Gene technology and future foods

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Molecular biology is revolutionizing biology, agriculture and medicine. It is now possible to isolate and sequence the basic genetic material (DNA) from any organism and techniques have been developed to copy and 'cut and paste' DNA molecules to produce new combinations. This has led to the development of genetically modified (GM) plants by the targeted introduction of a small number of well-defined genes directly into the cells of an existing plant variety to improve its quality or performance. Early efforts concentrated on major field crops, such as corn, soybeans and canola. Products from these plants, such as oil and flour, are components of many processed foods, so the rapid adoption of GM commodity crops in the United States has led to widespread appearance of GM plant material in foods. The initial traits targeted, such as herbicide tolerance and pest resistance, provide improved production efficiency with benefits for agrochemical and seed producers, farmers and the environment, but little obvious benefit to consumers. The second generation of GM plants will provide consumer benefits and will extend beyond bulk commodity crops. Genetically modified plants with improved flavour, nutritional composition and shelf life are currently being developed in a range of grains, fruits and vegetables. Genetically modified plants pose no risks for human health beyond those that we readily accept in other foods. In most developed countries, GM plants undergo thorough testing and evaluation, well beyond that required for a conventionally bred new variety, and this should ensure that the current high safety and quality of foods is maintained.

Key words: gene technology, food, plant, genetically modified.

Plant breeding

The plant varieties we use in modern agriculture bear little resemblance to their wild progenitors. Selection and breeding to develop improved plant varieties has occurred for over a thousand years, its effectiveness enhanced in the past two centuries by the discovery of the genetic basis of inheritance by Gregor Mendel in the late 1800s. The application of traditional genetics to plant breeding accelerated the development of new varieties with increased yield and better resistance to pests and diseases, as well as improved flavour, processing and nutritional properties. The yield of most of the major commodity crops such as corn, wheat, rice and soybeans has doubled in the past century, largely as a result of plant breeding, leading to the 'Green Revolution' of the 1960s. The potential to modify organisms has increased dramatically with the development of gene technology and this will accelerate plant breeding.

Gene technology

The gene is the basic functional unit of inheritance and each gene consists of a DNA molecule which enables an organism to make a particular protein together with the 'molecular switches' that determine when and where each gene is active. The DNA sequence (genetic code) of each gene specifies the protein to be made when the gene is active. All cells in an organism have the same complement of genes but the switches specify which genes are active and so specify which proteins will be made. This determines what each cell will become, giving rise to different tissues and ultimately different organisms. Organisms all use the same basic genetic code, with many genes being quite similar across a range of organisms. Plants typically contain more than 25 000 different genes and animals contain more than 50 000.

Conventional plant breeding involves cross-hybridization between two parents and selection of the best offspring for further breeding. In this process, large blocks of genetic material (i.e. thousands of genes) are mixed, generating numerous new combinations of genes. Over several successive generations, plant breeders are able to introduce and stabilize new genes, such as those providing disease resistance from a wild relative, into existing varieties and then gradually remove most of the unwanted new genes that were also transferred in the first cross. In a few cases, entirely new varieties of plant have been produced by the conventional breeding of plants which do not normally interbreed. An example of this is triticale, a hybrid of wheat and rye, now commonly grown in many countries.

The development of gene technology has provided a major advance in our understanding of genetics and is already revolutionizing biology, agriculture and medicine. It is based on recombinant DNA technology – the ability to copy, cut and paste DNA molecules in the laboratory. DNA can be isolated from an organism and its sequence (genetic code) determined. DNA molecules can be chemically synthesized and can be copied in a test tube or by using bacteria as 'DNA factories' to multiply specific DNA molecules. In this way, individual genes can be identified and new combinations of genetic material can be made ('DIY genes'). The

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order of the four constituent bases that make up DNA (its sequence) determines what product the gene will make in a cell, but the chemical and physical properties of DNA are essentially the same in all organisms. This common feature of DNA makes it possible to transfer genes from one organism to another. There is significant overlap in genes across a wide range of organisms; for example, bacteria, fungi, plants and animals all contain the same basic set of genes responsible for cell synthesis and function.

