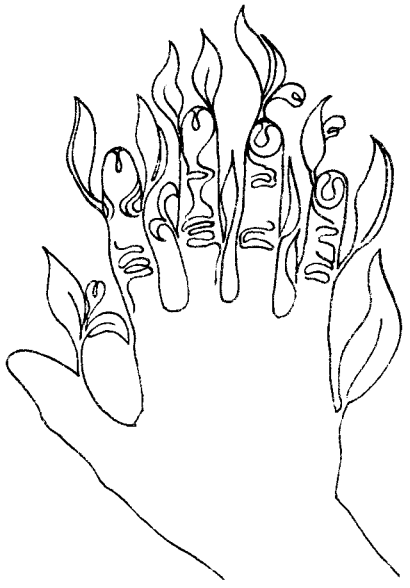
THE GENETIC ENGINEERING DEBATE

by David Straton



Genetic engineering has aroused an unprecdented controversy in the scientific world. It has been described by one Nobel prize-winner as creating the greatest ethical problem that science has ever had to face. (Wald, 1976). Another Nobel prize-winner has been quoted as calling its critics 'shits and incompetents'. (Golden, 1977). This article throws some light on this heated debate by describing some of the techniques involved, tracing the history of the controversy both overseas and in New Zealand, and then summarizing the arguments on each side. It concludes that a wider public debate is needed.

What is Genetic Engineering?

Some people reject this term as being emotive. (Bergquist, Petersen, 1977). But essentially, whether it is called genetic engineering or recombinant DNA research, it amounts to 'Research involving the combinations of DNA molecules from different biological origin using any methods that overcome natural barriers in mating and recombination to yield molecules that can be propagated in some host cell, and the subsequent study of such molecules'. (E.M.B.O., 1976). In simple words, the artificial transfer of genes from one species to another.

The groundwork for this was laid in 1944, when Avery, McLeod and McCarty succeeded in transforming the cell coat of the pneumococcus by adding purified DNA from a different strain of pneumococcus. (Avery and others, 1944). However, the significance of this research was not widely recognized at the time. Throughout the fifties and most of the sixties, attempts to manipulate the genetic structure of organisms used the technique of bombarding them with radiation in order to increase the mutation rate.

A series of important breakthroughs occurred in the late 1960s and early 70s. Paul Berg, and Stanley Cohen, both from Stanford University, and Herbert Boyer from the University of California at San Francisco, discovered between them how to cut strands of DNA, how to stick them together, and how to introduce them, using a specific vehicle, into a micro-organism. (Cohen, 1975). This laid open a much more precise form of genetic manipulation that has become known as recombinant DNA research.

How is Recombinant DNA Research Done?

To help explain this I will define some technical terms.

Restriction enzymes are naturally occurring enzymes produced by bacteria and other organisms as a defence against invading viruses. They work by cutting the virus DNA at a specific place, thereby incapacitating the virus and preventing the invasion. These enzymes have been known for some time, but it is only recently that they have been isolated and even more recently that scientists have known which specific points on a DNA chain they will cut. The first restriction enzymes discovered cut directly across both two strands of DNA, making it necessary to add a short length of single-stranded DNA to make a 'sticky end' before a new piece of foreign DNA could be attached. However, a recent development by Boyer was to find a new type of restruction enzyme which cuts the DNA obliquely, thereby leaving a 'sticky end' automatically. This makes the technique considerably simpler.

Ligases are enzymes that repair breaks or nicks in single strands of DNA. It was discovered in 1967 that these enzymes could be used to join together the ends of two separate pieces of DNA.

A plasmid is an intracellular particle which is a molecule of DNA that exists apart from the main bacterial chromosome. It replicates on its own, often carrying the genes for some supplementary activity such as resistance to antibiotics. These plasmids are the most popular vehicles for the recombinant technique.

A typical experiment will go as follows: (See Fig. 1)

1. The bacterial cell wall will be dissolved using a detergent-like liquid. This releases the DNA from inside the cell, both the long principle chromosome and also the

