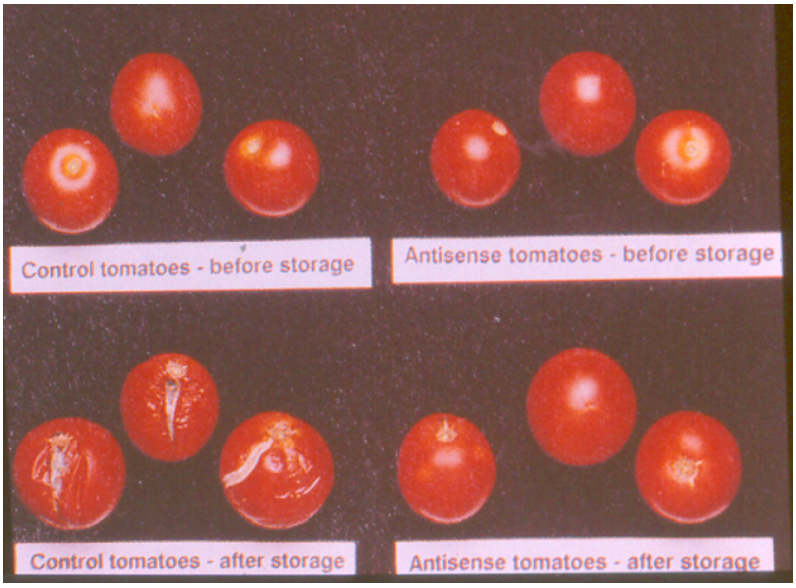
Viewpoint on Genetically Engineered Organisms Prof Doug E Rawlings

(This is a rather rapidly cobbled together piece that does not address many issues to do with whole animal cloning, stem cells and moralizing on many of these issues, but then this is not my own research field or major interest and I did not wish to let myself in for this).

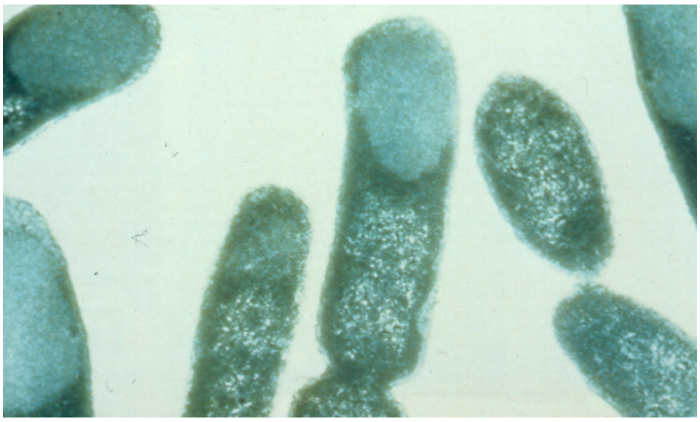
I am not someone who has strongly followed this debate internationally in recent times, because although I did when cloning first became widespread (I was amongst the first researchers in South Africa to use these techniques in bacteria), I long ago I formed the opinion that one can argue for or against and justify both points of view depending on the case. A general debate is therefore not of much value, a case by case debate is.

Some GMOs are so harmless, that they pose no threat to people or the environment. An example of a GMO that potentially falls into this category is the Flavr Savr tomato. Many fruits ripen due to the production of ethylene by the fruit. People who made the long-shelf life Flavr Savr tomato simply knocked out the gene responsible for producing an enzyme required for ethylene production. The result is that the tomatoes ripen slowly and have a greatly enhanced shelf life. There are different ways of 'knocking out' a gene, one is through the use of a gene that encodes for an iRNA (interference RNA, once considered to be antisense RNA). Alternately one could inactivate the gene *in vitro* by deletion of a portion and the insertion of an antibiotic resistance or similar (e.g. herbicide resistance) selectable gene. The inactivated gene is introduced into the plant where it will recombine with the natural gene such that the partially deleted antibiotic resistance containing homologue replaces the natural gene. This happens in a very small proportion of cells but the acquisition of antibiotic resistance gene enables one to select for the few recombinant cells in a population of normal cells. The trouble with this technique is that an unwanted gene, the antibiotic resistance gene, remains within the inactivated gene. A new set of techniques is now available where the antibiotic resistance gene is used to select for 'rare' recombinants and then once this role is completed the antibiotic resistance gene deletes itself leaving almost nothing behind but in a way that leaves the gene into which it was inserted inactive. Such a GMO would be considered harmless because in the final modified cells, nothing has been added but only a gene deleted that has increased the shelf life of the tomato. Nevertheless the tomato plant is a GMO. (I am not certain whether the original Flavr Savr tomatoes had all selectable markers removed before regenerating the tomato plant, but there would be nothing to stop a fully deleted construct to be made if this were not so.) The principle of making a 'harmless' GMO remains. Possibly all that is required in such a case is to label the plant as an approved GMO.