Genetic modification (also called genetic engineering) is the transfer of individual genes into an organism using non-traditional techniques. This may involve the modification of an existing gene, its replacement with an improved version, or the introduction of a new gene from a similar or a different organism. Importantly, these genes can be introduced without the large numbers of unwanted genes that are moved in conventional breeding. The introduced genes can come from another organism, allowing genetic material to cross species boundaries, which is generally not possible with conventional breeding. (In nature, there are a few instances where genetic material is transferred from one organism to another – usually by a form of infection. One of the most common methods used to insert genes into a plant exploits the natural ability of the gall forming soil bacterium, *Agrobacterium tumefaciens*, to incorporate its DNA into a host plant.) Genetically modified (GM) organisms are often described as 'transgenic'; that is, they contain genetic material from another organism. Further information on gene technology and its uses in agriculture are discussed elsewhere.[1,2]

Genetically modified plants

Genetic modification of plants involves the targeted introduction of a small number of selected genes (usually two) into an existing plant variety to affect its performance. This will normally involve the target gene, which will improve the plant, plus a selectable marker gene to allow scientists to rapidly identify and isolate those cells that have taken up the target gene. To date, the marker genes most commonly used produce a characteristic, such as herbicide or antibiotic resistance, to allow positive selection of the GM cells. New marker genes are presently being developed that do not involve antibiotic or herbicide resistance and are only manifested in the laboratory. In some crops, it is also possible to delete the marker gene after the genetic modification has been achieved.

Both the target and marker genes will have controlling elements (promoters and terminators) that are the 'molecular switches' to control when the genes are turned on and off and to specify the tissues where the genes will be active. The controlling elements from plant virus genes have been found to be effective in plants and are often used to switch on the introduced genes.

This is a relatively new set of techniques — the first GM plants were created in the laboratory in the late 1970s and the first commercial release of a GM plant was in 1994. Adoption of GM plants was initially quite rapid, increasing more than 15-fold from 1996 to 1998 (Table 1). The main commercial production of GM plants is in the United States, Canada and Argentina, although trials of GM plants have occurred in most countries. It is difficult to obtain reliable estimates of the extent of use of GM plants in China but it is known that significant areas of GM crops have been grown there since 1995. Because of the high initial costs in producing GM plants, the main commercial plantings have been in broad acre commodity crops such as corn, soybean, cotton and canola. Transfer of genes into the major cereals, such as wheat and rice, has been technically more difficult so these are not yet in commercial production to any significant extent.

Products from crops such as corn, soybean and canola are ingredients of many processed foods; hence the rapid adoption of GM plants for agriculture in major producing countries has led to the widespread inclusion of GM plant material in foods around the world. These commodity crops are marketed through bulk handling facilities so the GM products have generally not been segregated from their conventional counterparts. In foods, the GM material is often a processed product of a GM plant, such as oils, starches or protein extracts, and may only constitute a small proportion of the food.

There are now more than 150 different GM crops approved for production around the world, including cereals, oilseeds, fibre plants, pastures, fruits, nuts and ornamental plants. A range of new traits has been introduced into GM plants, which are aimed at increasing plant performance or improving plant product quality (Table 2).