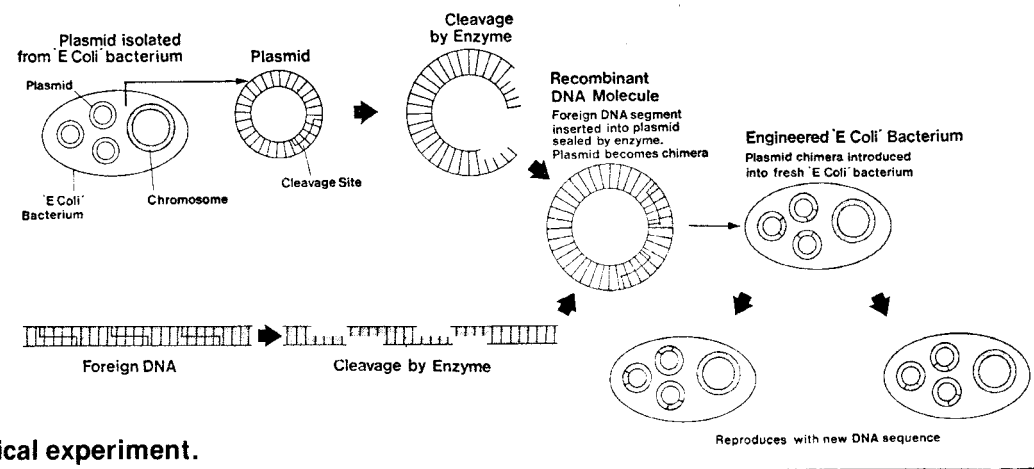


Fig. 1: A typical experiment.

smaller plasmids.

2. The plasmids are then separated out using an ultracentrifuge.

3. Next a restriction enzyme is added to the mixture containing the plasmids, cutting the DNA strands at specific points. This changes them from circles of DNA into linear molecules.

4. Meanwhile some foreign DNA has been prepared and similarly treated from either a virus, a bacterium, a plant, or an animal. The DNA has been cut, using restriction enzymes, and small pieces of DNA molecule obtained.

5. Next the foreign DNA segments are added to the linear plasmid DNA molecules.

6. A ligase enzyme is added to make them join. Once more the plasmid DNA strand becomes a circle, but this time the circle contains the fragment of foreign DNA. At this stage the plasmid is called a 'chimera'.

7. Finally the chimeras are placed in a solution of cold calcium chloride containing normal E.Coli bacteria. When the solution is suddenly heated the membranes of the E.Coli become permeable, allowing the plasmid chimeras to pass through and become part of the E.Coli's new genetic structure.

Not all plasmids are suitable for use as vehicles carrying foreign genes into the cell. One of the most popular ones is the plasmid pSC101 which was developed by Cohen. He produced it by chopping up a larger plasmid and sticking a small strand round into a circle.

Other vehicles have also been devised for carrying genes into bacteria. The bacteriophage 'Lambda' is particularly suitable for genetic modification before it is used to infect E.Coli. For higher types of cell, the polyoma virus of mice can be used, or the SV40 virus of monkeys. This virus was a contaminant of the polio vaccine given to nearly 2 million New Zealanders in the early 1960s. (Hamilton, 1974.)

Whichever vehicle is used to introduce new genetic material into the cell, the effect is much the same. The new genes are reproduced either at the same rate as the cell itself or sometimes independently and faster. The new cells become forms of life that are potentially different from before, with characteristics dictated not only by their own genes, but also by genes from an entirely different species. This process enables the scientist to do two things: firstly, to produce large quantities of identical genetic material as the plasmids are reproduced over and over again (the process is known as cloning); secondly, to examine the change in behaviour of the cell, thereby gaining some insight into the properties of the genes he has introduced.

The History of the Controversy

In 1971, Paul Berg was planning on an experiment. He wanted to introduce DNA of the SV40 virus into E.Coli. SV40 is a small virus with few genes. However, it is oncogenic and causes tumours in newborn hamsters. (Shah, Nathanson, 1976). Berg hoped that by studying the oncogenic gene he might learn how some viruses cause cancer.

A young cancer researcher called Robert Pollack heard of this experiment and phoned Berg to discuss its possible implications. Pollack was worried that if E.Coli were to acquire an oncogenic gene, and such a strain were to escape from the laboratory, it might lead to carcinogenic bacteria being widely spread through the human population. Berg was initially sceptical about this fear, but after discussing it with some colleagues he agreed it would be better to cancel the experiment.

In mid 1973, 140 leading molecular biologists met at a New Hampshire conference. Berg voiced some of his worries, and as a result the scientists asked the U.S. National Academy of Sciences to look into the risks of recombinant DNA esearch. The N.A.S. immediately set up a sub-committee with Berg as its head.

In April 1974 they called for a world-wide moratorium on obviously hazardous sorts of recombinant DNA research.

In February 1975, a conference took place in Asilomar, California. Scientists decided to continue the ban on the obviously dangerous experiments, and also to persuade the National Institutes of Health to establish safety guidelines. (Berg and others, 1975).

