GENETICALLY MODIFIED CROPS: FACT, FICTION AND PERCEPTION: GREEN GENES, RED HERRINGS AND BLUE CARNATIONS.

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The story of GM crops is a short one, no more than 20 years in total, with the principal elements dating back less than a decade. In that short time, the debate as to the desirability (or otherwise) of GM plants has become highly polarised. The proponents include the multinational seed companies, some governments and some scientists on one side, while the opponents of GM technology include the environmental movement, the organic farming industry and some other scientists on the other. Most of the public have understandably found themselves perplexed, frustrated and exasperated, in equal measure, unable to get a straight answer and confused by whom to trust. The same technology has been variously described as both the likely solution to world hunger and the greatest threat to the environment. Both sides have brought their big guns to bear on the issue, with Nobel laureates espousing each side of the argument. It's hard not to be confused.

DOMESTICATION OF PLANTS

Humans have been cultivating plants for at least 10,000, maybe 14,000 years, with primitive wheat (einkorn) being the first crop plant. The key step in the domestication of plants came when Stone Age farmers changed from merely collecting and eating grain from wild-grown wheat plants to also storing and planting seeds from their crops to establish the next year's crop. Not only did this give the people a predictable supply of the crop from year to year, allowing (indeed, forcing) the communities to settle down, but also leading to subtle genetic changes in the plant populations they grew. For example, the wild wheats were characterised by a brittle rachis (the part of the stem which runs through the ear), so that it shattered at maturity and the ripe grains were scattered, achieving seed dispersal which was invaluable for the wild plant, limiting competition between the offspring plants. Rare natural wheat mutants having a solid rachis kept the grains attached to the ear at maturity, enabling harvest of a higher proportion of the grains by the Neolithic farmer. As a consequence, this mutant would be represented (as a result of unconscious (i.e. not deliberate) selection) at a higher frequency in the harvested seed (and hence in each crop) at each subsequent generation. In this way started the process of plant domestication, in which crops became better adapted to agriculture (e.g. increased yield of seeds harvested) at the expense of reduced adaptation to nature (e.g. seed dispersal). Later, deliberate or conscious selection further improved domesticated plants, introducing, for example, the free-threshing character into cultivated wheat, so that the chaff could readily be separated from the grain. The quasi-religious basis of harvest festivals in agricultural cultures the world over meant that the largest heads of wheat or tubers of potato were selected (as offerings to the gods) for planting the next crop, resulting in inadvertent selection for increased yield.

Overall, it is believed that some 30,000 of the 250,000 plant species in the world have been used by man at some point for some purpose (food, medicine, fibre, fuel, for example), although currently more than 90% of the edible plant harvest worldwide is represented by less than 30 species. Some crops have been domesticated for thousands of years, such as wheat, barley (10,000 years) and potato (6000 years), but others are more recent, such as sugar beet (250 years) and oilseed rape (400 years ago). Very few crops originated in Europe: primarily the brassicas, including cabbage, cauliflower and oilseed rape, and the beets, mainly sugar beet but also fodder beet and beetroot. Most of our food crops originated elsewhere, such as potato (Peru/Bolivia), wheat and barley (Middle East) and peas (China).

MODERN PLANT BREEDING
Over the millennia, genetic crop improvement continued. Our modern-day crop varieties bear little resemblance to their wild ancestors. Wild bananas contain seeded fruits; the familiar cultivated bananas are sterile, producing no seeds. The first cultivated carrots were purple with an orange centre. It was only when Dutch plant breeders started to select for the patriotically coloured roots in the 17th century that all-orange carrots were developed.

Until the beginning of the 20th century, most farmers grew their own locally-adapted varieties ("landraces") of the major crops, and kept seed back from year to year for sowing. Commercial plant breeding occurred as early as the latter part of the 18th century, for example when the French developed sugarbeet varieties by selection from sweet fodder beet, but it was the 20th century which saw plant breeding placed on a scientific footing, with the rediscovery of Gregor Mendel's laws of inheritance. The result was a clearer understanding of how genetic traits such as plant height and seed yield were passed on from parent to offspring, and hence how this information could be used to develop, say, disease-resistant wheat varieties or high-yielding potato varieties.