The first round of commercial GM plants have added genes that provide tolerance to herbicides, which allow weeds to be sprayed without killing the crop, or genes to allow the plant to make its own insecticidal proteins to provide increased resistance to insect pests (Table 1). These traits improve plant performance and lower the cost of production so farmers and agrochemical and seed producers mainly see the benefits. They can also have a significant environmental benefit through an overall reduction in pesticide application, energy use and soil degradation. Consumers are usually unaware of any benefits as the savings from increased production efficiency, when passed down the marketing chain, often only maintain existing prices in the short term. The second generation of GM plants will include

Table 1. Commercial production of genetically modified plants

Total area			
1996	1997	1998	1999
2	11	28	40

Country	1998 area
USA	20.5
Argentina	4.3
Canada	2.8
Mexico	0.1
Australia	< 0.1
Europe	< 0.1
South Africa	< 0.1
Crop	**1998 area**
Soybean	14.5
Corn	8.3
Cotton	2.5
Canola	2.4
Potato	0.1

All areas are worldwide (excluding China) in millions of hectares.

improved quality traits (Table 2), which will have more direct benefits for consumers. The next wave of GM plants will also extend beyond the bulk commodity crops and include a much wider range of food products such as fruit and vegetables.

Genetically modified plants in Australia

Two GM plants are presently in commercial production in Australia — carnations with altered flower colour and insect-resistant cotton. The GM cotton, developed by CSIRO and industry partners, was released in 1997 and 100 000 hectares of GM cotton was grown in Australia in 1998, which was 20% of the total crop. The cotton fibre is used in the textile industry and the cotton seed provides oil that is used in cooking as well as meal which is fed to livestock.

Table 2. Plant traits modified using gene technology

Plant performance	Plant product quality
Increased yield	Delayed ripening
Herbicide tolerance	Modified oil content
Insect resistance	Increased starch content
Viral resistance	Modified starch composition
Fungal resistance	Improved protein composition
Bacterial resistance	Improved processing

The GM cotton contains a gene that provides the plant with in-built resistance to insect pests. The common bacterium *Bacillus thuringiensis* (Bt) produces a protein that is toxic to certain caterpillars, and this toxin has been extracted from bacteria and sprayed onto plants as a garden and agricultural insecticide for more than 20 years (Fig. 1). The gene which makes the toxin protein has been isolated and inserted into cotton plants so that the plant makes its own insecticide. Because the plant is making the Bt toxin, there has been more than 50% reduction in chemical sprays applied to the GM crop, resulting in more efficient production and lower pesticide use.

Current research in Australia is using gene technology in a wide range of plants including field crops, trees, ornamentals and horticultural products. Traits include herbicide tolerance, pest resistance, starch composition, protein composition, fruit ripening, seedlessness and virus resistance. Table 3 lists some examples of Australian research projects aimed at improving plants by genetic modification in a range of crops. Most are still at the research stage with insect-resistant cotton and modified flower colour carnations the only plants in commercial production at present.

Testing genetically modified crops

There is significant public concern about the food safety and environmental effects of the adoption of GM plants in