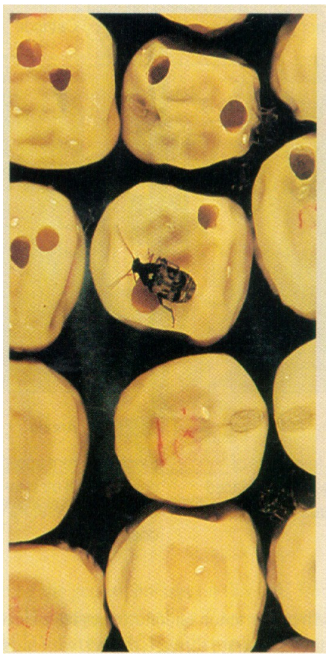


Another apparently harmless example is the genetic engineering of bacteria to produce useful products that they would not produce otherwise. This has been hugely beneficial. For example the gene for human insulin has been placed and expressed in the bacterium, *Escherichia coli*. Prior to this, diabetics were treated with insulin isolated from pigs. Although this worked well for most people, there is a single amino acid difference between pig and human insulin and some people mounted an allergic or immune response against pig insulin. Once it could be produced in bacteria, large quantities of safe, non-allergenic human insulin became available. Similar potential exists for producing other human proteins (e.g. human growth hormone) in bacteria, yeasts or other types of cells. This has become especially important given that AIDS and other infectious agents can contaminate samples isolated directly from humans.

From an advertisement in an old South African Airways in flight magazine, showing *E. coli* cells with insulin inclusion bodies shown in pale green. The advertisement was overprinted with the comment *E. coli*, your friend for life



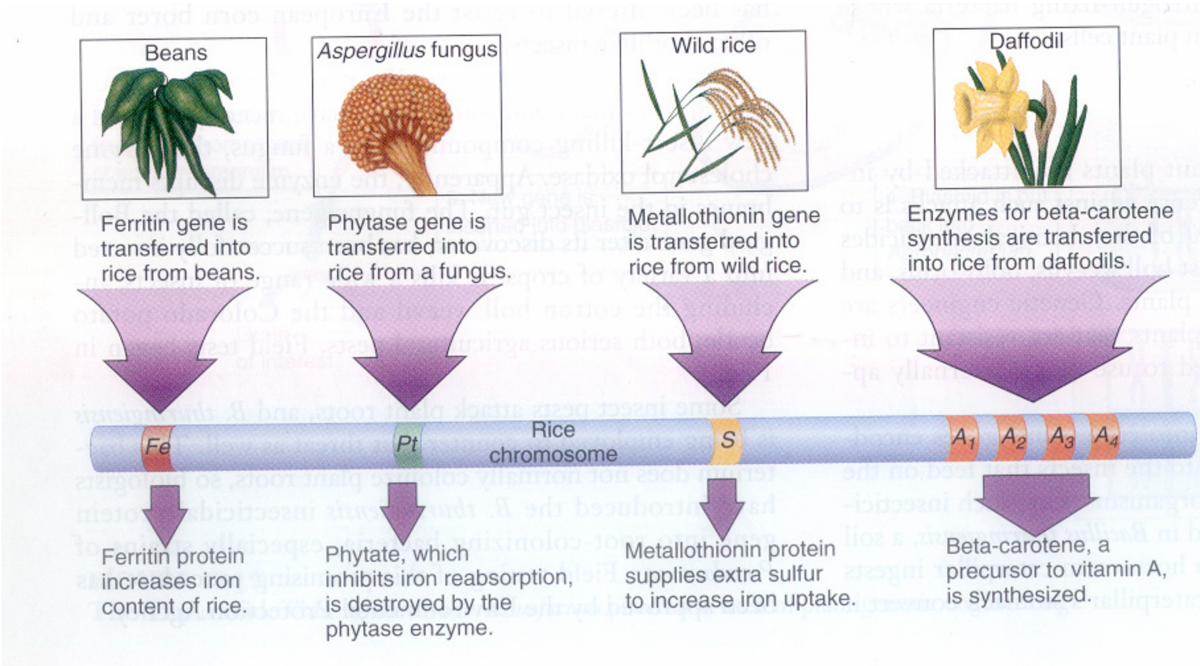
There are many examples of the modification of plants to herbicide resistance such as the insertion for a bacterial gene for an enzyme that is not sensitive to the herbicide glyphosate. The equivalent plant enzyme is sensitive to this herbicide and the plants into which the bacterial gene has been placed are resistant. Another is the insertion of a bacterial gene for a toxin (B.t. toxin) harmful to insects but not to people and which has been added to prevent insects from eating and damaging sugar cane, cotton, peas and other crops.



