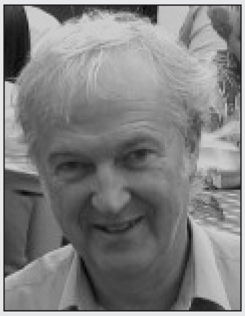
Ethical Issues In Genetic Modification

John Bryant

There is serious concern that some of these artificial recombinant DNA molecules could prove biologically hazardous.
Paul Berg *et al*., (1974)[1]

Summary

This paper surveys the origins and present applications of the Genetic Modification of plants, animals and humans. The ethical concerns raised from both secular and religious sources are considered. It is concluded that humankind has been delegated responsible stewardship for all the earth's resources, including DNA, and that there are strong theological motivations for using Genetic Modification wisely and for the benefit of others.



About the Author

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Background

In 1972, Paul Berg of Stanford University, California, reported the first construction in the test tube of recombinant DNA, meaning a DNA molecule recombined from pieces of pre-existing DNA molecules[2]. Very quickly, the methodology was taken up by another Stanford scientist, Stanley Cohen who, with Herbert Boyer (University of California, San Francisco) and their colleagues, showed that recombinant DNA molecules could be transferred very effectively into bacterial cells in the laboratory[3]. These first genetic modification (GM) experiments involved the transfer of recombinant DNA into cells of *Escherichia coli*, a bacterial species widely used as a model in biochemical and genetic research. Not only were the recombinant DNA molecules maintained and replicated within the bacterial cells but they also functioned normally.

Shortly after the invention of these techniques, there was a surprising development. Several leading biologists, including those who had developed recombinant DNA technology, wrote to the prestigious US journal *Science*.[4] They raised concerns about possible risks arising from some applications of the technology and suggested that some types of experiment should not be attempted. Initially, this research was self-regulated, but in 1975 the scientific community itself called a temporary halt to recombinant DNA work and a conference was held at Asilomar, California[5]. This meeting was widely hailed as a 'landmark of social responsibility and self-governance by scientists'[6], leading to the production of guidelines for evaluation of risk and for imposition of codes of practice based on each level of risk. These safety guidelines formed the basis of regulatory frameworks for conducting recombinant DNA work, which, although modified in the light of experience, are still in use today.

With regulatory frameworks in place, recombinant DNA technology/GM advanced rapidly. A key development was in the use of GM for the production of pharmaceuticals such as human insulin, one of the fastest commercial applications of biological knowledge on record, with a gap of only a few years between the isolation of the gene and the licensing of the product for use in human therapy. Insulin is now but one example of hundreds of therapeutic reagents created by GM and used in the pharmaceutical industry for the cure of both animal and human diseases.

Soon after its proven application to bacteria, it quickly became clear that GM techniques were applicable to a much wider range of organisms: GM of animals was first reported in 1976[7] and was well established by the early 1980s[8]; GM of plants was achieved in 1983[9]. It is now clear that at least some members of all the major groups can be genetically modified: bacteria, fungi (including yeast), invertebrate and vertebrate animals, uni-cellular and multi-cellular plants.

The recent sequencing of the genomes of more than 250 species (mostly bacteria, but including representatives of all the major groups), involving the determination of the precise order of the bases (the 'genetic letters') of the DNA contained in an individual organism, has only been possible because of the use of GM technology. The Human Genome Project has already been successful-

