Yale University

Tom Steitz and the Structural Biology of the Central Dogma

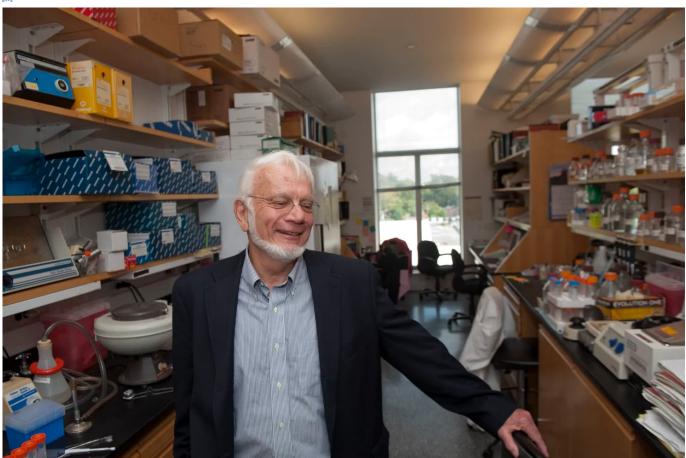
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October 11, 2018

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Biochemist Thomas A. Steitz at his Yale lab in 2009. He was awarded a share of the Nobel Prize in chemistry that year. (Douglas Healey/AP)

By Harrison Smith (https://www.washingtonpost.com/people/harrison-smith/)

October 11

Thomas A. Steitz, who won the Nobel Prize in chemistry for mapping the structure of ribosomes, molecular machines that translate genetic information into the thousands of proteins essential to living matter, died Oct. 9 at his home in Branford, Conn. He was 78.

He had pancreatic cancer, <u>according to a statement from Yale University</u>

(https://news.yale.edu/2018/10/10/nobel-laureate-thomas-steitz-dies-mapped-structure-ribosome), where he was a professor of molecular biophysics, biochemistry and chemistry and had served on the faculty since 1970.

Acclaimed as one of the finest biochemists of the late 20th century, Dr. Steitz was a kind of atomic cartographer, crafting three-dimensional maps that showed the location of tens of thousands of atoms within complex molecules. His work was credited with spurring the development of new antibiotics, but on a more fundamental level it shed light on the "central dogma" of molecular biology.

First stated by DNA co-discoverer Francis Crick in 1958, the dogma — a bedrock principle in the field — holds that genetic information passes from DNA to RNA, and from RNA to proteins. The latter, long

strings of amino acids, play an essential part in all aspects of life, transporting molecules, providing structural support to cells, transmitting signals across tissues, carrying out chemical reactions and battling pathogens such as viruses and bacteria.

While the dogma's general concept was long established, it took decades for Dr. Steitz and other researchers to fill in the details, using new computer-driven technologies to uncover the structures and functions of individual molecules. Their primary technique was X-ray crystallography, a method in which molecules are crystallized and bombarded with X-rays, resulting in pointillistic portraits that reveal the location of each atom.

Dr. Steitz worked with the HIV enzyme reverse transcriptase before turning to ribosomes in the 1990s, with some trepidation. If DNA is a blueprint for life, a ribosome is a factory, the final step in a process whereby genetic information is transcribed from DNA into RNA, ferried to one of a cell's many ribosomes, and translated into proteins.



Dr. Steitz and Sidney Altman, a fellow Yale professor who won the Nobel Prize in chemistry in 1989. (Douglas Healey/AP)

And that cellular factory, like its man-made counterpart, is imposingly large. A ribosome is composed of two subunits, and the larger section — which generates proteins, and which Dr. Steitz made the focus of his research — is about 50 times bigger than an average enzyme.

Dr. Steitz's work culminated in a pair of articles published in an <u>August 2000 issue of the journal Science (http://science.sciencemag.org/content/289/5481/905/tab-figures-data)</u>, in which he and his Yale colleagues (including chemist Peter Moore) reported discovering the structure of the ribosome's large subunit, down to the positions of all 100,000 atoms.

ADVERTISING

"I think we were amazed at each stage at the overwhelming complexity of the RNA folding in the ribosome," Dr. Steitz said in an interview with Yale's news office. "But I think the most surprising observation was that the proteins were embedded among the RNA helices, penetrating into the interior of the ribosome like tentacles."

His papers were published around the same time as related work by Venkatraman Ramakrishnan of the MRC Laboratory of Molecular Biology in Cambridge, England; and Ada E. Yonath of the Weizmann Institute of Science in Rehovot, Israel. All three scientists were awarded the Nobel Prize in chemistry in 2009, when the committee honored them for discovering "what the ribosome looks like and how it functions at the atomic level."

Because many antibiotics function by gunking up bacterial ribosomes, causing the pathogens to die, their work was credited with paving the way for the development of new drugs that could battle antibiotic-resistant bacteria. To that end, Dr. Steitz joined with two of his collaborators at Yale, Moore and William L. Jorgensen, to establish Rib-X Pharmaceuticals, now known as Melinta Therapeutics.

Notable deaths in 2018: John McCain, Aretha Franklin, Barbara Bush and other famous faces we lost this year



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"It may be hard for those who entered the ribosome field after 2000 to understand what it was like to work on protein synthesis in the Bad Old Days, uninformed by an accurate understanding of the architecture of the ribosome," Moore said in an email. "Prior to 2000, we had been blind, but now we could see. Tom was one of the pioneers that made this transformation possible."

