

MIT Faculty Memorial Resolution for Alexander Rich

Alexander Rich passed away on April 27, 2015 at the age of 90. Alex was a pioneer whose scientific discovery and theoretical insight traversed the spectacular arc of the field of molecular biology from its inception in the 1950s until the present day. He spent most of his remarkable career as a professor of Biology at MIT, where he served as a key leader and strong advocate for the growing field of molecular biology within MIT.

Alex was raised in a working class family in Springfield Massachusetts during the days of the great depression. His intellect and drive brought him to Harvard University, where he received his BA in 1946 and his MD in 1949. Alex embarked on a career in research when he joined the laboratory of Linus Pauling at Cal Tech as a research fellow. At that time, the Pauling lab was one of a handful of locations where the field, which would become known as molecular biology, was being born. This ambitious new field had two basic objectives: 1) to understand life processes in terms of the structures of the underlying biomolecules and 2) to understand at the molecular level how information flows from genes to all of working parts of a living organism. Alex worked for the next 60 years doing exactly this, and at the forefront of using X-ray crystallography to determine molecular structures of key components of genetic information transfer.

After launching his independent career at the National Institute of Mental Health (NIMH) and spending a short period on leave with Francis Crick at the Medical Research Council (MRC), Alex moved to MIT in 1958 to help lead a thrust in molecular biology. At MIT, Alex showed that DNA and RNA could form perfectly base paired two stranded structures. This discovery of hybridization not only gave clear experimental evidence for how genetic information encoded in DNA could be transcribed into an RNA copy, but also provided the foundation on which most modern technologies are based to detect and quantify specific cellular RNA molecules.

By 1972, Alex's laboratory at MIT was well established as one of the leading centers of X-ray crystallographic analysis of RNA structures. At that time he published the structure of an RNA double helix of sufficient resolution that the hydrogen bonding schemes that give specificity to base pairing could be seen. This was the first direct experimental confirmation of the chemical structures that had been hypothesized by Watson and Crick to give rise to complementary pairing of the two strands of double helical DNA.

A year later, Alex's group published what remained for decades as the only three dimensional structure of a functional RNA molecule. This molecule is transfer RNA, the key adaptor molecule, which reads the sequence of a messenger RNA and translates it into the amino acid sequence of a protein. The classic L-shaped structure of the transfer RNA, worked out contemporaneously with the group of Aaron Klug at the MRC, is now deeply ingrained in the visual imagery of molecular biology and is in every textbook.

Alex is perhaps best known for the discovery of Z-DNA. The structure of a fragment of Z-DNA was published in 1979; a time when there seemed to be nothing fundamentally new that could be learned about the structure of DNA, which was thought to exist exclusively as a right-handed double helix with a smooth twist. Alex's work showed that DNA of particular sequence could

form a stable left-handed helix with the backbone forming a zig-zag, hence the name Z-DNA. Even more astounding, his group went on to show that in a living cell regions of DNA could make the dramatic switch between the normal right-handed and left-handed conformations. This switch is thought to play an important biological role in the pathogenicity of certain human viruses.

Alex was best known for his discoveries based on rigorous and meticulous experimental science, but for the many who knew him well he was a visionary who had the foresight and courage to write down and publish prescient observations. In 1961 he speculated in a book chapter that life began with RNA as the only informational molecule, with DNA coming later as a chemically more stable form adapted for the storage of genetic information. This observation preceded by decades the now accepted concept that the so-called *RNA world* was a key stage in the origin of life. In another review, Alex proposed a role for an RNA double helix having an important part in the regulation of genes. This idea anticipated by 40 years the discovery of microRNAs as prolific regulators of gene expression.

In 1980, Alex received MIT's highest honor, the James R. Killian Jr. Faculty Achievement Award. Among many other honors, he received the US National Medal of Science (presented at White House by President Clinton), the Welch Award in Chemistry, the Rosenstiel Award in Basic Biomedical Research, and the Lomonosov Gold Medal of the Russian Academy of Science.

Alex was a treasured collaborator and colleague. His friends in the Biology Department would find excuses to visit Alex in his office, which was wonderfully cluttered with stacks of manuscripts, artworks, artifacts, fossils and ubiquitous molecular models – some made long ago of now yellowed paper and some elegant enough to be works of art. To spend time with Alex in his office was to be rewarded with wisdom, insight, and fresh new ideas usually about science, but also not infrequently about departmental and Institute politics and national science policy. But in his office there was also a sense of connectedness — to Alex's life of the mind, his pure joy in doing science, and his humanity. There was also a connectedness to science and scientists around the world and across the sweep of time. We truly miss having him among us.

Alex is survived by his wife of more than 60 years, Jane; two sons, Josiah and Benjamin; two daughters, Rebecca and Jessica; and seven grandchildren.

Be it resolved that the Faculty of the Massachusetts Institute of Technology, at its meeting of May 20, 2015, records its profound sense of loss on the death of our beloved friend and colleague, Alex Rich, and expresses its deepest sympathy to his family.

Respectfully submitted:

Chris Kaiser

Uttam RajBhandary

Phillip Sharp