1. Berg, P. 'Potential hazards of recombinant DNA molecules', *Science* (1974) 185, 303.
2. Jackson, D.A., Berg, P. & Symons, R.H. 'Biochemical method for inserting new genetic information into DNA of simian virus 40: circular SV40 DNA molecules containing lambda phage genes and lactose operon of *Escherichia coli*', *Proceedings of the National Academy of Sciences, USA* (1972) 69, 2904-2908
3. Cohen, S.N., Chang, A.C.Y., Boyer, H.W. & Helling, R.B. 'Construction of biologically functional bacterial plasmids *in vitro*', *Proceedings of the National Academy of Sciences, USA* (1973) 70, 3240-3244
4. Berg, *op. cit.*, (1)
5. Berg, P., Baltimore, D., Brenner, S., Roblin, R.O. & Singer, M.F. 'Summary statement of Asilomar conference on recombinant DNA molecules', *Proceedings of the National Academy of Sciences, USA* (1975) 72, 1981-1984.
6. Barinaga, M. 'Asilomar revisited: lessons for today?' *Science* (2000) 287, 1584-1585.
7. Jaenisch, R. 'Germ line integration and Mendelian transmission of the exogenous Moloney leukemia virus', *Proceedings of the National Academy of Sciences, USA* (1976) 73, 1260-1264.
8. e.g. Gordon, J.W., Scangos, G.A., Plotkin, D.J., Barbosa, J.A. & Ruddle, F.H. 'Genetic transformation of mouse embryos by microinjection of purified DNA', *Proceedings of the National Academy of Sciences, USA*, (1980) 77, 7380-7384.
9. Herrera-Estrella, L., Depicker, A., van Montagu, M. & Schell, J. 'Expression of chimaeric genes transferred into plant cells using a Ti-plasmid-derived vector', *Nature* (1983) 303, 209-213.

ly concluded[10], as has the DNA sequencing of other mammals, including primates[11]. The identification of DNA mutations causing human disease continues to increase rapidly. At the last count DNA-based diagnosis is available for 1033 different conditions (an increase of nearly 600 since 2002) with a further 296 under active research and development[12].

General ethical issues

In the early days of GM technology there was surprisingly little debate about ethical issues. Thus commentators have noted the absence from the Asilomar conference of professional ethicists (although some lawyers were present). Moral philosophy as such did not enter the discussions and the possibility of intrinsic objections to GM was barely raised. It was thus more or less inevitable that the basis for ethical discussion was consequentialism – 'what happens if ...' – with safety being the over-riding concern. The focus was on how the technology should be used rather than whether it should be used at all.

In respect of religious engagement with this topic, it is often assumed that religion in general will be opposed to GM technology. In fact this is not so. The situation is far more complex. Religious attitudes to GM are mainly concerned with what is done with the technology rather than whether it should be done. Indeed, some specific applications of GM have had strong support from religious people, especially those within the Judaeo-Christian tradition, as being a positive use of humankind's God-given talents used for the well-being of others. The topic of GM provides a very good example of the interplay between science, technology and religion in an arena in which the relevant scriptures (e.g. the Old Testament of the Bible in the Judaeo-Christian tradition and the New Testament in the Christian religion) have nothing *specific* to say.

Despite this general acceptance of GM technology there have been some opposing voices. There are people, often from a pagan or neo-pagan religious position, who have intrinsic objections to the whole idea of moving genes. In arguments with their roots in Aristotle, there is the view that an organism's genes are part of its essential nature, its *telos*[13], and that genetic modification distorts that essential nature. Others have a view of nature that regards the concept of a gene as a moveable entity as being far too reductionist; on this view, any gene is part of a complex web of life and moving it into another organism will disrupt that web and may thus disturb 'the balance of nature'.[14] Finally there are those who simply consider such activities to be 'off-limits' for humankind, a view generally based on particular views of the relationships between humans and the natural world.

Within the Christian religion there is a small minority who suggest that moving genes from one organism to another offends against the concept of God's creation of 'kinds' (Genesis 1). In the view of the present writer, this suggestion is untenable. The discoveries of micro-organisms and of genes occurred centuries after the writing of the New Testament, let alone the Old; such topics lay completely outside the knowledge of the biblical writers. Although doubtless the writer of Genesis equated kinds with the different sorts of animals and plants, it is difficult to square this with our modern understanding of species. Species are not fixed and indeed some are very blurred at the edges: in fact biologists have trouble coming up with a watertight definition of the word. This is especially true of bacteria, many of which indulge in gene swapping leading to rapid genetic evolution.