The oldest of five children, Thomas Arthur Steitz was born in Milwaukee on Aug. 23, 1940, and raised in nearby Wauwatosa. His father was a lawyer who worked as an administrator at Milwaukee County Hospital, and his mother was a homemaker.

In an <u>autobiographical essay (https://www.nobelprize.org/prizes/chemistry/2009/steitz/auto-biography/)</u> on the Nobel Prize website, he wrote that he was initially a poor student who cared little about grades, at least until his mother "applied the 'board of education' to the 'seat of knowledge' — my first and last spanking."

He went on to develop an aptitude for tools in shop class (a skill that he said served him well in the laboratory), and a keen interest in music, winning state saxophone competitions and founding a bigband dance group in high school. "I seriously considered becoming a musician," Dr. Steitz said, "but then concluded I could do music as a hobby if I went into science, but could not do science as a hobby if I went into music."

Dr. Steitz graduated in 1962 from Lawrence College (now Lawrence University) in Appleton, Wis. At Harvard University, he studied molecular biology and biochemistry under William N. Lipscomb Jr., who in 1976 won the Nobel Prize in chemistry for research on chemical bonding.

Dr. Steitz received his doctorate from Harvard in 1966, and that same year married Joan Argetsinger, a fellow biochemist with whom he formed a scientific power couple. She had worked with Crick and James Watson, and went on elucidate the way in which long strands of RNA are "read" by ribosomes and translated into proteins.

Both researchers were professors at Yale and served as investigators at the Howard Hughes Medical Institute in Chevy Chase, Md. Joan A. Steitz received the Lasker-Koshland Award for Special Achievement in Medical Science several weeks before Dr. Steitz's death.

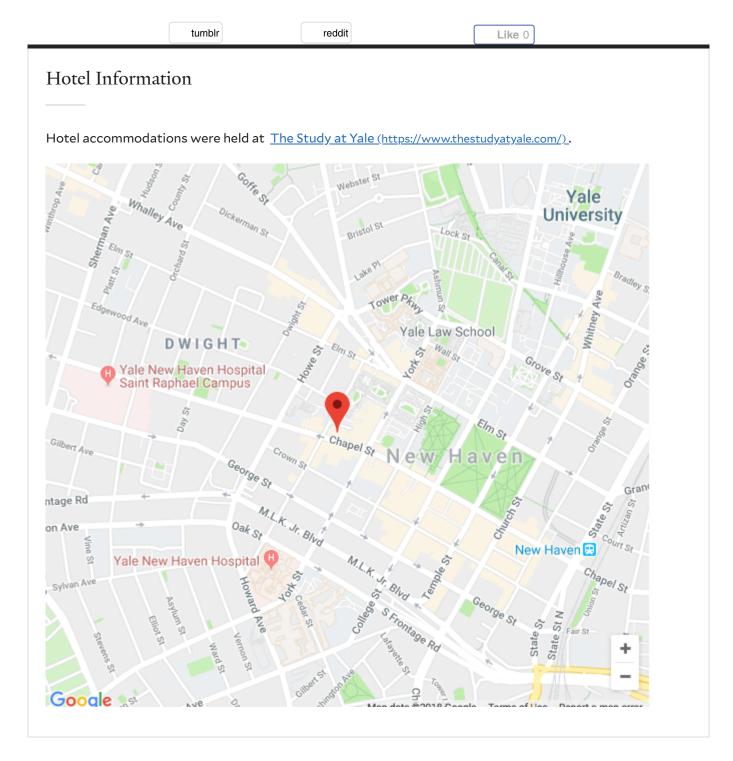
In addition to his wife of 52 years, of Branford, survivors include a son, Jon Steitz, a consultant and former minor-league baseball pitcher who lives in San Francisco, and two grandchildren.

Although Dr. Steitz was raised on the flat terrain of the Midwest and never left the region until college, when he took his first plane ride his senior year to attend a biochemistry conference at the Massachusetts Institute of Technology, he was fond of alpine metaphors and equally enamored of skiing.

His research on ribosomes, he once told the Milwaukee Journal Sentinel, was "like climbing a mountain. It looks very, very hard until you stand on top." Mapping the ribosome, he told Yale's news

office, was "like climbing Mount Everest or running the four-minute mile."

Indeed, Mr. Steitz wrote in his Nobel essay that he and his wife joined their "RNA-centric friends" on regular family ski trips, escaping from the lab to teach their children how to ski runs that were black diamond or tougher. Fittingly, these trips had a name that evoked the cellular site Mr. Steitz came to master: "Riboski."



Area Lunch options

These restaurants are within easy walking distance of the Law School:

Box 63 American Bar & Grill (http://www.box63.com/)

Tarry Lodge (https://tarrylodge.com/)

Ivy Wok (https://theshopsatyale.com/listings/ivy-wok/)

Maison Mathis (http://mm-yale.com/)

Salsa Fresca (https://www.salsafrescagrill.com/locations)

Junzi Kitchen (http://www.junzi.kitchen/)

Yorkside Pizza (https://yorksidepizza.com/)

Blue State Coffee on York (https://bluestatecoffee.com/pages/connecticut-cafes)

Blue State Coffee on Wall (https://bluestatecoffee.com/pages/connecticut-cafes)

Wall St Pizza (http://www.wallstpizza.com/)

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