OBITUARY

Arthur Kornberg (1918–2007)

Passionate biochemist with a love for enzymes.

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Arthur Kornberg was one of the greatest biochemists of the twentieth century. His career spanned more than 60 years, and such has been the impact of his work on modern biomedical science that his influence will endure for decades.

Kornberg was born in Brooklyn, New York, to a family of modest means. He had no exposure to science as a child; the young Arthur collected matchbook covers, the dominant flora of the Brooklyn streets, rather than the insects usually associated with a scientifically inclined youngster. He nonetheless opted to study chemistry and biology, and received his bachelor's degree from the City College of New York, one of three students from the class of 1937 destined to receive the Nobel prize (Herbert Hauptman and Jerome Karle were the others).

He went on to earn an MD from the University of Rochester, New York, where he wrote his first research paper on a mild form of jaundice he discovered in himself and classmates. For a short period he was a (self-described) attentive physician, first in New York, and then in the US Navy. But it was a transfer to the Public Health Service in 1942, which landed him at the National Institutes of Health (NIH), that was the turning point of his career.

At the NIH, and during research with Severo Ochoa at the New York University School of Medicine, and with Carl and Gerty Cori at Washington University School of Medicine, Kornberg turned to the study of enzymes, which he loved and considered the vital force in biology. He initially analysed enzymes involved in the synthesis of nucleotides and related small molecules. Nucleotides are the building-blocks of the molecule of heredity, DNA. Kornberg soon turned to the search for an enzyme that could synthesize this polynucleotide chain. His inspiration was not the 1953 Watson–Crick structure of DNA, but rather the Coris' work on the enzymatic synthesis of other biological macromolecules.

Kornberg had taken on a daunting task. A guiding principle of his research, however, was that a persistent biochemist could reconstitute any cellular event in a test tube. Moreover, he felt that the biochemist had the advantage of being able to optimize the reaction without the burden of working under the constraints imposed by cells. Kornberg set up a reaction containing DNA, radioactive thymidine (a nucleoside) and protein fractions obtained by breaking open *Escherichia coli*, an intestinal bacterium. Initially, only a tiny fraction of the labelled thymidine was converted into a form that seemed to be a DNA-like molecule. But, with this glimmer of activity (and many controls demonstrating reaction specificity) Kornberg persevered, and eventually found the proper form of the building-blocks needed for efficient synthesis.

Late in 1957, Kornberg's manuscripts describing the test-tube synthesis of DNA from precursor molecules by an enzyme — DNA polymerase — were rejected by *The Journal of Biological Chemistry*. Reviewers thought it premature to call the product 'DNA'. In the spring of 1958, however, a new editor stepped in and accepted the papers. Less than two years later, Kornberg's discovery, and the independent work on the synthesis of RNA polymers by Ochoa, were recognized by the Nobel Prize in Physiology or Medicine.

The enzymology of DNA replication remained Kornberg's passion for the next 30 years. His approach was to build up increasingly complex biochemical reactions that recapitulated cellular DNA replication processes. In 1967, he successfully replicated the DNA of a small virus, a feat that received much attention as it was (incorrectly) reported that he had created "life in a test tube". This was nonetheless a seminal achievement that defined many of the principles governing DNA replication of all genomes.

For example, the concept that special enzymes are needed to start DNA chains, which DNA polymerase then elongates rapidly and with exquisite fidelity, arose from this work. Likewise, Kornberg's work provided insight into the function of origins of replication, the sequences on a chromosome that direct the start of a cycle of DNA replication. In the 1980s, after ten years of effort, Kornberg's group reconstituted the replication of a DNA molecule initiated using a true origin 'cloned' from a cellular chromosome. The resulting model of the steps required for initiation of DNA replication at a chromosomal origin remains the paradigm for investigating replication in more complex organisms today.

From 1990, Kornberg's lab focused on the enzymes involved in polyphosphate metabolism. He continued this work until a week before his death on 26 October.

Kornberg's impact on modern biology has been enormous. He spearheaded the purification and characterization of many of the enzymes that have become essential tools of genetic engineering. He was also a visionary leader, who had an immense influence on the education of scientists. In 1959, he founded the biochemistry department at Stanford University. There, he forged a remarkable community, in which faculty limited the size of their research groups, pooled grants, and shared space and equipment.

He also successfully integrated his work and family life, bringing his children Roger, Tom and Ken, and then his grandchildren, to the lab and to conferences. His first wife, Sylvy (pictured here with him), was a gifted biochemist and worked alongside him for years. To Arthur's great pride and joy, Roger became a colleague at Stanford and, in 2006, received the Nobel Prize in Chemistry.

Then there is Arthur's extended scientific family. As a mentor he was passionate about both his science and his people, and held us to the same exacting standards as he held himself. Although fundamentally impatient, he was never too busy or too famous to discuss our data, edit our manuscripts (again, and again, and again), or to critique our presentations. He drove us crazy with his (not so gentle) homilies. "Keep your lab notebook with more accuracy than your cheque-book." "Only four lines per graph." "Don't go home until you find your enzyme activity." "Time is your most important resource." But we learned, treasure the memories, and now torture our own students with 'Kornbergisms'. I think Arthur would be pleased.

Tania A. Baker
Tania A. Baker is in the Department of Biology, Massachusetts Institute of Technology, and the Howard Hughes Medical Institute, 77 Massachusetts Avenue, Cambridge, Massachusetts 02139, USA.
e-mail: tabaker@mit.edu