The absence of specific prohibitions in the scriptures, however, does not necessarily mean that all is allowed. It is in such situations that the application of general principles becomes important. In both the Old and New Testaments, as well as the Qu'ran, there is the ongoing theme that God is the creator and sustainer of the universe; the natural world is his. Furthermore, he has given humans a particular place in it; we have the ability to use the natural world, the curiosity to find out more about it and the ingenuity and inventiveness to put that knowledge to use. However, we must use these gifts as stewards of God's world. That stewardship includes a right attitude to our fellow men and women, loving our neighbours as ourselves. So, as noted already, safety and risk will be as much concerns for scientists of Jewish or Christian faiths as for non-religious scientists. Would an appropriately informed and qualified group of Christians or religious Jews have come up with different conclusions from those that emanated from Asilomar? Almost certainly not. However, there may be specific religious concerns about some applications of GM technology and it is to those that we now turn.

Genetic Modification of plants

As mentioned above, the scientific community had to wait ten years from the initial report of genetic modification of bacteria to the first successful plant GM experiment. For plant scientists, the beauty of the technique was that, like the techniques originally developed for bacteria, it relied on a natural process in which a bacterium delivers DNA into the chromosomes of a host plant. Further, for plant breeders, the technique had the potential for delivery of specific genes into pre-existing elite strains. For technical details, interested readers are referred to Hughes and Bryant (2002)[15]. By 1985 some small-scale GM field trials were already under way in several countries and early successes had been achieved in regulating the expression of the 'foreign' genes. However, it was a further ten years before the first GM crop, the slow-softening tomato (and tomato paste derived from it) went on the market.

Today the use of GM crops varies greatly across the world. Although in the European Union only six countries have adopted GM crops, the use in the rest of the world increases annually. In 1996, GM crops were grown on less than 2 million hectares, nearly all in the USA where 1.7 million hectares were devoted to the main GM crop, herbicide-tolerant soybean. In 2006 GM crops were grown on 102 million hectares in 22 different countries[16]. In descending order of hectarage, the main countries involved are USA, Argentina, Brazil, Canada, India, China, Paraguay and South Africa, the largest crops being soybean (on 58.6 million hectares), maize (corn), cotton and oil-seed rape (canola). About 90% (9.3 million) of the growers of GM crops are resource-poor farmers working on small farms; 6.8 million of these are in China with significant numbers in India and South Africa. The first commercial production of GM rice took place in 2005 in Iran, and extensive field trials of GM rice are under way in China with approval expected soon for commercial growth on a large scale. The importance of rice in the world's food economy is such that there is likely to be a rapid increase in the land area devoted to GM varieties.

Background to the ethical debate on plants

The early days of plant genetic modification in 1983 received little public attention at the time, a situation that would eventually change dramatically. Indeed, the application of GM to commercially-grown crop plants alerted many people for the first time, in the mid-1990s, to the very existence of GM techniques, even though they had been in use in other contexts since the mid 1970s, and vigorous ethical debate continues. In the UK and other EU countries much of that debate has been hostile to GM crops, whereas reaction in many other parts of the world has been more favourable, as the statistics cited above suggest. Why is Europe different? The reasons are

10. See e.g. http://genome.wellcome.ac.uk/node30075.html (last accessed on 22/11/2006).
11. Dennis, C. 'Chimp genome: branching out', *Nature* (2005), 437, 17-19.
12. http://www.genetests.org (last accessed on 23/11/2006).
13. As discussed by Hauskeller, M. Telos: 'The revival of an Aristotelian concept in present day ethics', *Inquiry* (2005) 48, 62–75.
14. See, e.g. http://www.i-sis.org.uk/gaia.php (last accessed on 24/11/2006)
15. Hughes, S. & Bryant, J. 'GM crops and food: a scientific perspective', In Bryant, J., Baggott la Velle, L. & Searle, J. (eds.) *Bioethics for Scientists*, Chichester: John Wiley & Sons (2002), pp. 115-140.
16. ISAAA, 'Global status of commercialised biotech/GM crops, 2006', *ISAAA Briefs* (2006), 35. Available at www.isaaa.org (last accessed on 07/03/2007)

complex[17], but include the idea that we do not 'need' GM when we already produce too much food and a suspicion of science that has its roots in post-modernism. Such concerns are not so apparent in the USA with its more pragmatic and positive attitudes towards the introduction of new technologies.