COMMERCIALISATION OF PLANT BREEDING
Until the 1960's, variety improvement in Europe and the US was undertaken largely by universities (particularly the Land Grant universities in the US) and research institutions like the Plant Breeding Institute (PBI) in Cambridge and the Oak Park Research Centre (of An Foras Taluntais, now Teagasc) in Carlow. Although these new varieties enabled farmers to produce higher yields from the same land area, there was not much money to be made by the breeders. Breeding was time consuming (up to 14 years for a new potato variety) and expensive. In 1968, Plant Breeders' Rights were introduced in Europe (and similar schemes were introduced later in other parts of the world) by which plant breeders received a royalty payment per bag of seed sold of one of their varieties. PBR is not a patent, and there is a re-use clause which allows farmers to sow (but not sell) seed they produced from the crop grown from the seed they bought; this seed is known as farm-saved seed. The income from PBR established the commercial potential of plant breeding, and many of the major petrochemical companies, like Shell and ICI, moved into the area, buying up and expanding existing seed companies. These chemical companies already dealt with crop farmers, supplying them with fertilisers and pesticides etc.; it made good commercial sense to offer an entire vertically integrated package, including seed. The move from state-run breeding to the commercial sector was supported by conservative free-market governments like those of Thatcher and Reagan who cut support for state-run programmes e.g. the Land-Grant Universities in the US, and sold profit-making state-run breeding stations (e.g. the PBI), thus eliminating competition for the seed companies.

Conventional plant breeding is not the easiest business from which to make a profit. The aim is to cross, say, two parent wheat varieties and to select an individual with a much better combination of genes and hence characters from the two parents. Each inherited character is controlled by at least one gene, which is a tiny length of the chemical DNA present in the nucleus of every cell of the plant. The different genes are carried, joined end-to-end, on bodies called chromosomes. As an average plant contains approximately 25,000 different genes, conventional plant breeding is like having an enormous one-armed bandit, with 25,000 reels instead of three, and hoping to get all 25,000 lemons!! From 1.5 million hybrid wheat plants, a breeder would hope to produce one new variety; a good variety may then remain on the recommended list (from which farmers would select the varieties to purchase) for as little as four years before it is superseded by a newer, better variety. The breeder must recoup all the breeding costs and make a profit from the royalties paid over that short period. If that's not bad enough, seeds are one of the few self-replicating products. A farmer may buy certified seed of your wheat variety once but could then harvest enough seed from his first harvest to sell some to the milling company or for biscuit making or animal feed, and keep enough seed to sow next year; imagine the consternation of the automotive industry, if the consumer, after having owned the car for a year, went into the garage and found a brand new version sitting there! Certified seed purchased from the breeder (actually, from a seed merchant) has the advantage, however, of being certified to be free of disease, weed seeds etc., although it costs approximately three times the cost of farm-saved seed.

Up to the 1960s, conventional plant breeding consisted largely of classical hybridisation methods as described above. This strategy was effective but limited to the genes and characters present within the existing varieties of a particular crop (e.g. wheat, the so-called wheat gene pool). One could only cross wheat with wheat, not with closely related barley and definitely not with unrelated plants such as potato. Gradually, breeders adopted new techniques which enabled them to introduce novel characters into the crop gene pool, by permitting them to cross, say, wheat with closely related species (the other cereals, including rye and the wild wheats), to make hybrids not possible in nature. Most bread produced in Ireland, for example, is produced from wheat varieties containing some genes (from part of chromosome 1R) from rye, while the latest Irish-bred potato varieties, like Rooster and Cara, from the breeding programme at Oak Park, contain genes from wild potato species.

RECOMBINANT DNA TECHNOLOGY

These methods, though valuable, still only permitted the breeder to transfer genes from close relatives into a particular crop plant. In 1970, a new technology was developed which would have wide-ranging implications for plant breeding. Recombinant DNA (rDNA) technology enabled scientists to splice together DNA from two totally different species; no longer was gene transfer limited by the need for sexual compatibility between the donor and recipient. The first rDNA (or genetically modified, GM) organism was a bacterium (developed in 1970 by Paul Berg, Herb Boyer and Stanley Cohen). The first genetically modified (transgenic) plants were produced in 1983, in which a bacterial gene was cloned into a tobacco plant; tobacco is a widely used experimental plant in research. These first GM plants were experimental tools and were not planted outdoors; still, the enormous potential of this new technology was evident. Genes from any organism (animal (including human), plant, bacterium, virus, for example) could now be transferred into and permitted to work ("be expressed") in any plant.

