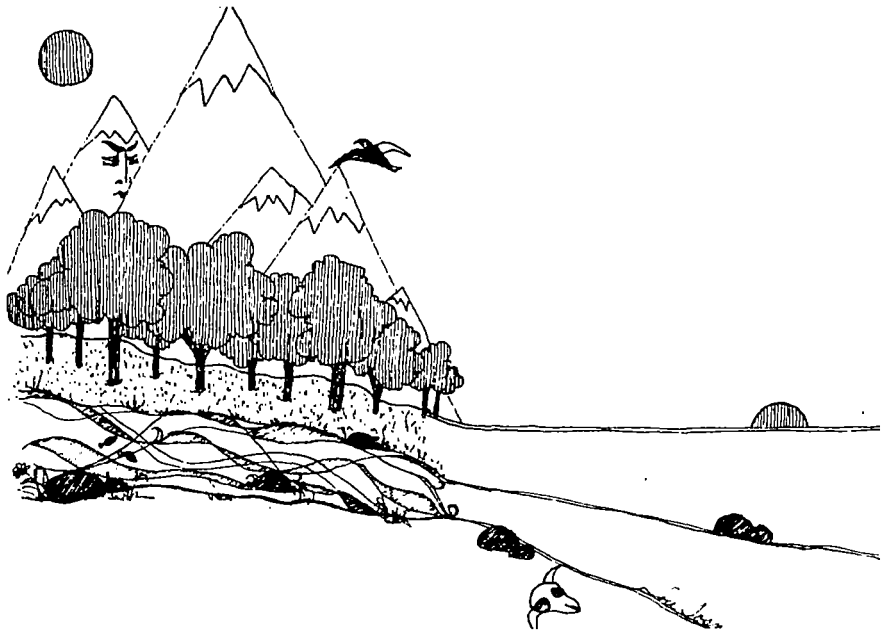

# You Shall Be As Gods

## Recombinant DNA: The immediate issue is safety; the ultimate issue is human destiny

Tabitha M. Powledge

Already the term "recombinant DNA" comes easily to the lips of legislators and television commentators. A few of them can even manage "deoxyribonucleic acid," which is what DNA stands for.

DNA is the genetic material, the miraculous self-replicating double helix of Watson and Crick, the marrow, soul, and substance of all earthly life. Molecular biologists have been tinkering with it for a couple of decades now, and only recently have they learned to slice it up and then stick it back together in new ways: hence recombinant DNA. Scientists have also discovered ways to transfer it from one living thing to another: to put genes from one kind of animal into a different kind, from bacteria into plants, or to put the newly spliced genes into just about any living cell. Bacteria that never before existed are being manufactured in molecular biology laboratories, and there are great plans for more to come: bacteria that will make human insulin for diabetics, bacteria that will gobble up oil spills and find gold and platinum in garbage, bacteria that will construct antibodies against the world's most burdensome diseases, antibodies that we can take by mouth just like vitamins.

That's the good news. And the bad news? It is equally speculative. Bacteria carrying genes for resistance to antibiotics might escape the lab and transfer that antibiotic resistance to bacteria living in the human intestinal tract. Or food plants genetically engineered to grow well without applications of fertilizers might be so successful that they will sweep the earth, driving out other vegetation and disrupting ecosystems. Or, says Erwin Chargaff, Emeritus Professor of Biochemistry at Columbia, "Were I not so averse to rancid science fiction, I should say that the spreading of experimental cancer may be confidently expected."

All of this—both risks and benefits—is conjecture; facts about recombinant DNA are next to nonexistent. Yet after nuclear power, and possibly the SST, recombinant DNA is the most torrid science policy issue around, rending academic departments, pitting Nobel laureates against one another, and setting scientists against their communities and against the Congress of the United States. It is a nice irony that it was the scientists who brought it up in the first place.

The scientists' concerns about these experiments have always centered around their safety, chiefly because the experiments usually involve transplanting new genes into a laboratory strain of *Escherichia coli* (*E. coli* for short), the common colon bacillus that is a normal resident of the human intestinal tract. Though the scientists' *E. coli* is not identical to the wild-type bacterium, there is some uncertainty about whether it retains its relative's ability to colonize the human gut, and so there is some legitimate cause for worry about splicing new genes (some of which might be harmful to humans or other life) into it.

