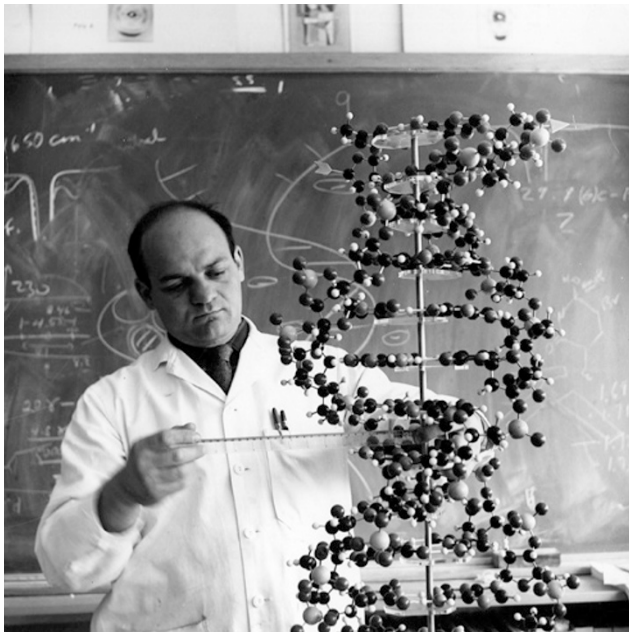
Alexander Rich

(1924–2015)

Biologist who discovered ribosome clusters and 'left-handed' DNA.



JOSIAH D. RICH

I first came across Alexander Rich in 1963. He was on the cover of that year's 13 May issue of *Newsweek* with his PhD student Jonathan Warner. The two of them had just discovered clusters of ribosomes called polysomes — crucial components involved in the building of proteins.

Rich, who died on 27 April, was born in 1924 in Hartford, Connecticut to immigrant parents from Russia and Eastern Europe. He grew up during the Great Depression in Springfield, Massachusetts, attending a technical secondary school by day, and working nights at a local rifle factory. At one point, his family went to live at a local YMCA club after being evicted from their home. Against the odds, Rich made it to Harvard University in Cambridge, Massachusetts, graduating with a bachelor's degree in biochemical sciences in 1947. Two years later, he received a medical degree from Harvard Medical School in Boston.

In 1949, Rich joined chemist Linus Pauling at the California Institute of Technology (Caltech), in Pasadena, where he stayed for five years, and learnt about X-ray crystallography. To his regret, he never published with Pauling; when asked what Rich had achieved during his tenure, Pauling apparently replied: "not much, but he must have learned a lot".

Indeed he had. From Caltech, Rich went on to lead the physical-chemistry section at the US National Institute of Mental Health (NIMH) in Bethesda, Maryland. In 1955, during a leave period at the Cavendish Laboratory in Cambridge, UK, he and Francis Crick determined the structures of two important proteins: polyglycine II and collagen. Back at the NIMH in 1956, three years after the discovery of DNA's iconic double helix, Rich and his colleagues discovered that RNA can also form a double helix, and even a three-stranded helical structure. The findings paved the way for studies that showed RNA's capacity to fold into complex architectures.

In 1958, Rich became an associate professor at the Massachusetts Institute of Technology (MIT) in Cambridge. There he showed that RNA could hybridize with, or bind to, DNA to form a double helix. From the early 1970s, this phenomenon was widely applied to the identification of DNA sequences, for instance using the northern blot technique. Today, it forms the basis of DNA chips, which are used to measure the expression levels of tens of thousands of genes at once.

Rich's work on polysomes, carried out in 1963, revealed how active ribosomes — the protein builders of cells — line up along a messenger RNA molecule, like beads on a string. As the ribosomes move along the mRNA, the corresponding amino acids are stitched together to produce proteins. The work established a defining mechanism in protein building.

In 1973, he made the first determination of an RNA double-helix structure at atomic resolution. This was followed, in 1974, by the solution of the L-shaped structure of a transfer RNA molecule, which was made simultaneously by Rich's MIT group and Aaron Klug's group at the Medical Research Council Laboratory of Molecular Biology in Cambridge, UK.

Rich is perhaps best known for his discovery of a DNA structure in which the double helix winds to the left instead of the right. In 1979, he, along with crystallographer Andrew Wang, revealed this stable, 'left-handed' DNA structure, dubbed Z-DNA, using X-ray crystallography. After showing that Z-DNA can influence the production and alteration of certain mRNA molecules, Rich worked out the structure of a Z-DNA fragment bound to an RNA-editing enzyme. He and his colleagues also showed how the pathogenicity of the vaccinia virus, and probably of the smallpox virus, correlated with a virus-specific protein binding to the host's Z-DNA.

Rich's interest in the latest discoveries across diverse disciplines was irrepressible. During the 1970s, he worked as an adviser for NASA, weighing in on projects exploring the possible existence of life on Mars. He also ventured into biotechnology and co-founded three companies: Repligen, Alkermes, and in his 80s, 3-D Matrix.

Rich received numerous honorary degrees and awards, including the US National Medal of Science, presented to him in 1995 by then US President Bill Clinton.

In spite of such a broad sweep of achievements, Alex was best known among close colleagues for his self-possession, large personality, critical intellect and humanity. He and his wife Jane held legendary parties at their classic brick house near Harvard Square, bringing together all sorts of people, including his four children and now seven grandchildren.

A few years after I saw him on the cover of *Newsweek*, Alex and I became faculty colleagues at MIT. We had endless conversations, ate as often as five times a week at a fish restaurant in Cambridge, and drove around in his dreadful old and enormous cars. On one occasion, the police stopped us, suspecting that his wild gesturing — to explain a theory of evolution to me — indicated drunk driving.

Alex was unstoppable. Once, because of a weeknight family obligation, I had to decline yet another of his dinner invitations. He responded immediately: "No problem, I will come instead to your home later in the evening to talk". And he did. ■

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