The Recombinant DNA Controversy: A Memoir — Science, Politics, and the Public Interest; 1974–1981

By Donald S. Fredrickson. 388 pp., illustrated. Washington, D.C., ASM Press, 2001. $39.95. ISBN 1-55581-222-8.

RECOMBINANT DNA technology began in the early 1970s, and it completely changed the world of biology and medicine. In essence, this technology allowed one to combine segments of genetic material from essentially any organism, using simple enzymatic reactions in test tubes, and to propagate the resulting recombinant DNA in living organisms such as *Escherichia coli* and mammalian cells. Recombinant DNA technology is used in virtually every area of biology, and it is hard to imagine the explosion of biologic information that has occurred over the past 30 years without it. Among the numerous practical benefits of recombinant DNA technology are the large-scale production of proteins of therapeutic value, the development of diagnostic tests for the human immunodeficiency virus, the sequencing of the human genome, the use of DNA testing in criminal trials, the creation of genetically modified plants, and current efforts in gene therapy. Recombinant DNA technology also initiated the change in biology from an academic discipline to a major industry.

The early days of the recombinant DNA era were marked by heated controversy related to the safety and morality of generating living organisms with combinations of genetic material completely unlike those occurring in nature. The National Institutes of Health (NIH) played a central role as referee in this controversy by forming a Recombinant DNA Molecule Program Advisory Committee (RAC) and formulating explicit guidelines for performing the experiments. Donald Fredrickson was the director of the NIH during this period, and his valuable memoir provides a unique perspective on the events.

As described in chapter 1, the initial practitioners of recombinant DNA techniques and other leading molecular biologists proposed and implemented a moratorium on certain experiments in order to assess the hypothetical hazards of the technology. This voluntary and unprecedented moratorium evolved into voluntary guidelines for performing experiments with recombinant DNA and a request for the NIH to become involved in an official capacity. Most of the remainder of the book describes, in great detail, how the NIH formulated the original guidelines and how these guidelines were relaxed over time as the hypothetical hazards became increasingly remote possibilities.

Although the book is largely a detailed description of events, Fredrickson does address the key issues. Should the NIH issue guidelines for handling recombinant DNA or should it or some other federal agency establish regulations that would be subject to federal law? Who should compose the RAC and make the judgments: scientists who were familiar with the technology, lawyers and politicians, or the lay public? Should the guidelines be federal, or should local communities be able to craft their own (typically more restrictive) versions? How should new knowledge about the risks and benefits of the technology be translated into modified guidelines and regulations? How could appropriate guidelines be extended to private industry and other countries, and how could such guidelines be enforced? Fredrickson's opinions on these issues are apparent, but unfortunately, they are somewhat buried and scattered throughout the detailed narrative.

The book closes with two brief chapters describing the evolution of the RAC to deal with new, pressing issues such as gene therapy and touching on the more general relation between scientific discovery and public participation. It is disappointing that Fredrickson devotes so little space to these fundamental issues, particularly given his unique perspective on the first defining case for regulating biologic research.

Fredrickson's account is meticulously documented, well balanced, and accurate. In a modest manner, he portrays himself as a fair and effective NIH director during these turbulent times. This self-portrayal is in accord with the general opinion of the molecular biology community during the controversy, and in retrospect, it is evident that Fredrickson skillfully played the cards he was dealt. Having myself conducted a nearly banned experiment that demonstrated functional expression of a eukaryotic protein in *E. coli,* I found it interesting to learn about the nonscientific constraints on the NIH director in his pursuit of a reasonable course of action. At the time, virtually all of us actually performing experiments with recombinant DNA thought the hazards were negligible, except perhaps in very special cases. Moreover, we thought that experiments involving single genes out of their normal context were much safer than conventional experiments on tumor viruses and other infectious agents, which are highly evolved threats. In the laboratory, the guidelines were followed grudgingly; the containment procedures were perceived as excessive and arbitrary, since there was no evidence of or belief in the risk. In addition, the guidelines were confusing with respect to whether the restrictions applied to free-living organisms, virus particles, or the recombinant DNA itself. In practice, recombinant DNA itself was not treated as a biohazard, because this would have required electron microscopes, ultracentrifuges, and other sensitive pieces of equipment to be disinfected after each use.

Fredrickson's memoir is a valuable historical document, but beyond that, it is unclear for whom it is intended. The science behind recombinant DNA is nicely introduced in the first chapter, but the scientific details throughout the remainder of the book will be impenetrable to nonscientists. Details of the federal bureaucracy, the relevant laws, and the long list of characters are difficult to follow and of limited interest, except to historians. The writing style — a curious mixture of federal document, legal brief, and diary — makes for difficult reading. Despite these deficiencies with respect to a general audience, Fredrickson's memoir is a unique and important contribution to our understanding of a pivotal moment in the history of biologic research.

Kevin Struhl, Ph.D.
Harvard Medical School
Boston, MA 02115
kevin@hms.harvard.edu