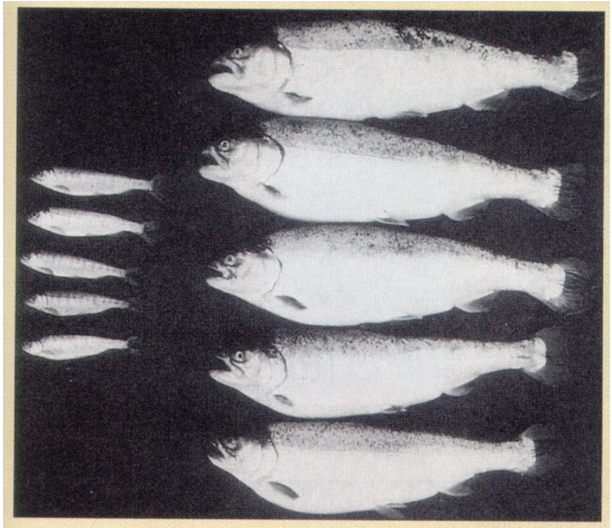
WEEVIL-PROOF PEAS

Not only has gene technology afforded agriculture viral and pest control in the field, it has also provided a pest control technique for the storage bin. A team of U.S. and Australian scientists have engineered a gene that is expressed only in the seed of the pea plant. The enzyme inhibitor encoded by this gene inhibits feeding by weevils, one of the most notorious pests affecting stored crops. The worldwide ramifications are significant as up to 40% of stored grains are lost to pests.

Below are some modifications that have been incorporated (or are possibly being considered for incorporation) into rice genomes with source of the 'foreign' genes and the potential benefits to the consumer given below the figure.



Then there is the possibility of making GMO's that might be concern many people. For example it may be possible to modify cattle or fish (see below) such that they produce enhanced amounts of growth hormone. Such animals produce body mass more rapidly than unmodified animals with clear financial benefits for a farmer. Sometimes, such rapidly growing animals may face skeletal problems because the strength of cartilage etc., is not able to cope with the increased loading. There is the possibility that such modification could be considered to be a breach of animal rights. Below is a well-known photograph of two mice that have been fed the same quantity of food but one is able to overexpress the rat growth hormone.



SUPER SALMON!

Canadian fisheries scientists have inserted recombinant growth hormone genes into developing salmon embryos, creating the first transgenic salmon. Not only do these transgenic fish have shortened production cycles, they are, on an average, 11 times heavier than nontransgenic salmon! The implications for the fisheries industry and for worldwide food production are obvious.

Then there are many other examples of using hormones to enhance milk production or provide other real or perceived benefits. The number of examples is extensive and these few are from first year general biology text books and a few other places.

