# Jonathan Widom

## (1955–2011)

Genomic map-maker and consummate teacher.

One of the fundamental paradoxes of DNA, life's most iconic molecule, is that nearly a metre of this polymer must be packed into the microscopic nucleus of every human cell while still granting access for the many biochemical and biophysical transactions needed to exploit its genetic information. Jonathan Widom rigorously and creatively applied physical and chemical principles to unravel the mystery of how genomes can at once be tightly packed and yet available for read-out. He did this over a 30-year career that ended unexpectedly and prematurely on 18 July 2011. He was 55.

Widom was born in Ithaca, New York, to parents who were, and still are, both chemists at Ithaca's Cornell University. The first of three children, who all became scientists, Widom's career reflects the intellectual curiosity fostered in his scientifically prolific home. Growing up near the Finger Lakes of upstate New York, he and his friends searched for crayfish, toads, butterflies and moths in the streams and fields, foreshadowing his future in biology. His passion for exploration, cultivated in his early days, only increased, as did the palette of topics he chose to investigate. In 1977 he obtained a bachelor's degree in chemistry, also from Cornell.

### UNPACKING DNA

Widom's lifelong interest in how organisms manage their genomes began during his graduate student days in the laboratory of Robert Baldwin at Stanford University in California. In viruses that infect bacteria, more than 10 micrometres of DNA is stuffed into a roughly 50-nanometre protein head, a process that has been likened to putting 500 metres of suspension-bridge cable into the back of a delivery truck. Widom's thesis work used electron microscopy and light scattering to test ideas about DNA packing, inspired in part by the startling observation that when surrounded by appropriate ions of opposite charge, DNA will spontaneously collapse into doughnut-shaped configurations.

After completing his PhD in 1982, he moved to the laboratory of Aaron Klug at the Medical Research Council Laboratory of Molecular Biology in Cambridge, UK. There he turned his attention to the geometry of eukaryotic DNA packing, setting the stage for the scientific questions that would dominate his career. Proteins known as histones compact DNA in eukaryotic organisms. Histones form stubby cylindrical octamers, and each octamer wraps up nearly 150 base pairs of DNA to form a nucleosome. Widom's beautiful seminars spelled out his vision for a physically based genome science. This vision spanned from the rules governing the assembly and accessibility of individual nucleosomes all the way to what dictates nucleosome positioning genome-wide, and how this positioning governs gene expression. In recent years, this vision has been coming to fruition, largely as a result of Widom's work.

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During the 1990s, one of the most important questions that Widom attacked with his "troops", as he affectionately called those working with him in his lab, was how the many proteins that copy, transcribe and repair genomic DNA reach sites within individual nucleosomes. As an independent investigator, first at the University of Illinois in Urbana-Champaign and later at Northwestern University in Illinois, he designed increasingly accurate experiments to measure the rate at which individual nucleosomes open up to render their sequestered DNA accessible. He probed the influence of packing depth and environment by burying recognition sites for DNA-cutting enzymes or fluorescent molecules at different spots within nucleosomes. He delighted in starting with simple models based on fundamental principles and seeing how far those models might go in explaining complicated biological problems.

Widom articulated the biological problem that most consumed him in recent years as: "Do nucleosomes care about their position on the genome and does the genome encode the positions of these nucleosomes?". As a prelude to answering these questions, Widom and his troops performed one of his most well-known experiments, revealing the extent to which different DNA sequences favour the formation of nucleosomes. These results sowed the seeds for his seminal genome-scale efforts to seek out the rules for nucleosome occupancy in organisms ranging from yeast to humans. At the time of his death, he and his collaborators had just introduced a groundbreaking chemical-mapping strategy using engineered histones to investigate this question and produce maps at base-pair resolution.

### LEGENDARY GENEROSITY

Jon was the best of colleagues. He was noted for his honesty, kindness and insatiable curiosity. He loved life, and everyone around him felt happier and smarter in his presence. His generosity was legendary. As a tiny but telling example, each year he and his wife Daphne bought four season tickets for the opera and took a pair of friends or colleagues to each performance. At work, he always had time to help anyone who asked, never hinting that he had his own prodigious workload.

He loved cooking and there was no better dinner companion. He read insatiably, and his resulting broad and penetrating knowledge, scientific and otherwise, often gave others the feeling that he knew more about their work than they knew themselves. His passion for exploration took him all over the world, with recent trips to India and China merging his love of food and the outdoors. For many of us, his attendance at a meeting was a prerequisite for our own.

An ancient Greek definition holds that happiness is "the exercise of vital powers along lines of excellence in a life affording them scope". Jonathan Widom had extraordinary vital powers which he exercised along lines of excellence in a way that was an inspiration to all. ■

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