In June 1976, the NIH guidelines were released. (Federal Register, 1976). They are voluntary and classify different types of experiment into a number of categories. The most dangerous should not be done at all, and the four categories below that should only be done under appropriate containment conditions. The guidelines describe four levels of physical containment, and three levels of biological containment.

The experiments banned are those where there is some scientific basis for expecting danger, such as the implantation of oncogenic viruses or toxin-producing genes

into bacteria that might infect humans. As for containment, the highest level is called p4. Laboratories classified p4 are similar to those that are currently used for extremely dangerous organisms such as Lassa Fever virus, Marburg virus, and Zaire Haemorragic Fever virus which can cause nearly 100 per cent mortality in infected individuals. A P4 laboratory is specially built with airlocks and filters, biological safety cabinets, clothing changes for personnel, and autoclaves inside the building.

A P3 laboratory is also specially constructed with double doors, negative air pressure, and special air filtration devices.

P2 laboratories are similar to those that have been used for many years for work with bacteria such as Salmonella Typhosa and Clostridium Botulinum. The NIH guidelines require that P2 laboratories be used for research involving recombinant DNA molecules from separate species.

P1 laboratories have the lowest level of containment. These can only be used for experiments involving recombinant DNA from two strains within the same species. Essentially this is where the new bacteria could possibly have occurred naturally.

The American NIH guidelines also specify levels of biological containment. This means the use of specially crippled bacteria, and other organisms, so that in the event of one of them escaping from the laboratory it would not be able to survive long. The three levels of biological containments are: E.K.1. This means using the K12 strain of E.Coli which has been shown to be naturally feeble. E.K.2 would involve using more extensively crippled bacteria that require specific laboratory nutrients in order to reproduce it all. They may also require specific temperatures to survive. Some crippled bacteria of this sort have been produced already, although it is disputed whether they meet the E.K.2 standards. (Goldstein and others, 1976). E.K.3 Biological containment is similar to E.K.2 except that it has been rigorously field tested. This has not been done yet.

A few days after the NIH guidelines were released, an eminent Nobel Prize winner, Professor George Wald, launched his attack on them. (Wald, 1976). I will leave some of his argument until later, but will say at this stage just this:

1. The guidelines discuss the conditions under which the research should be done, but they do not address the question of whether the research should be done at all.

2. They involved no public discussion.

3. They are voluntary, not compulsory.

4. He went into a detailed criticism of both physical and biological containments.

5. The techniques are unpredictable.

6. Their consequences are potentially unprecedented.

7. Because of these factors a much wider debate and more stringent controls on this research was necessary before it went ahead.

Wald persuaded the Cambridge (Mass.) City Council to place a temporary ban on P3 and P4 experiments planned at Harvard University. The Mayor of Cambridge, Mr. Vellucci, who has had a number of battles with the University in the past, became a vocal and powerful opponent of the research. The decision by the Cambridge City Council immediately made the debate more public and also extremely heated.

Meanwhile in Britain the debate was also going on. (Lewin, 1976). In July 1974 when the American National Academy of Sciences urged a world-wide moratorium on hazardous Recombinant DNA experiments, a committee of enquiry was set up in Britain under Lord Ashby, to investigate the potential risks and benefits of genetic manipulation. This working party reported in January 1975 giving general approval of genetic engineering while affirming the need for adequate safeguards.

The British Department of Education and Science then set up a second working party chaired by Professor Williams to suggest ways in which this research could be monitored and regulated. This working party published the Williams Report in August 1976. But there is not just one 'British Report'; in the same month, the British Health and Safety Commission also published a consultative document, which in many important ways was completely different from the Williams Report. The Williams Report recommended the setting up of a Genetic Manipulation Advisory Group, known as G.M.A.G. The membership of G.M.A.G. includes people to take into account the interests of employees and also the general public. The Williams Report also specifies four levels of laboratory containment, but unlike the American NIH guidelines, it does not specify precisely the types of laboratory needed for each category of experiment. Instead, it offers more 'flexibility'. The Williams Report emphasizes physical containment methods, rather more than the physical and biological containment systems in the NIH guidelines.