Ethics, Risks and Safety

For GM techniques in general, there was, as noted already, very little expression of intrinsic objections to the technology, that is, the idea that these techniques are in themselves wrong, although some of the objectors to the use in agriculture of GM crops have expressed such views. The main objections have generally fallen into two other categories. The first of those concerns risk and safety, and the second concerns issues that arise not from the technology itself but from the ways in which it is commercialised. These ways include gene patenting, the ownership of the technology and its products in a small number of commercial organisations, possible exploitation of less-developed countries and the relationship between the economically strong and the economically weak. These are all immensely important topics, worthy of extensive analysis from ethical standpoints, but space here precludes more than this passing mention.

Attention is thus refocused on risks and safety. Amongst those who campaign against the commercialisation of GM crops this has been a major concern. Three themes may be distinguished. First, the incorporation of a foreign gene is inherently dangerous because the long-term effects are completely unpredictable. Second, plant metabolism may be altered so that there are risks to consumers. Third, the GM crops may pose environmental risks by becoming 'superweeds' or by outcrossing with wild relatives so that the latter become superweeds or by affecting biodiversity in some other way.

Proponents of the technology argue that these concerns are unfounded. First, plant genomes are not destabilised by the addition of exogenous genes; indeed, uptake of foreign genetic material has been, and presumably still is, part of plant evolution. Further, in those crops into which foreign genes have been introduced by 'conventional' breeding techniques, there have been no problems. Second, introduction of a foreign gene, unless specifically selected to have an effect on biochemistry, does not of itself lead to changes in metabolism. Indeed, it is argued that the interbreeding of two strains, albeit of the same crop, is as likely to perturb metabolism as is GM. In addition, proponents point out that any food company that markets a product that they do not know to be safe is heading for commercial disaster. Third, varieties created by GM techniques are no more or less likely to become superweeds, to outcross with wild relatives or to have other effects on the environment than conventionally bred crops. This was illustrated by the extensive farm-scale evaluations carried out in the UK, purporting to examine the effects of GM crops on biodiversity, but actually showing how the husbandry of a crop carrying the specific trait of herbicide-tolerance affects biodiversity[18]. Of course, in these trials, that trait had been inserted by GM techniques, but the breeding method was not actually evaluated. Had that trait been available in the same crop via conventional breeding, it is very probable that the same results, that is, a reduction in biodiversity, would have been obtained.

Conducting the debate

It also needs to be stated that neither side in this polarised debate emerges with honour. Both have presented misleading and in some cases downright untruthful propaganda[19], and have misrepresented the other side, making genuine debate difficult[20]. Nevertheless, in the UK there is still a majority who do not wish to see the introduction of GM crops and it has almost become part of 'politically correct' liberal thinking to be opposed in this way.

Religious attitudes to GM crops

In the absence of specific scriptural instructions, the focus within the Abrahamic faiths is once again based on more general principles. It is interesting that an Islamic state such as Iran has adopted GM rice, while the Muslim Council of Indonesia, the world's most populous Islamic nation, has approved the consumption of GM crops and their products. British Muslims, however, have been generally more cautious, perhaps reflecting the views of the wider British public. In Judaism, current rabbinical teaching indicates that GM technology is an acceptable use of God's gifts to humankind and that GM crops are compatible with the kosher food laws.

Amongst Christians, views are mixed. Several Christian writers have concluded that the genetic modification of crops is itself an acceptable set of technologies provided they are used with due care[21]; others have been more neutral[22] while some have expressed clear opposition[23]. However, what all these writers have in common, along with Muslim and Jewish writers, is their concerns about the issues relating to the commercialisation of GM crops, reflecting the words of the Jewish prophet, Micah: 'And what does the Lord require of you? To act justly and to love mercy and to walk humbly with your God.' (Micah 6:8) A critical question to ask is: 'Who will the new technology really benefit – the poor and the needy? Or will it be used to place yet more power in the hands of the rich?' Each case has to be judged on its own merits, but this is the key biblical question, as important for GM as it is for the application of any other new technology.

