Structural Chemistry (2022) 33:1385–1387
https://doi.org/10.1007/s11224-022-01954-8

OBITUARY

Sidney Altman (1939–2022)—molecular biologist, discoverer of catalytic properties of RNA

Istvan Hargittai[1]

Accepted: 28 April 2022 / Published online: 16 May 2022
© The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2022

Abstract
Sidney Altman(1939-2022) was a physicist turned molecular biologist. He was born in Canada, studied at MIT and at the University of Colorado, and did his most important work at the MRC LMB and Yale University. He shared the 1989 Nobel Prize in Chemistry for the discovery of catalytic properties of RNA.

Keywords Sidney Altman · Leonard Lerman · Enzymatic RNA · Ribozyme · MRC LMB · Yale University · 1989 Nobel Prize

Sidney Altman (1939–2022, Fig. 1) [1, 2] was born in Montreal, Canada, in a poor East European immigrant Jewish family. He attended schools in Montreal, but for higher education, he moved to the USA. He studied at the Massachusetts Institute of Technology in Cambridge, Massachusetts, and earned a bachelor's degree in physics in 1960. The nuclear physicist, pedagogue, and innovator Lee Grodzins supervised his senior thesis. After spending a frustrating year and a half at Columbia University, he continued, still in physics, at the University of Colorado in Boulder, and enrolled in graduate studies. In the summer of 1962, he attended a summer institute in theoretical physics where he met George Gamow. It was a casual meeting, but impacted Altman's path in science profoundly. Gamow told him about the interesting work in molecular biology in the Medical School of the University of Colorado. This prompted Altman for a change in his career path even if he had to do a great deal of catching up in studies of organic chemistry and biochemistry. He joined Leonard Lerman who was studying the consequences of acridine-intercalation in DNA. This was a research area, which later became the source of Altman's important discoveries. Altman received his PhD in biophysics in 1967. Postdoctoral stints followed, including one with Matthew Meselson at Harvard University.

✉ Istvan Hargittai
stuceditor@gmail.com

[1] Department of Inorganic and Analytical Chemistry, Budapest University of Technology and Economics, POBox 91, Budapest 1521, Hungary

Altman's most significant postdoctoral period was in the years of 1969–1971 when he worked at the Medical Research Council (MRC) Laboratory of Molecular Biology (LMB) in Cambridge, UK [3]. He was assigned to the unit of the LMB led by Sydney Brenner and Francis Crick. They gave him complete freedom in selecting his research project, and he chose to work with transfer-RNA (tRNA), the nucleic acid that participates in protein synthesis. He wanted to search for acridine-induced mutants of tRNA. In this, he followed Lerman's example who had done similar work with DNA at the University of Colorado when Altman was working in his laboratory. Altman's project was very timely as by then, Frederick Sanger had solved the problem of sequencing RNA (and continued his work on DNA sequencing). Altman found himself at the center of molecular biology, and he made good use of this unique opportunity. Initially he had only a one-year fellowship at the MRC LMB, but his work showed so much promise that Brenner and Crick offered him an extension of his stay using LMB funds.

Altman's research eventually led to the discovery of Rnase P and the enzymatic properties of the RNA component of ribozyme—thus demonstrating the capability of RNA as an enzyme. Even the initial results were significant enough to help him land an assistant professorship at Yale University. He had a most successful career, served as professor, department chair, and dean. He discharged his administrative duties as dean just in time before he received the Nobel Prize in 1989. There were two co-recipients of the chemistry prize, Altman and Thomas Cech who, in an independent work, also demonstrated the enzymatic capabilities

Fig. 1 Sidney Altman in his office at the Department of Biology, Yale University, New Haven, Connecticut, 1998 (photograph by I. Hargittai)

of RNA. The motivation of the prize read as follows: "for their discovery of catalytic properties of RNA."