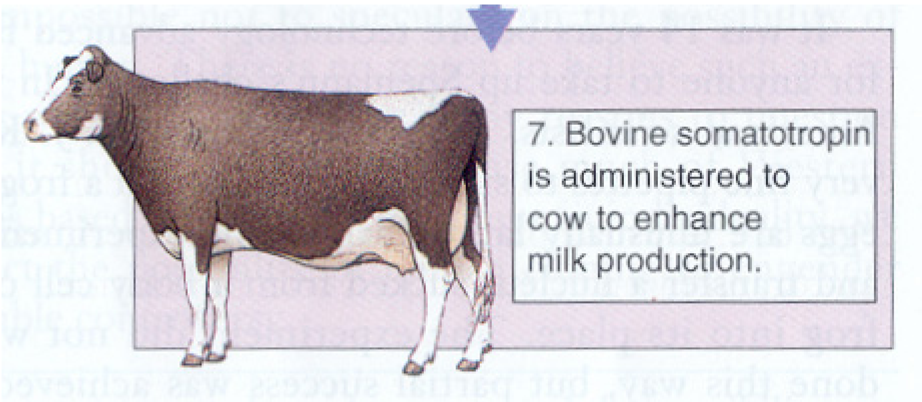


FIGURE 14-15 **Transgenic "pharm" cows.**

These cows contain a human gene that codes for lactoferrin, a protein found in human mothers' milk and in secretions such as tears, saliva, bile, and pancreatic fluids. Lactoferrin is one of the immune system's lines of defense against disease-causing organisms. The cows secrete human lactoferrin in their milk.

The question is then, which of these are dangerous and should not be carried out? Scientists are generally careful about what they do and precautions are taken to ensure that genetically modified bacteria are not viable outside of the laboratory. There no examples of accidentally cloned hazardous genes, although this does not exclude that something harmful might be carried out in the future, either unintentionally or maliciously.

Clearly careful attention needs to be paid to organisms for release in the wild. Genes could be transferred via pollen to close wild weed relatives. To date, it appears as though these transgenic weeds are not competitive with respect to non-transgenic weeds. However, care needs to be taken that this could not happen on a case by case basis. What is clear, is that plants are not harmful simply because they are transgenic, it is the nature of the modification that needs to be taken into account.

There was a concern that the placement of genes for insecticides into plants may negatively affect unintended targets. A well-advertised case was whether genes encoding bacterial insect toxins would affect the fate of 1000's of monarch butterflies during their immigration if they alighted on transgenic crops. So far this has not appeared to be the case.

What if fast growing fish escaped into natural water bodies and what affect would that have on the ecological balance or rivers? The answer to this is not yet known but to address this concern, transgenic salmon produced in the USA are non-reproducing females.

My own research field, the use of microorganisms in the extraction of metals from ores (also called biomining) exploits a natural processes that has been taking places for many millennia. That is the ability of certain bacteria to obtain their energy through the oxidation of minerals containing either iron or sulphur. The ferric iron and sulphuric acid produced is able to solubilise certain metals such as copper, zinc or nickel (and others depending on the ore). The Rio Tinto river in the south of Spain is red, highly acid, undrinkable and void of all macrolife (it teams with microbial life) as a result of these bacteria. This is not a result of man-made pollution, it has been like this since prehistory. In spite of the organisms responsible for the production of ferric iron and acid being natural, we would not consider using GMOs in the processes used to recover metals for the following reasons. The public considers the use of bacteria in mining operations as being unnatural and are therefore very suspicious of any attempts to manipulate such organisms. When certain members of the public have heard about how efficient microbial based mineral recovery processes are, a question that has been asked is, 'what if the bacteria escape and eat the mountains?' Of course, if they could, they would have done so already, because the organisms are natural and occur ubiquitously. Fortunately, for us these microorganisms have access to a substantial horizontal gene pool and it has not been necessary to 'genetically manipulate them by introducing, for example, metal resistance genes. It has been possible to isolate suitable organisms from the many natural variants that exist without deliberately genetically engineering any of the bacteria. The main point being made is that public perception is critical and if the public is suspicious of GMOs. It is danger to the company share price is so severe that a self-imposed ban exists which would require a successful public education program to reduce concern before genetic manipulation of any nature is carried out.

Risk assessment techniques have been developed and are in place in most first world and some other countries where the ability to carry out work described here exists.

References

P.H. Raven and G.B. Johnson. 2002. Biology 6th Edition, McGraw-Hill.

E.P. Solomon, L.R. Berg and D.W. Martin. 2005. Biology 7th Edition, Thomson Brooks/Cole.