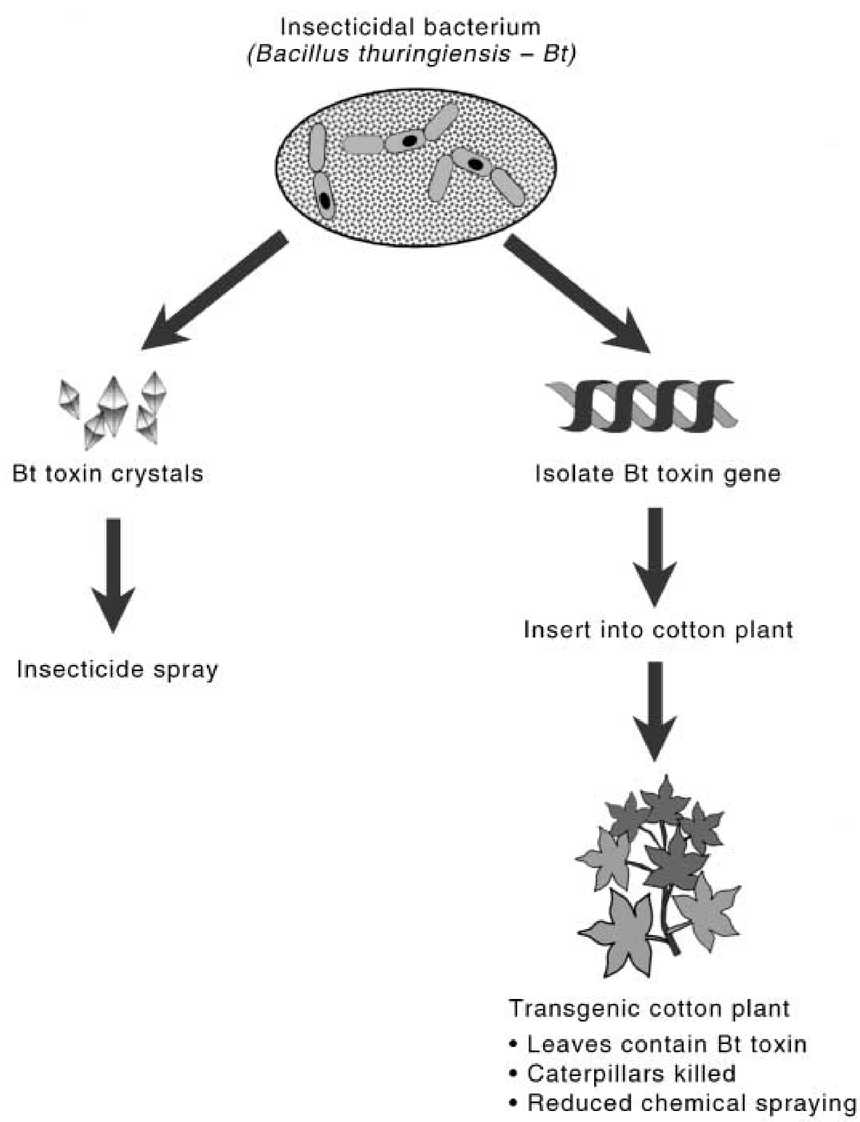

Figure 1. Development of insect-resistant cotton.

agriculture.[3] This has led to an unprecedented level of scrutiny of these plants, well beyond that which would occur for a new plant developed by conventional breeding. Development of a GM plant is a lengthy process with extensive testing at each step and the progression from initial laboratory studies to commercial release of a GM plant can take up to 15 years. Research is initiated in the laboratory to identify useful genes and determine their function in minute detail. From a gene sequence, the type of protein it will make can be determined and sophisticated computer models are used to predict how the protein will behave in the plant and as a food product. The protein a gene encodes can be made in the laboratory in large quantities and its nutritive properties, allergenicity, toxicity and other health effects can be readily evaluated. Following this testing, the gene is introduced into the target plant to produce a GM plant in the laboratory. The plants are evaluated in the laboratory and in glasshouse trials to check that they are true to type and perform as well as their conventional counterparts. The GM plants will then undergo small-scale field trials to evaluate their performance and the material produced can be used in laboratory trials to check its safety as a food product. If the plants perform satisfactorily, development will proceed to larger field trials. At each step, regulatory approval from all of the relevant authorities is required and the eventual commercial use of the GM plant as a crop depends on the GM plant passing all of these tests. It is important that this rigorous testing of GM plants continues. This will provide a rational scientific basis for regulation of GM foods, but it will also be important in reassuring consumers about the safety of the food they eat.

Safety of genetically modified foods

In countries such as the United States and Canada, evaluation of the safety of GM plants has been based on the principle of substantial equivalence. The United States Food and Drug Administration (FDA) ruled in 1992 that food products from GM plants that are essentially the same as their conventional counterparts by all criteria relevant to their use in food (composition, nutritive value, functional characteristics, taste) need not be specifically labelled as genetically modified. In contrast, European laws introduced in 1997 require specific labelling as genetically modified if food contains significant amounts of the introduced DNA or protein.