The Health and Safety Commission Report, on the other hand, is much more stringent. It proposes to control with statutory powers all forms of genetic manipulation. This H.S.C. document has antagonised large numbers of scientists in Britain who are afraid that their research might come under bureaucratic control. A heated debate has been going on in Britain, although whereas the debate in America is between those in favour and those against the research, in Britain it has been between scientists who want flexible voluntary guidelines and government administrators who want statutory powers. The spectre of international competition has been raised in Britain, with scientists claiming that if their research is restricted, other countries will move ahead and Britain may lose out economically. Reports are currently being prepared in France, West Germany, the Netherlands, Sweden, Norway, Belgium, Denmark, Switzerland, Italy, Israel, and the U.S.S.R. (Tooze, 1977).

The New Zealand Situation

Genetic manipulation has been going on in at least two centres in New Zealand; Auckland University and the Plant Physiology Division of the D.S.I.R. in Palmerston North. Over the last ten years, Professor Bergquist in Auckland has been researching the regulatory controls of DNA replication using small plasmids from E.Coli and cloning them in other E.Coli of the K.12

strain. This research does not involve any genetic material crossing a species barrier, and as such, is not as hazardous as research which does. (Bergquist, 1977.)

The work in Palmerston North has been largely concerned with increasing the abilities of plants to take up nitrogen from the air, thereby requiring less nitrogenous fertilizer. One such experiment involved the introduction of nitrogen fixing bacteria into the cytoplasm of a mycorrhizal fungus which normally lives in association with pinetree roots. (Giles, Whitehead, 1975). The idea was that if the fungus could be enabled to fix nitrogen from the air, then when it was reapplied to the pinetree roots, some of this fixed nitrogen might be made available to the pine trees, thereby increasing their rate of growth without the need to apply nitrogenous fertilizer.

The first of these experiments was successful in so far as some strains of fungi were produced and could live on nitrogen deficient medium. They also were able to reduce acetylene which is the specific test for nitrogenaze activities. Later these strains of modified fungus were applied to the roots of some pinetree seedlings. (Giles, Whitehead, 1977). Some of the pinetrees have appeared to acquire some slight nitrogen fixing ability. However, in the case of one strain of the modified fungus, all the pinetree seedlings that came into contact with it died. It was found that this strain of modified fungus was pathogenic. Hyphae had penetrated to all parts of the plant. The scientists destroyed all the trees and the fungus that had affected them.

I have no reason to suppose that the containment systems of the laboratory were breached, but this gives a nice example of the sort of danger that can occur as a result of this type of research. These scientists were trying to produce a fungus that would have assisted our forest industry. However, they inadvertently produced a fungus that might, if it had escaped the laboratory, have caused a disease affecting pinus radiata trees in this country and destroyed large areas of forest.

Another scientist in Palmerston North has been bombarding pollen with radiation, thereby breaking chromosomes into short lengths and sometimes single genes. Using this technique, he has selectively produced hybrids between types of plants that normally hybridize with difficulty. This technique is relatively simple and could be done by plant breeders without the need for any complicated microbiological training. In the paper (Pandey, 1976) describing this work he mentions 'The essential thing is that this exploratory work be done as speedily as possible, if the initiative is not to pass into the hands of more ambitious laboratories overseas. I believe it may be a unique opportunity for the D.S.I.R. and for agricultural technology in New Zealand. Such an opportunity should not be allowed to pass us by'. This illustrates some of the pressures put on scientists by international competition. It may encourage them to be more hasty in developing this research than might otherwise be desirable.

In 1975 the New Zealand Medical Research Council commissioned a sub-committee to look into the need for guidelines for genetic engineering in New Zealand. This subcommittee consisted of Professor Bergquist from Auckland and Professor Petersen from Otago. Their deliberations occurred in private, and it was only in February 1977 when an article was published in *The NZ Listener* (Booth and others, 1977), that the issue of genetic engineering came to the attention of the public in New Zealand. This article proposed that an enquiry should be held to consider whether genetic engineering should continue in New Zealand. It went on to say that if such an enquiry decided that genetic engineering could continue, then a regulatory authority should be established with legal duties and powers to investigate and control all future research. The authority should have at least the following features:

A. Satisfactory funding to set up independent staffing,

B. Entirely public meetings and records,

C. Representation but not domination by those scientists interested in doing genetic engineering,

D. A majority representation from those groups and viewpoints with a clear understanding of the ethical issues, but not involved in the actual research.

On the 5th March, 1977, the Council of the New Zealand Association of Scientists discussed these proposals, and wrote to the Prime Minister asking for an open enquiry to be held immediately, to consider the implications of genetic engineering, and also calling for a moratorium on the research pending the enquiry.