Furthermore, expression of the transferred gene ("transgene")could also be controlled, so that it happened in large or small amounts, in specific tissues or organs (e.g. only in petals) or under specific circumstances, such as at maturity or when the plant was attacked by a pathogen. A gene consists both of a so-called coding sequence (which determines the character controlled) but also a regulatory sequence (the promoter) which controls when and in what part of the plant the gene is expressed. A gene can be customised by adding a particular promoter so that the gene only works when and where it is needed. Although every cell of a single plant contains exactly the same genes (usually two copies, one from the maternal, one from the paternal parent) of each of the approximately 25,000 genes, expression of most genes is restricted to particular tissues or environmental conditions; in an average plant cell, perhaps only 1-5% of the genes will be expressed (i.e. will generate their product) at any one time.

The gene product is usually a specific protein (the protein is said to be "encoded" by the gene) and that protein can control the particular inherited trait in one of two principal ways. The protein can either control the character directly, e.g. the wheat glutenin protein (encoded by the gene *Glu-1D*) controls the ability of the flour to make a loaf, or indirectly by controlling a chemical reaction which generates a chemical product which, in turn, determines the phenotypic trait. In the latter case, the *Dfr* gene in petunia encodes the protein dihydroflavonone reductase, which, in turn, controls a chemical reaction which produces the blue-coloured pigment delphinidin, determining blue flower colour. Proteins such as this which control the rate of chemical reactions are known as enzymes, examples of which (called lipases because they break down fats,or lipids, on dirty clothing) are found in biological washing powders.

The seed companies embraced the new technology and the resulting genetically modified (GM) plants with enthusiasm. Not only could new characters be introduced which were impossible by other means, but the various patents offices decreed that utility patents could be granted to GM plants and the isolated gene, providing seed companies with a legal means to prevent farmers re-using farm-saved seed. When purchasing GM seed, farmers sign a legally binding contract, guaranteeing that they will not sow farm-saved seed; this agreement ensures that seed would need to be purchased each year, resulting in potentially large increases in income for the seed company. The parent companies, now re-labelled "Life Science" companies, started to develop their own GM crop varieties. Interestingly, though Monsanto has always been to the fore in the GM story (and currently produces 90% of GM varieties) and, for many, is synonymous with GM, European-based multinational companies such as the French-German Aventis, the German Bayer CropScience and the British Syngenta have all been very active.

STRATEGIES FOR PLANT GENETIC TRANSFORMATION

Two strategies were quickly developed for modifying plant genes using this new technology. By inserting the new gene ("transgene") in the correct orientation ("sense construct"), the new gene product and its character could be introduced. On the other hand, if an existing character in the plant was undesirable, it could be eliminated by inserting an extra copy of the plant's own version of the gene in question into the plant but upside down ("antisense construct"). The first commercial GM plant was the blue-flowered carnation variety, Moondust. In nature, carnations are incapable of producing blue flowers because they lack the *Dfr* gene which controls production of the enzyme dihydroflavonone reductase which produces the blue pigment delphinidin. The gene (as a sense construct) was transferred by an Australian company, Florigene, from petunia into carnation to produce the first blue- (actually a muddy lavender colour !) flowered carnation. The first commercial GM food crop variety released was the Flavr-Savr tomato produced by the Californian plant biotechnology company Calgene in 1994. Tomatoes, allowed to ripen naturally on the plant, change from green, hard and bitter to red, soft and sweet under the influence of the natural hormone ethylene, which switches on specific ripening-associated genes in the fruits. A major problem for tomato growers was that, because ripe fruits are soft, they are easily damaged during transport, resulting in a short shelf-life. To overcome this, tomatoes were harvested and transported unripe (in which state they are hard and hence resistant to damage) and then artificially ripened by being exposed to the natural hormone ethylene; the disadvantage was that flavour did not develop fully under such conditions. Calgene employed antisense technology to switch off the *Pga* gene which encodes the enzyme polygalacturonase; this enzyme causes fruit softening during ripening by digesting the "glue" (pectin) which holds the fruit cells together. The fresh Flavr-Savr tomatoes were marketed for several years in North America, but were eventually dropped because of their high price. Zeneca (formerly the UK-based multinational ICI), now Syngenta, brought out a similar GM tomato which was given permission for marketing in the UK as tomato paste, and which sold well in Sainsbury supermarkets (voted the top supermarket in 2002 for organic produce by the UK organic certification body, the Soil Association!) for a number of years, on the basis that it was cheaper (because the GM plant produced more pectin, a major component of tomato paste, as a result of the reduced polygalacturonase activity) than conventional tomato paste.

