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## Recombinant DNA Revisited

Thoughtful people might well begin to wonder at yet another celebration marking a new generation of major discoveries in molecular genetics. But it is true that since 1953, when the Watson-Crick model for DNA structure was proposed, there has been a dizzying succession of advances, each deepening our understanding of biology at the molecular level. It has been a 30-year high for those who participated, although for the most part we did poorly in imparting to others the reasons for our excitement.

In this regard, the recombinant DNA debate had a happy effect. The daily papers and television now report frequently on the activities of biologists. Lately, these reports have been upbeat, as the production of rare and medically significant materials nears reality. This is a marked change from the hair-raising headlines of a few years ago. Most people now understand that the extreme views heard at the height of the debate were groundless. No novel hazards have emerged from the research, and the cautious approach instituted at Asilomar in 1975, and continued by national guidelines in many countries, has not seriously hampered the progress of research.

Dramatic differences exist between the reports appearing in the mass media and those in this issue of *Science*. The manufacture of important biological agents like insulin and interferon by recombinant DNA procedures is the fruit of the basic research of the past. Here are reported the foundations for the future. It would be foolhardy to try to predict specific outcomes. We can be certain only that they will be unexpected and astonishing. And we ought not fear these unknowns. Rather we should work to ensure that the singular intellectual bounties of our era are exploited for the good of all.

The present articles, regardless of any future impact, stand on their own for their originality and remarkable insights into how the genes of all organisms, including man, are arranged, expressed, and regulated. Once we thought the DNA of complex organisms was inscrutable. Now we cope with it readily. We thought of DNA as immovable, a fixed component of cells. Now we know that some modules of DNA are peripatetic; their function depends on their ability to move about in a genome. There are already sufficient examples of peripatetic DNA for us to be certain that it is a universal element in differentiation and development. We thought genes were continuous stretches of DNA. Now we know coding regions may be interrupted dozens of times, and spliced together in the form of messenger RNA when needed. We have learned that genes are fungible; animal genes function perfectly well within bacteria and bacterial genes within animal cells, confirming the unity of nature. We need no longer depend on chance events to generate the mutations essential for unraveling intricate genetic phenomena. Specific mutations can be constructed at will, and millions of mutant genomes readily produced for study. We already see that some standard questions about evolution must be rephrased to account for new information.

Recombinant DNA techniques alone did not accomplish all this. Coincident improvements in methods for the chemical and enzymatic manipulation of DNA were equally important. First, the discovery and exploitation of restriction endonucleases allow us to cut up large genomes into reproducible small segments. The segments are ready-made for insertion into a recombinant DNA vector because of the special termini generated by the endonuclease cleavage. Next, it is feasible and indeed common to determine with precision the sequence of thousands of base pairs on a DNA segment. Finally, there is the matter of scale; nanogram, even picogram amounts of DNA can be characterized with precision because of the availability of highly radioactive phosphorus-32 and simple electrophoretic techniques carried out on semisolid gel supports. Together, these methods have opened opportunities unimaginable even 5 years ago. And molecular biologists alone did not accomplish all this. They had unprecedented support from enlightened societies and governments. It has been a joint venture, and we should celebrate together.—MAXINE SINGER, *Chief, Laboratory of Biochemistry, National Cancer Institute, Bethesda, Maryland 20205*