In early March, 1977, the subcommittee of the M.R.C. presented its recommendations to the Medical Research Council itself. (Bergquist, Petersen, 1977). The recommendations were accepted. Essentially they are fairly similar to the British Williams Report, and the emphasis is on physical rather than biological containment. Also the regulations stress flexibility rather than a rigid classification of experiments. There are some differences from the Williams Reports. In general the New Zealand recommendations are more stringent, and in particular, although scientists could do P1 and P2 type experiments in appropriate laboratories here, the suggestion is that type 3 and type 4 laboratories would be uneconomic in New Zealand and scientists wishing to do experiments in those categories would have to use laboratories overseas.

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The M.R.C. guidelines suggest the setting up of a two tier control system. At the top would be a 'Genetic Manipulation Advisory Committee', containing scientists, medical scientists, trade unionists, representatives from industry, from the public, and from the Department of Health. The committee of half scientists and half non-scientists would continually review research and developments involving recombinant DNA.

The second level of control would

be called the 'Recombinant DNA Advisory Committee' consisting of scientists representing the M.R.C., the government scientific departments, and also universities. These experts would vet all research proposals and advise the level of safety precautions necessary for them. In this way each separate piece of research would be evaluated rather than fall into a general category. In addition, the proposals recommend that each institution doing this research should employ a biological safety officer to ensure that all staff working there knew of the research and who would also be responsible for supervising the safety precautions.

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Professor Bergquist tells me that the recommendations are different in another respect as well. They are compulsory as far as M.R.C. work is concerned, whereas in Britain and America the guidelines are at present voluntary, although in America at least legislation is being prepared. (Wade, 1977). The D.S.I.R. in New Zealand have asked the Minister for Science to apply the M.R.C. guidelines to research done by the government departments, and there is talk about possible legislation being produced for New Zealand in order to control the activities of industry. (Gandar, 1977).

The present position in New Zealand is that with Professors Bergquist and Petersen having accepted the British standards, Professor Bergquist's research has been stopped while his laboratory is being modified. I understand the research in Palmerston North is continuing. The New Zealand Association of Scientists is still awaiting a decision by the Prime Minister as to whether he will institute a public enquiry. It seems unlikely that this will now take place, although the Royal Society is setting up a sub-committee to investigate genetic engineering and it is possible that the public will be able to make submissions to it.

A Summary of the Arguments

The arguments seem to me to fall into three main groups: The first is the issue of containment within the laboratory, and the consequences if it were breached: The second is the issue of control, that is to say, who should decide if the research should go ahead, and if so under what conditions. Should it be the scientists who are doing the research themselves? Should it be experts from that area of science? Should it be the general public? Should the controls be voluntary, or should they be compulsory under law? The third area of controversy concerns the technological and social implications of this research.

Containment

The advocates of genetic engineering like Cohen (1977), who was one of the originators of the recombinant technique, claim that the benefits will be so great that the risks involved are justified. The benefits, he claims, would be of two types: Firstly the advancement of fundamental scientific and medical knowledge especially in the areas of genetics, the mechanism of carcinogenesis, and drug resistance. The second area of possible benefit is in the practical applications which I will mention later.

As far as the risks are concerned, advocates of the research tend to emphasize the unlikelihood of any major catastrophe occurring. They talk about the risks of being one in a million, or one in a billion (Holliday, 1977). They emphasize the importance of strict guidelines and laboratory control. (Curtiss, 1976.) They say that with P4 containment the physical escape of micro-organisms could be completely prevented and that with biological containment systems as well if such an escape did occur, then the micro-organism would not survive long enough to cause an epidemic.

Some advocates in New Zealand believe the risks to be minimal because inter-species genetic exchange may occur naturally. (Sutton, 1977). If 'natural genetic engineering' is widespread anyway, the argument goes, then dangerous new organisms are unlikely to be produced by researchers because if they could survive they would exist already. This 'she'll-be-right' attitude is rarely mentioned by advocates outside this country.

The more sober of the proponents take pains to disclaim that they mean that all experiments should be freely permitted. They say that they want controls, but that they should not be too restrictive. (Cohen, 1977.)

On the other side of the debate, critics of the research claim the risks are so great that no amount of security would be adequate. Professor Cavalieri, Professor of Biochemistry at Cornell University, warns that 'A single unrecognised accident could contaminate the entire earth with an ineradicable and dangerous agent that might not reveal its presence until its deadly work was done'. Professor Robert Sinsheimer, Chairman of the Biology Division at the California Institute of Technology, says that 'Because of human fallibility, these new organisms are almost certain to escape. Once they have escaped there is no way to recapture them, and so we have the great potential for a major calamity'. (Cavalieri, 1976.)