Better-tasting tomatoes and blue-flowered carnations were not the ground-breaking developments expected of GM. The first GM crops which made a significant impact on agriculture were herbicide-resistant and insect-resistant crops, and still more than 98% of GM crops contain these characters. Monsanto lead the way with their RoundUp-Ready family of crop varieties resistant to their best-selling herbicide RoundUp (in which the active ingredient is glyphosate). This herbicide kills all plants and some bacteria because it interferes with a vital enzyme (EPSPS) present only in these organisms; the rapid immobilisation of glyphosate when in contact with soil means that the effect on soil bacteria is minimised. Because of its very broad-spectrum effect on plants, glyphosate had only ever been used on crops as a pre-emergence herbicide, applied before weed and crop seedlings had emerged. The inclusion of a EPSPS gene from a soil bacterium (isolated by Calgene scientists from a glyphosate dump) which was resistant to glyphosate made the transgenic crop resistant to the herbicide. As a result, the herbicide could then be used as a post-emergence herbicide after the weed and GM crop seedlings had appeared above ground. This opened up a huge new market for the herbicide and the sales of the GM crops (soyabean, maize, cotton, sugarbeet) were tied in with increased sales of the herbicide. Because RoundUp has no effect on animals, using RoundUp Ready varieties reduced risk to farmers and people surrounding crop land; because it kills all plants, fewer application (1-2) of RoundUp were needed than previously. The public was often confused by Monsanto's claim that the RoundUp Ready varieties would result in reduced usage of herbicides; why would a chemical company want farmers to use **less** herbicide? What actually happened was that the farmers would use less herbicide in total but more of the Monsanto product, which, previously, could not be applied to crops; the incentive for Monsanto was that RoundUp, which contributed approximately 30% to the company's total profits, was coming to the end of its period of patent protection, which meant that the market would soon be swamped with generic forms of glyphosate from other companies. By introducing RoundUp Ready varieties and recommending RoundUp as the only form of glyphosate for use on them, Monsanto have managed to maintain sales of RoundUp. GM crops resistant to other herbicides such as Liberty have also been released by other companies.

The other main class of input traits in the first generation of GM crops is the insect resistant varieties achieved by incorporating a gene from the bacterium *Bacillus thuringiensis* (Bt). This bacterium is usually a natural parasite of caterpillars; other forms of Bt are parasites of other insects. When ingested by the insect, the bacterium releases a protein pro-toxin; whereas the pro-toxin is safe, it is converted in the alkaline gut contents of the insect into the caterpillar-specific toxin, which kills the caterpillar. Bt has been used in organic farming and gardening for more than 40 years as a safe and environmentally protective caterpillar control measure. Incorporation of the gene for the toxin (not the pro-toxin) into maize, potato, cotton etc. enables the GM plant to generate its own insecticide, yet the effect is specific: only caterpillars which eat the leaf or stem tissue of the plant (which actively produces the toxin) are killed, so that Bt varieties are much more specific than the insecticides they replace.