Genetic modification of animals

The genetic modification of mammals is now considered a routine procedure, albeit with relatively low success rates. There are two basic methods by which this genetic modification in non-human mammals can be achieved[24]. The more widely used procedure is the introduction of the foreign DNA into the newly fertilised egg[25] (following *in vitro* fertilisation, IVF). The embryo, which now carries 'foreign' (exogenous) genes randomly integrated into its DNA, is introduced into the uterus of a suitable potential mother. If a pregnancy is established successfully (and it should be noted that the success rate for GM embryos is significantly lower than for non-GM embryos) a transgenic (genetically modified) mammal will eventually be born; furthermore, it will pass on the new gene to subsequent generations. The second main approach, most often used to disrupt an existing gene in mice for research purposes, is to insert the gene into stem cells (generated from a normal embryo) by a process known as homologous recombination. The modified cells are replaced in the embryo which is then introduced into the uterus and brought to term. The foreign gene is passed on to the next generation via the germ-line. Although not generally applicable to larger animals such as sheep or cattle, it is a useful alternative procedure for animals with a short generation time, such as mice.

In addition, foreign genes introduced into mammals may be regulated so as to confine the expression of the gene to particular cells or tissues or to particular phases of growth and development. However, there are still problems with the level of expression of the foreign genes (i.e. how well the foreign gene works) and these are not likely to be overcome until it becomes possible to insert the

17. See Barnes, B. 'The public evaluation of science and technology', In Bryant, J, Baggott la Velle, L. & Searle, J. (eds.), *Bioethics for Scientists*, Chichester: John Wiley and Sons (2002), pp. 19-36.
18. Discussed in Bryant, J., Baggott la Velle, L. & Searle, J. *Introduction to Bioethics*, Chichester: John Wiley and Sons (2005), pp. 93-98.
19. Bryant et al., *op.cit.*, (18)
20. Bryant, J. & Searle, J. *Life in Our Hands*, Leicester: Inter-Varsity Press (2004) pp. 82-86.
21. e.g. Perry, J.N. 'Genetically modified crops', *Science and Christian Belief* (2003) 15, 141-163.and pp. 78-107
22. e.g. Deane-Drummond, C.E. *Biology and Theology Today*, London: SCM (2001).
23. e.g. Christian Ecology Link: GM crops briefing paper (2003). Available at www.christian-ecology.org.uk/GM-Crops.rtf (last accessed on 23/11/2006)
24. Maclean, N. (ed.) *Animals with Novel Genes*, Cambridge: Cambridge University Press (1994), pp. 4-7.
25. This is often called Pronuclear Injection (PNI). At this early stage, the genetic material from the sperm and the egg have not yet merged but is still located within the egg cell in individual structures called pronuclei (singular: pronucleus). The 'foreign' DNA is actually injected into one of the pronuclei.

gene(s) into specific sites in the animal's chromosomes. Nevertheless, GM rodents carrying mutant human genes that cause diseases such as cystic fibrosis or genes which when activated cause cancer (oncogenes) are in routine use in medical research. According to figures from the Home Office (which regulates animal research in the UK), there were in 2005, 957,000 regulated procedures involving GM animals, 96% of which were mice. Only one-third of the procedures involved direct experimental testing, the majority being associated with breeding of the animals. Other applications include modifying sheep so that they produce pharmaceutical proteins in their milk while active research on genetic modification of pigs is aimed at changing their immunological make-up so that their organs can be used for transplant into humans. On the other hand, attempts to increase yield in large farm animals have not been successful because of growth abnormalities and skeletal aberrations that were side-effects of the particular genetic modification.

GM and Animal Welfare

There is no doubt that the creation and subsequent use of GM animals, whether in medical research or in the production of pharmaceuticals, is based on an instrumental view of animals: they are being used to serve the needs of humankind. In that respect, the GM of animals raises no issues that are not already raised by our use of animals in other contexts. In general the ethical responses to the GM of animals vary widely amongst people of religious faith and of no faith, ranging from total opposition, as expressed by the British theologian, Andrew Linzey[26], to general, albeit often qualified, acceptance. For Christians, Jews and Muslims there is no scriptural prohibition of the use of animals. Jesus himself used a donkey as a beast of burden and also ate meat. However, this must be set against the respect for domestic animals embodied in Jewish law and the general biblical theme that God cares for the creation, including the wild animals and birds. Similar themes also occur in the Qu'ran. This implies that even if animals are used instrumentally, that use should be tempered as far as is possible by consideration of their welfare. In the UK that welfare is enshrined in the very tight Home Office Regulations that govern the use of all animals in research, including research involving GM.