The case of the critics can be reduced to the following principle points:

1) *ABSOLUTE CONTAINMENT IS IMPOSSIBLE.* When you take into account all the human factors and the possibilities of mechanical failure as well, there is no way that complete containment can be guaranteed. That might be permissible if the consequences of an accident were severe but not potentially disastrous. However if the consequences of the accident are potentially intolerable, the risk of a breach of laboratory containment, however minute that risk might be, becomes a strong argument against doing the research.

The critics point to the fact that Fort Detrick biological warfare laboratories, which developed P4 high-level physical containment, had at least 423 accidental infections over 25 years (Cavalieri, 1976). Biological containment relies on the nature of the host organism for its success. That nature is genetically deter-

mined, yet the genetic makeup of the organism is being modified during the course of an experiment. The nature of the host may change in unpredictable ways, reducing the reliability of the biological containment. It has been shown that the cripple cell E.Coli 1776 can survive better after a certain plasmid has been introduced into it. (Goldstein and others, 1976.)

2) *THE CONSEQUENCES ARE UNPREDICTABLE.* Many of the lengths of DNA that are inserted into new cells contain genes whose function is poorly understood. They are certainly not understood in conjunction with the host cells genes.

Sinsheimer theorises that some of these experiments are crossing what he suspects is an absolute biological barrier — the barrier between the lower forms of life, the Prokaryotes, like bacteria and blue-green algae, and the higher forms of life, like animals and plants, which are called Eukaryotes. He suggests some of the possible consequences of breaching this natural barrier. (Sinsheimer, 1976.) One is that Prokaryotic viruses might acquire the capacity to infect Eukaryotes. In other words, viruses that currently only infect bacteria could acquire the ability to infect higher plants, animals and humans.

Another fear is that bacteria might acquire the capacity to act as a reservoir for the common Eukaryotic viruses, which would then be much more difficult to eradicate.

Apart from the danger of new infectious diseases being created and spread the biggest fear is that an oncogenic gene might escape. Veteran DNA researcher Professor Chargaff of Columbia has been quoted as saying 'the spreading of experimental cancer can be confidently predicted'. (Cavalieri, 1976).

3) *AN ACCIDENT COULD BE IRREVERSIBLE.* As Chargaff put it: 'You can stop splitting the atom, and you can stop visiting the moon, you can stop using aerosols, you may even decide not to kill entire populations by the use of a few bombs. But you cannot recall a new form of life. Once you have constructed a viable bacterium carrying a plasmid DNA into which a piece of foreign DNA has been spliced, it will survive

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you, and your children, and your children's children. An irreversible attack on the biosphere is something so unheard of, so unthinkable to previous generations that I could only wish that mine had not been guilty of it'. (Chargaff. 1976).

4) *THE HOST CELL IS E.COLI.* Much recombinant DNA research currently taking place uses Escherichia Coli (E. Coli) as the host cell. The reason is that E.Coli is the best understood bacterium available. More is known about the composition of its chromosomes and plasmids than about those of any other type of cell. Unfortunately it is also a normal inhabitant of the human bowel. The chances of a modified strain of bacterium escaping the laboratory is therefore increased, because it could be carried out in the gut of a laboratory worker. In addition if a pathogenic E.Coli was created, the chances that the disease would affect humans and possibly cause a human epidemic would be increased. Many critics of genetic engineering say that if the research is to go ahead, it should not be done using organisms that are known ever to infect humans.

E.Coli also is known to transmit its plasmids to at least 40 other organisms. This for example, is what occurs when multiple drug resistance is transmitted from strains of E.Coli to other bacteria. One of Wald's criticisms of biological containment is that if E.Coli, however weak or crippled, still have the ability to transmit genetic material to other strains, then this so-called 'biological containment' might not amount to much. The danger might not be from pathogenic bacteria escaping the laboratory so much as healthy bacteria getting in. Such healthy bacteria might acquire the pathogenic genes and then be in a position to escape and cause an epidemic. (Wald, 1976).

An example of the danger that can arise from using E.Coli occurred in New York two years ago. (Wade, 1977). Researchers were trying to develop a strain of E.Coli that could digest sewage and produce methane gas for fuel. A desirable project. In the course of their experiments, they produced a strain of E.Coli that possessed the enzyme cellulase, which can break down cellulose. After this had been achieved, it occurred to the scientists that such a bug would be very unpleasant to have in one's gut. It would break down roughage producing cellulose breakdown products which would be likely to cause at least wind and probably chronic diarrhoea. They decided to destroy the organism.