The discovery was truly important, but its significance and impact multiplied because it helped to overthrow a dogma that all enzymes were always proteins. Back in 1958, Crick came up with the idea about the one-way direction of the flow of genetic information as DNA → RNA → protein, and called it "the central dogma." This was an unfortunate choice of name and became the source of long-standing misunderstandings. The meaning of dogma is something impossible to doubt whereas Crick used it in the meaning of a mere hypothesis [4]. The academician of the Royal Swedish Academy of Sciences, Bertil Andersson, who presented the achievements of the two prize-winners at the award ceremony in Stockholm, on December 20, 1989, alluded to the paradigm-change character of what Altman and Cech found, saying that it was not only a great surprise, but was met initially with skepticism. The discovery helped to understand complex processes of genetics. It gave also a new insight into how life might have begun billions of years before. Andersson stressed this aspect of its significance [5]:

> The discovery of catalytic properties in RNA also gives us a new insight into the way in which biological processes once began on this earth, billions of years ago. Researchers have wondered which were the first biological molecules. How could life begin if the DNA molecules of the genetic code can only be reproduced and deciphered with the aid of protein enzymes, and proteins can only be produced by means of genetic information from DNA? Which came first, the chicken or the egg? Altman and Cech have now found the missing link. Probably it was the RNA molecule that came first. This molecule has the properties needed by an original biomolecule, because it is capable of being both genetic code and enzyme at one and the same time.

Of course, originally, Altman did not set out to solve the origin of life problem and referring to the speculations about the significance of his work in this respect he said "I still take all these discussions with a grain of salt because it's impossible to do conclusive experiments on the origin of life" [6].

I first met Sidney ("Sid") Altman in 1998 when I recorded a long conversation with him in his office at the Department of Biology, Yale University, in New Haven, Connecticut [1]. Subsequently, we met on a number of occasions, such as the centennial festivities of the Nobel Prize in December 2001 in Stockholm, and the 50th anniversary of the discovery of the double helix structure of DNA in April 2003, in Cambridge, UK. I found him a very private person who gradually opened up more and more with every successive meeting. About being a private person, he said "I'm not interested in spending my time to make myself well known or to become very active in organizations that are engaged in the politics of science. I don't get much satisfaction from that. There are many more important things to do" [7].

He was very good in assigning credit to his mentors and to his students when discussing his achievements. Of his mentors, he singled out Leonard Lerman, Matthew Meselson, Sydney Brenner, and Lee Grodzins in his Nobel autobiography. He stressed his indebtedness to his wife, Ann M. Körner, and to his two children, for their support.

Sidney Altman was a member of the National Academy of Sciences (1990), the American Academy of Arts and Sciences (1988), and the American Philosophical Society (1990). The dates may indicate that most of his recognitions came after and not prior to the Nobel Prize. He was the recipient of the Rosenstiel Award of Basic Biomedical Research (1989) and of the National Institutes of Health Merit Award (1989), and had other distinctions. He served on the Board of Governors of the Weizmann Institute of Science (1990–1995) and as President of the Yale Hillel Association (1995–1997). He had memberships on the

scientific advisory boards of research funds and biomedical companies. He left a marked footprint in twentieth-century science.

References

1. Hargittai I (2002) Candid science II: conversations with famous biomedical scientists. Edited by M. Hargittai. Imperial College Press, London, 2002. Chapter 22, "Sidney Altman," pp 338–349
2. Altman S (1992) In: Malmström BG (ed) Chemistry 1981–1990: Nobel Lectures. World Scientific, Singapore, pp 623–625
3. Hargittai I, Hargittai M (2022) A unique venue of discoveries in structural chemistry and structural biology: the 75-year and 60-year jubilees of the MRC Laboratory of Molecular Biology—a personal tribute. Struct Chem 33:281–289
4. Crick F (1988) What mad pursuit: a personal view of scientific discovery. BasicBooks, pp 109
5. Andersson B (1989) In: Malmström BG (ed) Chemistry 1981–1990: Nobel Lectures. World Scientific, Singapore, p 620
6. Hargittai I (2002) Candid science II: conversations with famous biomedical scientists. Edited by M. Hargittai. Imperial College Press, London, 2002. Chapter 22, "Sidney Altman," pp 338–349, actual quote, pp 349
7. Hargittai I (2002) Candid science II: conversations with famous biomedical scientists. Edited by M. Hargittai. Imperial College Press, London, 2002. Chapter 22, "Sidney Altman," pp 338–349, actual quote, pp 348

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.