If a GM plant is derived from an existing cultivar with an established record of use in food, the evaluation focuses on the added gene and its protein product. As discussed earlier, this can readily be assessed in a GM plant as a small number of well-characterized genes have been introduced and their protein products evaluated thoroughly. Many of the different GM crops contain the same or similar introduced genes, such as those providing herbicide tolerance or insect resistance. The products of these genes have been extensively evaluated, particularly in the United States, prior to their use in commercial crops and there is a large amount of data on their safety in food. The evaluation has been similar to that required for registration of a new agrochemical or drug and has involved *in vitro* studies, animal feeding trials and toxicity testing. Three examples of safety issues relevant to many GM plants are given below.

Virus genes

- Many GM plants contain a gene promoter from a plant virus;
- We already ingest millions of plant viruses in conventional foods;
- Only a small part of the virus is used in GM plants;

Table 3. Some examples of current plant gene technology research in Australia. Most of these projects are in the research phase. The only genetically modified plants grown commercially in Australia at present are carnations with modified flower colour and cotton with insect resistance

Plant	Trait	Application
Cotton	Insect resistance	Caterpillars
	Herbicide tolerance	Weeds
Carnation	Petal colour	New flower colours
	Senescence	Extended vase life
Canola	Herbicide tolerance	Weeds
	Lipid metabolism	Oil content and composition
	Pod shatter	Increased yield
	Resistance to fungal pathogens	Blackleg
Clover	Virus resistance	Alfalfa mosaic virus
	Pasture quality	Cattle bloat
	Herbicide tolerance	Weeds
	Protein composition	Animal nutrition
Peas	Insect resistance	Weevils
	Protein composition	Animal nutrition
	Herbicide tolerance	Weeds
	Resistance to fungal pathogens	Blight
Wheat	Resistance to fungal pathogens	Rusts
	Starch and protein composition	Processing quality
	Resistance to root pests	Cereal cyst nematodes
Barley	Starch and protein composition	Malting quality
	Virus resistance	Barley yellow dwarf virus
Soybeans	Herbicide tolerance	Weeds
Lupins	Amino acid composition	Wool and meat production
Sugarcane	Resistance to bacterial pathogens	Leaf scald
	Virus resistance	Sugarcane mosaic virus
	Sugar content and colour	Sugar yield and quality
Rice	Increased iron content	Improved nutrition
Tomatoes	Ripening	Improved flavour
	Insect resistance	Various insect pests
Citrus	Seed development	Seedless fruit
Potatoes	Virus resistance	Leaf roll virus
	Tuber quality	Blackspot bruising
Grapes	Resistance to fungal pathogens	Powdery and Downy mildew
	Resistance to root pests	Nematodes and Phylloxera
	Grape quality	Improved colour and flavour
Apples	Insect resistance	Codling moth
Papaya	Virus resistance	Papaya ringspot virus
	Ripening	Improved shelf life
Lentils	Herbicide tolerance	Weeds
Pineapple	Flowering induction	Uniform ripening
Lettuce	Virus resistance	Lettuce necrotic yellows virus

- It is not infectious in any way;
- There are no credible risk scenarios.

Antibiotic resistance genes

- Antibiotic resistance genes are used as markers in producing GM plants;
- There is concern about transfer of the genes to other organisms;
- This group of antibiotics is not commonly used in medicine;
- Extensive studies have been carried out;
- The protein does not survive in the digestive tract;
- Transfer of the gene to pathogenic bacteria is highly unlikely;
- Risk and consequences (if any) are minimal.

Herbicide tolerance genes

- Herbicide tolerance comes from a modified version of an existing protein;
- The gene for the modified protein is from bacteria;
- The modified protein is neither toxic nor allergenic;
- No change occurs in the nutritive value of the plant products;
- Extensive testing indicates the modified protein has no adverse health effects;
- Transfer of the genes to weeds *is* a potential problem.

Where a GM plant contains a protein that is not normally found in food, the plant should be considered to be a new food or additive and more extensive testing would be required. Examples would include plants carrying vaccines or those with genes from a wild plant not normally consumed as food.