It is incidently interesting to note that, because the experiment was done in vivo and because it used plasmids but not restriction enzymes, it would not have been covered by the NIH guidelines.

5) *A LABORATORY LEAK MIGHT BE INDETECTABLE.* As well as being irreversible, the escape of a pathogenic organism from a laboratory may be hard to detect, since many of the organisms being used in this research are already, in an unmodified state, widespread in the environment. If a leak occurred involving some modified E.Coli, it could be extremely hard to trace. This argument is used to criticize the proposed containment systems. The critics say that in order to establish whether the proposed containment systems are adequate, it should be possible to test the safety systems empirically. During normal operation, it is likely that most laboratories would be able to contain pathogenic organisms. However, the fear is not so much about the normal operation of safety systems as those unexpected and unpredictable situations where things go wrong.

A useful analogy is made here with the problem of radiation and its possible escape from a nuclear power station or a nuclear waste disposal site. If radiation were to leak from a nuclear power station, it could be detected with a geiger counter. It could be concluded then that the safety systems had broken down and needed improving.

But with recombinant DNA, a leak could occur, and nobody know about it. If the organism was already

widespread in an unmodified form in the environment, it could be hard to show immunologically, or in any other way, that anything unusual had happened. Of course, if the organism was dangerous in the sense that it had immediate toxic effects, then a new and unknown disease might appear. However, it is well known that some oncogenic viruses have incubation periods of up to twenty years before the cancer becomes detectable. An example is Herpes Simplex Type 2 and carcinoma of the cervix. (Aurelian, 1976).

In effect, if it is possible for a leak from a laboratory to be both highly dangerous and indetectable in the short term, then it is difficult to prove that safety systems are satisfactory.

Control

Who is to control this research? Should it take place at all? Who should make that decision? Who is to control the conditions under which the research is done?

Not all advocates of genetic engineering agree about this. Some feel that the pursuit of scientific knowledge should not be controlled in any way, and that freedom is vital if science is to remain vigorous. There are others who concede that if 'pure' scientific research involves risk to the public, then it is reasonable to have controls over the types of research done, and the conditions under which it is done. Within that group, some believe that restrictions should be voluntary guidelines drawn up by scientists who are doing the research.

Richard Novick, Chief of Plasmid Biology at New York's Public Health Research Institute, disagrees: 'Given that I would like to do certain R-DNA experiments that I believe to be non-dangerous I am unable to distinguish between the following two alternatives as the basis for this belief:

1) I am convinced they are not dangerous, so it is okay to do them.

2) I have convinced myself that they are safe precisely because I want to do them!'

He defies anyone with a self-interest to make that distinction. (Novick, 1977).

Critics of the research tend to emphasize the importance of public involvement in decision-making, both as to whether the research should be done at all, and also the conditions under which it should be done.

The critics tend to emphasize that the public are to be put at risk by these experiments and that it may be an extreme risk. The public should therefore have the right to veto at least some of this research and to scrutinize the controls on any that is done.

Future Implications

This goes beyond the question of laboratory containment, and the activities of a few scientists to consider the possible long term effects of this research on future technological and social developments. Advocates are optimistic about possible practical applications of genetic engineering. A number of possible benefits have been mentioned (Cohen, 1977), including cheap and plentiful supplies of drugs, antibiotics, hormones, insulin, vitamins, vaccines and many other biologically active agents. These could be produced using specially designed and engineered bacteria as miniature pharmaceutical factories. They would be equipped with the genes to create directly the compounds required.

Other attractive prospects include the possibility of designing bacteria to clean up oilspills, bacteria that could produce methane from sewage, techniques that could enable plants to fix nitrogen from the atmosphere instead of requiring nitrogenous fertilizers, and also possible bacteria or algae that could produce hydrogen from water using the power of photosynthesis. This prospect is particularly attractive to people who are aware of the fact that world petroleum production is expected to start declining in ten to fifteen years time, and the need to find alternative energy supplies that can be used for transport.

Another suggested application for this research is the treatment of genetic diseases. The hope is that in diseases caused by an enzyme deficiency, or even a chromosome deficiency, the patient might be able to be given the genetic material that he is lacking. In fact one attempt at this has already been made in two children suffering from hyperargininaemia, a genetic defect of the enzyme arginase. An attempt was made to correct this enzyme defect by injecting Shope Papaloma virus into the children in the hope that the arginase present in this virus might help the children. In one of these patients the arginine level fell, indicating some partial success. (Nevin, 1977).