GM of humans

In the UK, there is nearly thirty years' experience of working with human embryos *in vitro*, thanks to IVF. Genetic selection of embryos for couples who are at risk of having a child with a severe genetic condition has been available for several years. So, if the technical difficulties are overcome, are there any reasons not to go ahead with human GM, that is, to change the genetic make-up of a future human being in such a way that the change is heritable? The Human Fertilisation and Embryology Act of 1990, although permitting genetic experimentation on early embryos, forbids the use of GM embryos for establishment of a pregnancy. However, as experience has shown with stem cell research, the terms of the Act may be altered if Parliament deems it appropriate. Further, the Christian ethicist Robin Gill[27] is not alone in suggesting that human GM would be acceptable if it was directed at correcting a genetic disease, a process known as germ-line ***gene therapy***. However, there are some who would go further than this. Atheist philosopher John Harris equates genetic ***enhancement*** with paying for music tuition or ballet classes[28], while Gregory Stock, Director of the Programme on Medicine, Technology and Society at the University of California (UCLA), self-confessedly 'relatively permissive about these technologies', suggests that it is just a matter of time and money: it should be left to the market[29]. Given such views, taken with the ongoing technical development, it is little wonder that Christian medic Gareth Jones believes that human GM is inevitable[30].

In evaluating these issues, the following points need to be considered:

First, the power of genes should not be overstated. Humans are much more than our genes, even though it is acknowledged that genes have some influence on some of our behaviour[31]. Second, even if gene therapy is approved, the distinction between therapy and enhancement is difficult. Third, extensive experience with IVF indicates that human GM is not likely to become mass technology in the near or even medium-term future. IVF is not an easy, nor a pleasant procedure for the woman. Couples electing for genetic modification of embryos would need to be highly motivated, for whatever reason. Fourth, the advent of preimplantation diagnosis, which involves IVF and the screening of embryos for genetic diseases at the very early 8-cell stage, followed by implantation of only the 'healthy' embryos in the mother, renders germ-line modification for correction of genetic disorders unnecessary. Fifth, although it is possible to envisage that germ-line gene therapy may be available via public or insurance-based health provision (as it is for somatic cell gene therapy), any manipulation involving genetic enhancement is likely to be a commercial activity. This raises the possibility of small numbers of wealthy people buying enhancement for their children, but there needs to be realism about what is and is not possible. The complexities of attributes such as musical talent or sporting prowess make them unsuitable targets for genetic modification, at least in the foreseeable future.

Conclusions

God has given humankind a mandate to care for the earth and its resources, utilising them wherever feasible for the good of others. This stewardship extends to DNA as much as to any other resource. Therefore there are strong theological motivations for using GM positively and wisely. At the same time, theology provides ethical resources for defining the limits of what is acceptable, and injects a note of realism to counter inflated views as to the possible benefits of GM for humankind.

26 Linzey, A. *Animal Theology*, London: SCM (1994), esp. p. 143; see also Compassion in World Farming: www.ciwf.org.uk/campaigns/other_campaigns/genetic.html (last accessed on 23/11/2006)

27. Gill, R. *Moral Communities: The 1992 Bishop John Prideaux Lectures*, Exeter: Exeter University Press (1992)
28. Harris, J. *Clones, Genes and Immortality*, Oxford: Oxford University Press (1998), esp. p. 194
29. Stock, G. *Redesigning Humans: Choosing our Children's Genes*, London: Profile Books (2002) and 'Unnatural birth', *RSA Journal* (2003) April, 34-37.
30. Jones, D.G. *Designers of the Future*, Oxford: Monarch Books (2005).
31. Nuffield Council on Bioethics, *Genetics and Human Behaviour*, London: Nuffield Council on Bioethics (2002).

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