Opposition to GM

GM is presented by proponents as a much more specific and precise form of plant improvement than conventional breeding, incorporating two additional well-defined genes (the target gene plus a marker gene essential to identifying which plants contained the target gene during the initial transformation process) into the variety, compared to the random re-shuffling of thousands of genes in conventional breeding. GM varieties are widely grown, with more than 140 million acres (12% of the total arable area world wide) sown to GM crops. Four countries (USA, Canada, Argentina and China) account for 99% of the GM acreage, although increasing numbers of developed and developing countries are growing GM crops, including Australia, New Zealand, Spain, Colombia, Uruguay and Chile. Of the US crops, 75% of soyabean is GM, compared to 71% cotton and 34% maize. In North America, more than 60% of all processed food products are reported to contain GM ingredients. Why then are there no GM food crops grown in the EU (although Spain grows 100,000 acres of GM maize for animal feed)?

After a period in which a GM tomato paste was marketed, and numerous GM crops were trialled around Europe, a moratorium on the cultivation of GM food crops was implemented in the EU in 1998. This was largely the consequence of a consumer-led backlash against the "backdoor" introduction of (largely US) GM products into Europe, in the form of GM soyabean, maize and canola (oilseed rape) products (principally oil, food additives, etc.). Public concerns about GM foods fall into two main categories:

1. effects on human health (novel toxins, allergies, antibiotic resistance);
2. effects on the environment (effect on non-target organisms, gene escape into the wild);

In addition, there are social/ethical concerns (e.g. ethics of GM, effect on developing countries, dominance of multinationals, increased intensification of agriculture).

In this paper, I will try to give a balanced view (although necessarily a personal one) of the pros and cons of GM. I won't pretend to be able to give a definitive answer, but I hope to provide a degree of perspective in which to put the facts, to help you distinguish fact from fiction and, in the end, to help you make an informed choice.

RISK ASSESSMENT OF GM CROPS

Everything in life can represent a risk. In the US each year, 400,000 people are injured by their bedding and 40,000 by toilets – are we to put government health warnings on duvets? The proponents of GM, of course, emphasise the potential benefits of GM crops, while the opponents emphasise the potential hazards.

In risk assessment, there are four main points:

1. What is the chance of the proposed hazard (in this case, some unexpected harm associated with GMs) happening?
2. Is the risk greater with GM crops than with non-GM crops?
3. If it did happen, how serious would be the consequences?
4. Are there any mitigating circumstances (principally, benefits) to weigh against the hazard?

We carry out risk assessments every day – crossing the road, for example: can I make it across the traffic in that gap between the cars or should I wait until the little green man appears? Cost –possibly being knocked over. Benefit - crossing the road sooner. We carry out the cost-benefit analysis automatically, and usually get it reasonable correct.

Often in the GM debate, scientists are portrayed as being irresponsible, as having a cavalier attitude towards the effect of GMs on the environment and on humans. The truth is quite different. Within two years of the generation of the first recombinant organism in 1970, one of the three scientists involved, Paul Berg, called for a moratorium on rDNA research until the risks had been assessed. Leading researchers in this area drew up strict safety guidelines for this type of research, and, at a meeting in Asilomar, in northern California, in 1975, they refused to carry out rDNA research until their recommendations were implemented.

The obvious question to ask of any new technology and its products (including GM crops) is: are they safe? Unfortunately, it is impossible to prove a negative (will GM crops constitute no risk?). Trying to convince members of the public of the benign nature of GM crops is made more difficult by the training of scientists. When asked if something can happen, a scientist will talk in terms of probability: "It is highly unlikely…The chances are vanishingly small…." These are acceptable assessments in scientific terms, but, to the public, even if something is unlikely to happen, the converse means that it **can** happen. When this is put against the comment from opponents of GM, that the threat is a racing certainty, then the public feel that both sides are saying more or less the same thing (that GMs constitute a risk), when, actually, they are not saying the same at all. Trials can be carried out to answer a specific risk assessment question (e.g. do GM crops contain higher levels of natural plant toxins than non-GM varieties?), but not to determine whether GM plants are safe for human health and/or for the environment.

