Thomas A. Steitz

(1940–2018)

Crystallographer who shared the ribosome Nobel.

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One Nobel prize sometimes leads to another. As a student in 1963, Thomas Steitz heard Max Perutz talk about the structure of myoglobin, the first protein to be solved at the resolution of individual atoms. Perutz had shared the Nobel Prize in Chemistry the year before with his colleague John Kendrew, of the MRC Laboratory of Molecular Biology in Cambridge, UK. Steitz later recalled that he was stunned, thanks to the diminutive Perutz's stereoscopic slides, to see the structure "pop out in three dimensions over Max's head".

Grasping that this technique could answer questions about the molecular basis of life, Steitz joined a protein crystallography lab for his doctoral research. His scientific insight and deft hand with the notoriously tricky experiments led him eventually to the Sterling Professorship of Molecular Biophysics and Biochemistry at Yale University in New Haven, Connecticut.

In 2009, he received his own Nobel Prize in Chemistry (shared with Venkatraman Ramakrishnan and Ada E. Yonath) for his contribution to solving the immensely complex structure of the ribosome, the structure that translates genetic information into proteins in cells.

Steitz had an unerring eye for important problems. He set himself the task of unravelling the molecular basis of what Francis Crick had dubbed the central dogma of biology: that genes, made of DNA, direct the production of proteins through the mediation of RNA. His early work confirmed predictions that enzymes would change their 3D shape on binding to their substrates, and this led to work on interactions between proteins and nucleic acids. His group was the first to solve the structure of a protein that binds to DNA (a transcription factor), and the first to solve the structure of one of the enzymes that synthesizes DNA molecules, a DNA polymerase.

Born and raised in Milwaukee, Wisconsin, Steitz spent his school holidays picking radishes and weeding onions on his grandfather's nearby farm. At his local high school, he played the saxophone in the school band, and briefly considered becoming a professional musician. Instead, he won a scholarship to Lawrence College, a small liberal-arts school in Appleton, Wisconsin, where he majored in chemistry but also took courses in a range of humanities subjects. This brought opportunities to question the narrow beliefs of his upbringing, and to experience laboratory research.

At a summer school in Cambridge, Massachusetts, taught by faculty members from Harvard University and the Massachusetts Institute of Technology, he came across the field of biophysics and decided to go to Harvard for his doctoral work in that field. It was in his first year at Harvard that he had the lecture-room epiphany that determined the course of his career. He joined the lab of 'The Colonel' William Lipscomb, and became a protein crystallographer, helping to solve the structure of the versatile enzyme carboxypeptidase A.

On receiving his PhD, Steitz married fellow Harvard graduate student, Joan Argetsinger. She had been working on bacteriophage RNA in the laboratory of James Watson. Argetsinger was also a Midwesterner with a bachelor's degree from a small liberal-arts college; their careers continued to progress independently, yet in parallel. Both went to the United Kingdom for postdoctoral work at the MRC Laboratory of Molecular Biology. Tom worked with David Blow on interactions of the enzyme chymotrypsin with its substrates, and Joan with Francis Crick, Sydney Brenner and Mark Bretscher on messenger RNA.

Tom started an assistant professorship at the University of California, Berkeley, but soon resigned, on the grounds that the institution would not accept Joan into a faculty position because she was a woman. Yale was only too pleased to recruit them both, and from 1970, they each developed their own research groups. Tom's was part of the Yale Center for Structural Biology, with colleagues including Donald Engelman and Peter Moore. He continued to work on enzymes and their substrates, increasingly focusing on enzymes involved in DNA synthesis and RNA transcription.

In 1995, he began to collaborate with Moore on the structure of the ribosome, the 'final frontier' in sorting out the molecular basis of the central dogma. By 2000, their team had solved the structure of the '50S subunit' of the bacterial ribosome, the part that assembles amino acids into proteins.

This immediately clarified the action of antibiotics that work by binding to this subunit in the bacterial cell and inhibiting the synthesis of proteins. Steitz and his team founded a company, Rib-X Pharmaceuticals (now Melinta Therapeutics, in New Haven), to develop new antibiotics targeting the same binding site.

Steitz was genial, generous and gregarious, and a scientific mentor to many. His beard gave him the look of an Amish farmer or a New England whaler. As well as music, he loved sport and the outdoors, playing baseball with his son Jon (who later became a professional player); impersonating his wife as 'Dr Steitz' to gain access to the tennis courts of the University of Cambridge college that had admitted her as its first woman member; and skiing with scientific friends and their families.

He was not deflected from his fascination with new problems, either by the demands of his status as a Nobel laureate or by the diagnosis of pancreatic cancer that led to his death on 9 October. His long-standing colleague Peter Moore called him "the most accomplished structural biologist of his generation". ■

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