In 1973, when work on recombinant DNA was just getting started, Stanford University's Paul Berg decided against transplanting animal tumor viruses into *E. coli*; although he thought the risk of harm was low, he could not persuade himself that it was

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nonexistent. By the summer of 1974 concern had grown to the point where an ad hoc committee of the National Academy of Sciences, chaired by Berg and composed of several other prominent molecular biologists, called for a moratorium on recombinant DNA research until an international meeting could be organized to devise adequate safety procedures. It is an indication of the extraordinary nature of that request that it was published simultaneously in *Science* and in *Nature*, the two most illustrious technical journals in the world. Even more extraordinary, the moratorium seems to have been largely observed. It was the first time in the history of science that an entire group of researchers voluntarily refrained from a particular type of experiment, an experiment, furthermore, that was the most technically challenging and theoretically exciting in their field. (For comparison try asking physicists to stop looking for elementary particles.)

The process leading up to and following that international meeting, held in February, 1975, was named after the meeting site, Asilomar, a conference center on California's raw and foggy Monterey peninsula. In three days a handful of lawyers and nearly 140 molecular biologists (including a quiet delegation from the Soviet Union) hammered out draft safety guidelines. They did so in full view of the press. Coverage was widespread, thorough, and careful, with superb reports carried in publications as disparate as the *Washington Post* and *Rolling Stone*.

Since the National Institutes of Health (NIH) was at that point paying for a large percentage of recombinant DNA research, an NIH committee took over from there and spent the next eighteen months reworking the guidelines, although never without criticism from those who thought the guidelines too strict and those who thought them too lax. NIH even (the recombinant DNA story is brimful of precedents) held a public hearing to which it invited consumer representatives, philosophers, and other types not usually asked for comment on the conduct of science. In their current form the guidelines, which will continue to be revised and updated, provide for two kinds of procedures designed to keep the experimental organisms—and their newly inserted DNA—from getting out of the lab: physical containment and biological containment.

The physical containment procedures specify four levels of stringency, designated P1 through P4 (the last the most rigorous), depending on the degree of theoretical risk in the experiment. (Many of the procedures are similar to those imposed on researchers who normally work with pathogens. One of the effects of the safety discussion has been to raise the consciousness of molecular biologists, who traditionally have not thought of themselves as dealing with dangerous organisms and who have therefore not been careful about smoking and eating in the lab, or pouring cultures willy-nilly down the sink, or doing other things that horrify experimenters accustomed to research with pathogens.) No P4 (highest containment) labs yet exist, though one is being constructed in an NIH trailer, and a laboratory at Fort Detrick, Maryland—site of the government's past biological warfare experiments—is being modified to meet P4 standards.

Still, given the fact that people make mistakes in labs, and that Murphy's Law (If anything can go wrong, it will) operates in scientific experiments just as in other areas of life, many scientists believe that the second kind of protection—biological containment—will offer the closest thing to a guarantee of safety. First proposed at Asilomar, this clever notion involves manufacturing an experimental organism—in this case an *E. coli*—with an assortment of needs (such as temperature, nutrients, pH) so peculiar that they can only be provided within the artificial confines of the lab. The idea is that if such a creature does by accident escape, it will perish immediately. At Asilomar it was assumed that it would take only a few weeks to come up with such a novel bug (which is what the scientists call the bacteria they experiment on), but it proved much more difficult than had been imagined. It was not until 1976 that Roy Curtiss of the University of Alabama Medical School bred χ 1776, the bicentennial bug, which needs five more chemical nutrients than the usual laboratory *E. coli* and is also laid low by detergent, the bile found in the human gut, and sunlight. Despite the importance of devising laboratory-dependent creatures like χ 1776, Curtiss's is the only lab in the world doing this work.

In addition to devising safer procedures for much recombinant DNA work, the NIH guidelines also prohibit certain kinds of experiments. For instance, it is prohibited to transfer drug resistance to an organism that is not known to acquire it naturally, or to deliberately release into the environment any organism containing recombinant DNA.

In short, the NIH guidelines appear to most (though of course not all) of the interested parties to be quite stringent and to err, if at all, on the side of caution. They are a powerful weapon. In order to get money from NIH a research group will have to demonstrate that it is observing the guidelines. In addition there are several moves under way to write the guidelines into law and make them mandatory for all recombinant DNA research. Such legislation has already been introduced in New York and California and is being considered in other states. Such local efforts appear likely to be superseded, however, by federal legislation that has received the enthusiastic endorsement of senators and congressmen, government officials, and even the scientists themselves. There are several good reasons for such a move, restrictive as it may at first appear. For one thing, proliferation of local option might very well result in recombinant DNA research being concentrated in states with the least restrictive policies, and that would defeat the whole purpose of the lengthy safety debate.