Some supporters of genetic engineering think that an understanding of the mechanisms of carcinogenesis will lead to a cure for cancer.

Critics of the research, in particular Francine Simring of Friends of the Earth, have emphasized (Simring, 1976) the long term and possibly immense changes that this research might bring. She has pointed out that the proponents of the research have tended to concentrate on laboratory containment as being the key issue, in much the same way as early researchers into nuclear power concentrated upon reactor safety. Now, of course, the nuclear debate encompasses issues such as terrorism, the inevitability of human mistakes, problems of waste disposal and transport, and the economic and military implications of a nuclear programme.

By analogy with this, she says, we must consider right at the beginning of the genetic debate all the possible ramifications. In particular, questions she has raised include:

THE REDUCTION IN THE DIVERSITY OF THE GENE POOL. A key element in the stability of an ecosystem is the size of the gene pool that it contains. That is to say, in a natural ecosystem there is usually a large variety of different organisms living together and interacting with one another. If this complex ecosystem is simplified and replaced by a monoculture, then the system as a whole becomes much less stable in the face of some possible change in its environmental conditions. Examples of the sort of minor ecocatastrophe that has occurred when a simplified monoculture has been affected by a new situation include the invasion of rabbits in Australia, and the invasion of gorse into New Zealand. In such cases, a single organism possessing an advantage over the existing over-simplified ecosystem can sweep through the environment.

INTERFERENCE WITH NATURAL EVOLUTIONARY PROCESSES. This issue has brought theologians and philosophers into the debate. Up to now, the direction of development in plants and animals has been largely a matter of random mutation and natural selection, although modified by artificial breeding. But with genetic manipulation techniques easily available, the design of plants and animals, and even humans, become theoretically possible. This places a whole range of new powers into human hands and will lead to a whole new dimension of ethical problems as a result.

MILITARY EXPLOITATION. In the past, biological warfare research has been relatively crude, usually involving the use of radiation to increase the mutation rate and thus create novel pathogens. Recombinant DNA technology could make this much more precise and therefore more deadly in the hands of a government or terrorist group. In addition P4 laboratories containing dangerous organisms could make attractive targets for terrorists who wished to hold society to ransom.

INDUSTRIAL EXPLOITATION. When recombinant DNA techniques are widely used by industry, the scale of production of modified micro-organisms will increase immensely. The problems of containment, regulation and inspection of these factories will be much greater. The pursuit of profit or national advantage in a competitive situation may lead to corruption or to regulations being ignored. As in the case of nuclear power systems, some possible accidents would be fairly minor. But it is also true that with genetic engineering, a single release of a pathogenic organism may lead to an unprecedented disaster.

When industries wish to deploy their new organisms, some very complex decisions will need to be made. For example, if the proposed oil-eating bacteria can be created, should they be spread on an oil-slick? What would be the consequences for marine ecology, and what if oil in pipelines or petrol-tanks was also to get infected? Likewise with nitrogen fixing plants. It would be very hard to predict the long-term consequences for the world's flora if some plants suddenly acquired a significant advantage. Could nitrogen-fixing pinus radiata trees take over areas of native forest?

Questions such as these are incredibly complex, yet they would need resolving before genetically engineered organisms could be released from containment conditions. One of the principles of a democratic society is that major decisions should be made by public representatives. With decisions in this area being so complex and with such far-reachig consequences, it will be hard for our democratic institutions to cope with them. It will be all too easy for commercially motivated people to press ahead in spite of that.

Conclusion

Fortunately, the responsibility of the scientists involved has brought the dilemma to public attention before it is too late. The research has not yet progressed so far that it could not still be controlled. The scientists' very responsibility, however, should not blind us to the fact that genetic engineering has implications that extend way beyond the field of molecular biology to affect interests outside the scientific world as well. Nor can the dilemma be avoided by claiming that the pure research is one thing, while what is done with it is another. In this case, even the 'pure' research carries public risks and therefore moral responsibilities.

In the face of all the ethical difficulties that genetic engineering creates, many scientists and other concerned individuals are saying we should take a long, hard look at it before it goes any further.

Robert Sinsheimer put it very simply: 'The Atomic Age began with Hiroshima. After that no one needed to be convinced that we had a problem. We are now entering the Genetic Age; I hope we do not need a similar demonstration.'

David Straton

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