Piers Nye

David H. Dressler 1941–2014

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The year 2014 represents an unfortunate landmark in the study of genetics: two scientists who together clarified our understanding of genetic recombination, Robin Holliday and David Dressler, passed away this year, on 9 April and 27 May, respectively.

David Dressler was born in Cincinnati, Ohio, in 1941, graduated from Columbia University in 1963 and went on to graduate school at Harvard University, joining the developing molecular biology group headed by James Watson and earning his doctorate in 1969. David's dissertation experiments showed that the Φ X DNA replication intermediate was not, as was dogma at the time, a double-stranded circle of unit genome length but included a much longer linear positive strand that was synthesized in a continuous fashion from a circular negative-strand template. This discovery led to the now established 'rolling circle model' of DNA replication but not without setbacks.

Difficulties arose because Robert Sinsheimer, the avowed leader of Φ X DNA replication studies, promoted the standard model. Accepting this authority, David's official mentor disbelieved David's results and terminated his fellowship. Walter Gilbert then gave David the space and resources to continue the experiments that proved the rolling circle model and were one of the first demonstrations of the asymmetric growing point, in which one daughter strand is elongated continuously and the second daughter strand is elongated discontinuously. Today we view these results as axiomatic, but they were highly controversial at the time of their finding.

David continued his research on DNA, using molecular biology and electron microscopy to demonstrate the application of the rolling circle model to ribosomal DNA amplification in *Xenopus*, the bidirectional and asymmetric growing points during the replication of bacteriophage T7 DNA, the structure of the origin of DNA replication in phage G4 and the inverted repeats on the ends of adenovirus DNA. When I joined David's laboratory in 1972, I expressed interest in studying recombination, and we chose as the experimental system one of the newly discovered *Escherichia coli* plasmids that had a single restriction site. The many double-sized DNA molecules we observed through the electron microscope started out with the configuration of a figure eight and changed upon digestion to an X shape (which we termed a 'chi form'). The fact that chi forms were only present in RecA-positive cells established them as recombination intermediates. Partial denaturation then showed that the two recombining double helices had exchanged and religated single strands to generate the very structure that Robin Holliday had proposed in 1964 as part of the recombination model that he developed on the basis of genetic studies in fungi. The physical demonstration of the Holliday junction thus solidified the Holliday model and its subsequent modifications as fundamental to both prokaryotes and eukaryotes.

In addition to being dedicated to research, David was also a devoted teacher. Together with James Watson, Guido Guidotti and

Konrad Bloch, David initiated the first biochemistry and molecular biology course at Harvard, Biochem 10, which over the next decade with David's leadership became one of the most popular and successful courses at Harvard. David's approach to teaching was that students should learn not

only the outcomes but also the hypotheses, the methods and the experiments that led to groundbreaking discoveries. His students appreciated this approach as providing a valuable and far-reaching training in scientific thinking.

David's conviction that it was possible to present the logic and experimental design behind discoveries of molecular biology in ways that all interested people could understand also led him to a remarkable teaching moment for the public. In 1976, with the ending of the self-imposed ban on recombinant DNA experiments initiated at the Asilomar conference, many researchers were eager to move forward under the new US National Institutes of Health guidelines, with the hopes of not only understanding more about fundamental biology but also applying that knowledge to developing treatments for human diseases. This intention elicited a backlash from some scientists and populists who claimed that recombinant DNA might create monsters in the laboratory that could escape and wreak havoc and also that there was something possibly unethical about playing God and speeding up evolution artificially. The ensuing debate before the Cambridge City Council pitted titans of biology such as Nobelist George Wald and other Science for the People proponents against David Baltimore, Walter Gilbert, Matthew Meselson and Mark Ptashne. In this environment, David decided to take his research to the street and set up a table just down the way from the Science for the People booth at an outdoor fair near the Massachusetts Institute of Technology. There he showed passers-by how to spread Petri dishes with *E. coli* and what phage plaques and bacterial colonies looked like. With this real-life demonstration, David helped to reduce and counteract the mystery, fear and uncertainty that others were trying to use to have such techniques banned. By presenting science to nonscientists in an understandable way, David showed that science itself was already for the people.

After a short time at Princeton University, David returned to Harvard, where together we wrote the Scientific American Library book *Discovering Enzymes*. In the last stage of his professional life, he taught for almost fifteen years as a lecturer in the Biochemistry Department and as a tutor at Balliol College at Oxford University in the UK, where he then retired. David Dressler will be fondly remembered and appreciated by the thousands of students who learned from him at three major universities.

Electron micrograph of the chi form

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