In some countries, particularly in Europe, regulatory examination has been process-based, rather than the product-based approach in the United States. The view has been that the process of modifying a plant using gene technology introduces new risks so the process itself must be regulated. This view gained momentum following the release in 1998 of controversial data from a study carried out in Scotland by Dr Arpad Pusztai. Regrettably, Pusztai initially announced his findings to the media rather than the normal procedure of submitting the results to a scientific journal, where his scientific peers would review the data. The Pusztai experiments involved feeding rats with potatoes genetically modified to produce an insecticidal protein from snowdrops. These rats were compared to another group fed conventional potatoes with the snowdrop protein added. The results appeared to show that the GM potatoes affected the immune system of the rats as a result of the genetic modification itself, beyond the effect of the insecticidal protein. Because these claims raised serious concerns about the health effects of GM foods, and were not subjected to the normal scrutiny of a scientific publication, the Royal Society carried out a review to investigate the study. The review, carried out by six independent experts, found that the Pusztai experiments were flawed by poor experimental design, small sample sizes, dietary deficiencies, uncertainty about the chemical composition of the potatoes and inappropriate statistical treatment of the data. The Royal Society review concluded that there was no evidence of adverse health effects from consumption of GM potatoes.

It is quite feasible to produce plants that have a lower nutritive value or are toxic or allergenic by genetic modification. It is equally possible to produce such plants by conventional breeding. In all of the studies that have been carried out so far, there is no reliable data to suggest that the process of genetic modification itself has any adverse effects on human health.

Regulation of genetically modified products

There has been a great deal of discussion as to whether existing regulations for food and agriculture are sufficient for GM organisms. Because gene technology has developed rapidly, new legislation to deal with regulatory issues has often lagged behind the production of GM foods. In all, some 30–40 countries have regulations governing experimentation and use of GM products. The remaining 130 or more countries have no regulations for GM organisms.

In the United States, the FDA and the US Department of Agriculture (USDA) have been involved in approval of GM plants. The responsibility for testing has mostly rested on the developer of the GM product and the principle of substantial equivalence has been accepted. The FDA has indicated that labelling of GM food would only be required where the product is materially different from its conventional counterpart.

In Australia, the Genetic Manipulation Advisory Committee (GMAC) was established in 1987 as a non-statutory committee reporting to the Minister for Industry, Science and Tourism. The Committee comprises leading scientists in a wide range of disciplines as well as members of the wider community with expertise in areas such as law and journalism. The GMAC has had oversight of all gene technology research and also provides advice on gene technology to Commonwealth agencies. The GMAC has developed a range of guidelines for laboratory and field experiments involving GM organisms. Research agencies using gene technology are required to form Institutional Biosafety Committees (IBC) to assess the safety of the research, to regularly inspect facilities and to ensure that the GMAC guidelines are followed. The IBC can approve low-risk research in contained facilities but seek approval from the GMAC before any field trials are carried out. Adherence to the GMAC guidelines is voluntary but there has been a very high level of compliance to date.

Where GM organisms are to be used in food, the regulatory responsibility primarily rests with the individual states and territories. The Australia New Zealand Food Authority (ANZFA) develops uniform food standards and these are essentially specific performance standards relating to safety, composition, labelling and permitted residues in food. The ANZFA also coordinates food surveillance undertaken by the various authorities and advises the Commonwealth Minister on food matters. In this regard the ANZFA is consulted on the safety and identification of food produced through gene technology.

The only two GM plants presently grown commercially in Australia, carnations and cotton, do not have major impacts on our food supply. However, GM products have appeared in a range of foods as a result of the use of imported foods and ingredients. With the commercial development of GM organisms accelerating, the Federal Government announced in 1997 that it would introduce a national legislative framework that would provide protection for humans and the environment, assure scientifically based risk assessment, and specify a clear regulatory path for industry, investors and researchers. The establishment of the Office of the Gene Technology Regulator (OGTR), and associated legislation, will provide an effective system to regulate gene technology, including the use of GM organisms in food. The OGTR will develop regulations to cover research, testing and labelling of GM organisms and food products. The Federal Government has also established a coordinating body, Biotechnology Australia, to help ensure Australia captures the benefits of biotechnology while protecting the community and the environment from any risks.