Opponents of GM foods propose the application of the Precautionary Principle to the introduction of GM crops; that GM crops should not be grown if it cannot be proved that they are safe. This certainly sounds like common sense but, as I said earlier, it is impossible to prove a negative point such as: are GM crops safe? If the Precautionary Principle were to be applied to other developments, I doubt if any would be allowed to operate. Organic farming, for example, would fail the most stringent interpretation of the Precautionary Principle which is being applied by some sectors to the GM question. Two of the characteristics of organically produced crops highlighted by their proponents, are that they are more disease resistant and better tasting than their conventionally produced counterparts. This is largely because the slow supply of nitrogen to organic crops from organic nutrient sources such as manures, compared to the rapid supply from artificial fertilisers, results in higher levels of production of natural plant chemicals grouped under the heading “secondary plant metabolites”, which are responsible for traits such as colour, flavour, scent and defence. Unfortunately, many secondary plant metabolites (particularly the defence chemicals intended to ward off potential herbivores) have negative side effects on humans, such as the defence chemical solanine present in potato tubers, which causes damage to the human digestive and central nervous systems. Elevated levels of solanine are the reason for avoiding green potato tubers, but solanine levels in organic tubers are also higher than in conventionally grown potatoes. Furthermore, the greater emphasis on manures in organic farming increases the risk of contamination (internal as well as external) of organic produce, particularly important in plant products, such as salad material, consumed raw. In 1996, the US Center for Disease Control in Atlanta reported that one-third of all reported cases of the serious food poisoning organism *E.coli* 0157 were associated with organic produce, although such produce represented only 1% of food consumed in the US. Do these observations mean that organic food is dangerous? As a scientist, I would say almost certainly that it is not. Clearly, a balanced cost-benefit approach is necessary when applying the Precautionary Principle to either organic (benefits include no pesticide residues, beneficial effects on biodiversity) or GM crops; the Rio Declaration on the Environment (1992) stated that a lack of full scientific certainty should not be used as a reason for postponing the introduction of cost-effective measures.

GM AND HUMAN HEALTH

The concerns of the consumer about the effects of eating GM food fall, broadly speaking, into three main categories:

1. the effect of GM on levels of natural toxins already present in non-GM varieties of the crop;
2. the possible introduction into GM food of novel allergens and toxins;
3. the transfer of GM genes (particularly those for antibiotic resistance) from GM food (via digestion products) to human cells or to natural gut bacteria (horizontal gene transfer).

Natural Toxins

GM foods are the most closely regulated of all foods. Products from GM plants are checked for levels of natural toxins (such as solanine) present normally in crop plants to ensure that the genetic transformation has not resulted in an inadvertent increase. Such checks are not carried out on conventionally bred crop varieties and there have been cases where such varieties have had to be taken off the market after elevated levels of toxins were discovered, e.g. solanine in the potato variety Magnum Bonum and psoralens (causing UV-sensitivity of the skin) in a disease-resistant celery variety.

Novel Toxins and Allergens

Any novel protein encoded by the transgene is assessed for potential toxicity, using techniques which can include short-term animal feeding trials Although this is more than is done for conventionally bred varieties, no allowance is made for specific effects on humans nor for long-term exposure. There is no direct testing for novel allergens in GM (nor non-GM) crops. Nearly all allergens are proteins, but most ingested proteins are rapidly degraded in the acidic contents of the human stomach, eliminating the risk of allergenicity. Furthermore, because almost all allergens have characteristic features of their structure or chemistry, proteins encoded by the transgene in GMs are screened for evidence of such characteristics. Interestingly, when direct allergenicity testing was carried out on Bt products, the Bt toxin in GM plants was shown to be non-allergenic, unlike the preparation used by organic growers which contains the pro-toxin plus bacterial cells, the latter causing allergic responses. One aspect of allergen testing which is not included in GM evaluation but which deserves greater attention with regard to both GM and non-GM crops is the risk of inhaled allergens, e.g. in the form of pollen.

In addition to the direct effects of the novel protein encoded by each transgene, more attention needs to be given to the possibility of unexpected side-effects of transgene incorporation into a crop plant. But, if the GM process is so precise and specific, why would there be concerns about "unexpected" effects? The process of gene insertion into the plant is less precise and controlled than the proponents of GM crops would care to admit. The number of copies of the transgene inserted into a plant cell and the location of the site of insertion of the transgene into the plant chromosome, both of which could affect the expression and possible side effects of the gene, are not well regulated. The trialling procedures for GM crops by the companies are designed to identify such side effects of gene transfer, but it is possible that some could be over-looked. Secondly, unexpected negative side effects could also occur as the result of the end result of genetic manipulation (GM and non-GM); for example, the GM tomato paste sold in Sainsbury's would probably provide lower levels of the natural anti-oxidants (valuable in protecting the body against cell damage which can lead to cancer) in tomato, such as lycopene, because the high pectin would reduce the bioavailability of these chemicals in the human diet.