Even more important, there seems to be no other way to impose the guidelines on research over which NIH has no control. Recombinant DNA research is being supported by three other government agencies: the National Science Foundation, the Veterans Administration, and the U.S. Department of Agriculture. Furthermore, commercial organizations are showing enormous interest in recombinant DNA. Several corporations—

mostly drug companies—are already involved in the research, and others are planning to begin soon. One company, Genentech, has already been specifically set up to explore its commercial possibilities, and early this spring a Wall Street research firm sponsored a seminar for major institutional investors in which prospects for investment opportunities in recombinant DNA were a topic. Some of these organizations say they are inclined to adhere voluntarily to the NIH guidelines, but legislation would make the guidelines applicable to everybody doing the research. Clearly that is a more desirable state of affairs than hit-or-miss voluntarism.

But there is one big danger in legislation. It may lull people into feeling that the problems with recombinant DNA research have been solved. In fact, they are probably only beginning. Legislation mandating compliance with the guidelines by itself doesn't mean much unless it also stipulates effective enforcement procedures; but enforcement of recombinant DNA safety regulations is going to be very tough. National legislation is likely to give the federal government power to license labs to do recombinant DNA research. That could mean—provided enough money is budgeted for proper inspection—perfectly adequate supervision for university and much commercial research, but whether it will do the whole job is doubtful. For instance, competitive pressures may provide powerful incentives to keep some industrial research secret, particularly if the commercial applications of recombinant DNA turn out to be anything like the hopes for them.

Although they haven't been much discussed, the military applications of recombinant DNA, which would also be covert, also seem obvious. If it is possible to construct a lethal or debilitating bug by accident, it is surely possible to do so by design. The biological warfare conventions now in force would probably apply to recombinant DNA, and the Department of Defense says it is not presently funding any recombinant DNA research and has no immediate plans to do so. But the recent record of government agencies is not one that inspires trust in their candor, and a certain amount of skepticism toward such declarations seems only prudent. Nor, of course, would U.S. enforcement procedures be of much use against possible terrorist uses of recombinant DNA, or against experiments—military and other—carried out in other countries.

The noise over recombinant DNA is largely confined to the U.S., though the work is certainly going on elsewhere in the world, particularly in Europe. The British have developed a set of guidelines called the Williams Report that place more emphasis on physical containment and less on biological containment than the U.S. guidelines. They are being observed voluntarily in some places, but, says Sir John Kendrew, director general of the European Molecular Biology Laboratory, which is supported by ten Western European countries, "In Europe the difficulty in this, as in so many other spheres, is that the region consists of a large number of sovereign states with different science policies, different legal systems, different national interests, and different national temperaments. Various international organizations exist at different levels that offer the possibility of united actions and policies, but all of these organizations have more or less limited geographical coverage and extremely limited authority."

The European Molecular Biology Organization (EMBO), the European Science Foundation (ESF), and the European Economic Community (EEC) have all done some work on the subject, but they have not coordinated their efforts. And, of course, none of this work applies to Eastern Europe, let alone anywhere else in the world. In addition, many European countries have their own national committees, and the USSR is also said to be at work on guidelines. Some first steps toward worldwide control have been taken: A committee of the World Health Organization is considering the public health implications of recombinant DNA research, and a Committee on Genetic Experimentation (COGENE) has also been set up by the International Council of Scientific Unions.

One very great difficulty with control of recombinant DNA research is that, as modern scientific work goes, it is not very expensive or complicated. Nor does it rely heavily on elaborate technology (except for the containment procedures, which will increase costs and complexity). Labs in underdeveloped countries will be able to undertake the work. Some of the experiments are the sort of thing bright high school students will be doing in a few years. What some people find most worrisome is that terrorists will resort to recombinant DNA, either to devise actual weapons or for blackmail.

In short, since bacteria are not limited by national boundaries, and recombinant DNA work will be going on in many places, the U.S. safety restrictions, even if they were completely effective, cannot guarantee that disaster will not result from work with recombinant DNA. However, since outlawing the work would be fruitless, it would also seem wise to press for the toughest possible restrictions in order to reduce the risk.

Troubling as the questions of safety are—and the discussion so far has centered on safety—those questions may not be the most important ones to be asked about recombinant DNA research. In recent months there has emerged from the debate a second set of questions. These deal with the morality of future designed genetic change, particularly designed genetic change of human beings. Molecular biologists tend to brush off these questions because purposeful gene change is not now possible. While conceding their ultimate importance, some researchers think such ethical inquiries should be put off another decade or two, until true genetic engineering is closer to reality. Still, what is likely to begin soon as attempts to cure genetic disease by substituting functioning genes for malfunctioning ones—a laudable goal—will very probably lead in the not-too-distant future to the ability to direct the evolution of all living things on this planet, our own included. We are fond—perhaps excessively fond—of attributing to ourselves godlike powers. But control of evolution is surely the quintessence of deity, and it can hardly be too early to start reflecting on what it might mean to accept such a challenge. Or to bear such a burden.