Gene technology in the future

The production of GM plants can be considered in three phases. The first phase concentrates on improving crop performance, involves traits such as insect resistance and herbicide tolerance, and is targeted at the major field crops such as corn, soybean and canola. These crops have direct benefits for producers but only limited benefits for consumers. The second phase of GM plants, most of which are still being developed, have a range of traits aimed at improving product quality. These will have direct benefits for consumers and are likely to provide healthier and safer foods. For example, an estimated 2 million people die and 8 million go blind each year as a result of vitamin A deficiency. A GM rice plant has been developed that produces carotenes in the seed. In humans the carotenes are converted into vitamin A so this 'golden rice' will benefit the millions of people worldwide who suffer from health problems caused by vitamin A deficiency. Similarly, it is estimated that 30% of the world's people are afflicted by iron deficiency as a result of the low levels of bioavailable iron in their food. Most of these people also have vegetarian diets with rice as a major component. Proteins that have a high level of bioavailable iron, such as ferritin and plant haemoglobins, have now been introduced into rice to provide a higher level of dietary iron in a suitable form to correct iron deficiency. We are also likely to see the application of gene technology extended beyond the common field crops to a wider range of plants, including fruit and vegetables. Gene technology will improve the shelf-life of many foods by delaying ripening and senescence, hence reducing the significant postharvest losses that occur in a range of crops, particularly soft fruit and vegetables.

The third phase of GM plants involves new products and new industries. Examples of future GM plants include:

- The production of oral vaccines and other pharmaceuticals in plants;
- Crops producing feedstocks for the chemical industries, hence reducing reliance on fossil fuels;
- Production of biodegradable polymers for the plastics industry;
- Forest trees with enhanced growth and improved timber properties;
- Plants that can be used in bioremediation of polluted sites.

Gene technology will also have a major impact on agriculture in other ways. DNA-based diagnostic procedures are already in use, which allow rapid detection of pests and pathogens and the identification of plant cultivars using 'DNA fingerprinting' techniques. DNA markers will also greatly accelerate traditional plant breeding through the use of marker-based selection of improved plants. The techniques used in gene technology continue to improve at a rapid rate and have now made it feasible to study 'the genome' — the complete collection of genes in an organism. The complete sequence of the genome of the *Arabidopsis* plant will be known before the end of 2000 and the entire rice genome will be sequenced within the next year. This information will provide a vast amount of new knowledge and will greatly streamline traditional breeding. Indeed, the 'biotechnology revolution' that will occur in this century has the potential to change our lives to a greater extent than the electronic and information eras of the past century.

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Appendix I

Gene technology and food sites

CSIRO biotechnology: http://genetech.csiro.au
Genetic Manipulation Advisory Committee (GMAC):
http://www.health.gov.au/tga/gene/gmac/gmac.html
Australian Biotechnology Association (ABA):
http://www.aba.asn.au
Australian Food and Grocery Council: http://www.afc.org.au
Australia New Zealand Food Authority: http://www.anzfa.gov.au
US Department of Agriculture Biotechnology:
http://www.nal.usda.gov/bic
US Food and Drug Administration: http://www.fda.gov
Therapeutic Goods Administration:
http://www.health.gov.au/tga/gene/genetech
Biotechnology Australia: http://www.isr.gov.au/ba/
Interim Office of the Gene Technology Regulator (IOGTR):
http://www.health.gov.au/tga/gene/genetech/iogtr.html
Genethics: http://www.zero.com.au/agen/
Biosafety Information Network: http://binas.unido.org/binas/
Ag Biotech Infonet: http://www.biotech-info.net/