Food labelling legislation for GM foods currently only covers material which includes DNA and/or protein from the GM organism, though there are plans to broaden this to include other materials. Refined sugar from GM sugarbeet or oil from GM soyabean or oilseed rape would not need to be labelled under the existing regulations because of the absence of DNA and protein, although genes work by affecting chemical products as well, which may be toxic. Most vegetarian cheese is produced by using GM rennet (produced in bacteria containing the rennet gene from cows rather than the rennet enzyme from calves' stomachs) but does not need to be labelled as GM because the cheese does not contain the gene for rennet nor the GM rennet itself. Material containing less than 1% (by weight) GM DNA does not need to be labelled as containing GM; similar limits operate with respect to organic produce, where a maximum of 1% contamination with non-organic material is acceptable.

Ironically, GM material, which has not been proven to damage human health, is subject to mandatory labelling, whereas other products containing known toxins, carcinogens, etc., such as caffeine in coffee, are not.

Horizontal gene transfer

Another fear from anti-GM groups is the transfer of genes from the GM food to cells of bacteria living within our gut, a possible example of horizontal gene transfer (HGT); HGT involves transfer of genes other than by sexual means. Whereas HGT has been shown to be a natural if very rare event in evolution, transferring genes, say from infectious microbial pathogens to their plant hosts, its significance as a potential risk in GM foods has brought HGT to a much wider public. It must be kept in context, however; nearly all our food contains DNA from plants, animals, bacteria or fungi (we each eat approximately 10 mg of foreign DNA per day!), and there is very little evidence, over the past few hundreds of thousands of years, that it has had any effect at all on the genetics of ourselves or our gut bacteria.

The principal concern for GM-specific HGT, however, is the risk of transfer of antibiotic resistance genes from GM material to our gut bacteria, reducing the effectiveness of clinical antibiotics. But how did antibiotic resistance genes get into GM food in the first place? Earlier on, I mentioned that two genes are transferred into a GM plant: the target gene and a marker gene. The marker gene is used because the gene transfer method is so inefficient. Antibiotic resistance was used because at high levels certain antibiotics, such as kanamycin, are toxic to plant cells; by including a kanamycin resistance marker gene plus the target gene, the scientist can add kanamycin to the plant cells after the transformation process; the only cells which will survive are those containing the marker gene, which is piggybacked onto the target gene, so the survivors will also contain the target gene. Unfortunately, the choice of antibiotic resistance as the marker gene showed very poor judgement. The antibiotic resistance gene can now be eliminated from GM plants and the next generation of GMs will carry different marker genes.

From a PR point of view, the use of antibiotic resistance was a bad mistake. From a safety point of view, the risk is very small. Nearly all DNA in food is quickly destroyed in the acid conditions in the human stomach, and studies showed that the traces which survived were not taken up by gut bacteria; on the other hand, much larger amounts of food DNA survived passage into the gut in people who had had their stomach removed surgically, and there was evidence that antibiotic resistance marker genes from GM food had been incorporated into their bacteria in their large intestines. Because of the over-use of kanamycin in the past, kanamycin resistance is a common characteristic (arising as a result of natural mutation) in all bacteria, and we each naturally contain billions of kanamycin-resistant bacteria (each containing the same piece of DNA as in GM food) in our guts. Furthermore, we each eat approximately 1 million naturally kanamycin resistant bacteria per day, more in the summer when salads are more plentiful. If kanamycin resistance can transfer from food into our gut bacteria, it would have happened long ago and would not need GM foods.

GM and the Environment

The principal concerns about GM crops and the environment are as follows:

1. GM crops (especially herbicide resistant crops) could become pests in the wild or as weeds in crops;
2. genes from GM crops could be transferred to wild plants by cross-pollination
3. GMs could have a detrimental effect on non-target organisms, reducing biodiversity.

GM Crops as Pests

Most crops have been domesticated for so long that they would no longer be able to survive in the wild (for example wheat, where non-shattering of the ripe ear would prevent seed dispersal), so the risk of GM variants with an additional trait developing into dominant plants in the wild, disturbing the balance of the ecosystem, is generally very low. The only exception would be for recently domesticated crops, such as oilseed rape, which have retained sufficient wild traits to survive, as evidenced by feral populations of oilseed rape which have developed along roadside verges in the UK after seed spills from lorries. Even so, the risk is small compared to that associated with garden plants introduced into Ireland, from wild areas of other countries. Such alien introductions hold much greater risks because the plants are adapted to the wild and are often not regulated by pests and pathogens in their new environment, unlike the situation in their natural habitat. In Ireland, serious weeds introduced as garden plants include Japanese knotweed, giant rhubarb, giant hogweed and rhododendron, while wild plants which have become serious weeds when introduced from Europe include purple loosestrife and ivy in the US.

In crop situations, seed shed from herbicide-resistant GM crops could germinate and cause a problem in subsequent crops of other crops. These “volunteers” would be susceptible to and hence controllable by other herbicides but problems could develop for farmers. In Canada, cross-pollination between two different GM herbicide resistant oilseed rape varieties has resulted in weed populations resistant to both RoundUp and Liberty herbicides, causing problems of weed control.

Gene Transfer

Gene transfer by cross pollination between closely related species is known as vertical gene transfer, as opposed to horizontal gene transfer mentioned earlier. Concerns have been raised regarding the transfer of, say, insect resistance from a GM crop to a wild plant, and the consequences on the natural ecosystem. At the start of the GM debate, many scientists considered the probability of such events to be negligible, but recent studies have shown that the frequency of such transfers can be quite high.

For cross pollination between GM and wild plants to be an environmental hazard, two requirements would need to be met; the hybrid would need to be fertile and would need to be viable. The crop and the wild plant would need to be different but related species to have a chance of producing fertile offspring; the concept of “species” is that sexual gene transfer should not be possible between different species, but it is known that this can occur, but only between very close relatives. Very few of the crops grown in Europe evolved here; as a consequence, for most crops in Europe, the risks of cross-pollination with wild relatives is non-existent. For potato, for example, which evolved in the region around Bolivia and Peru, although wild relatives, e.g. the woody, black and deadly nightshades, exist, they would not produce hybrids with cultivated potato. The only exceptions to this general rule are the European crops, the brassicas and sugarbeet. Of the brassicas, only oilseed rape (and mustard, grown to a very limited extent) are allowed to flower and hence risk cross pollination, and viable hybrid populations between GM oilseed rape with several wild species, including wild cabbage, wild turnip and charlock have been reported. Sugarbeet could cross with sea beet. Whether the hybrids would survive is open to debate; the presence of domesticated traits in the GM crop could reduce the fitness of the hybrids, although the relatively undomesticated nature of oilseed rape could make hybrids with this crop relatively fit.

The risk of cross pollination between GM crops and wild relatives, therefore, depends on the country and differs between different crops. In Europe, oilseed rape appears to be in a unique position of risk, being both native and relatively undomesticated. In developing countries, where most of the major crops evolved, however, the risk of hybridisation between GM crops and wild crop relatives would be greater and could involve a larger number of crops, for which wild relatives exist. A recent development could prevent all risk of gene escape by cross-pollination. Most genes in a plant are in the nucleus of each cell, but a small number are also found in cells within the tiny organelles called chloroplasts where photosynthesis takes place. The advantage of targeting the transgene into the chloroplast is that the gene transfer of chloroplast genes does not occur during pollination, unlike the situation with nuclear genes.

It is important again to put the risks in perspective. Conventionally bred (i.e. non-GM) oilseed rape varieties would also have cross-pollinated with wild brassicas and transferred potentially useful characters, such as disease resistance. To date, no effect on the wild populations has been reported, supporting the hypothesis that single genes would have little effect on the adaptive fitness of a plant in the wild. On the other hand, cross pollination between cultivated and wild species can cause problems, for GM or non-GM crops. In parts of Canada, it has now become impossible to grow conventional rye crops because cross pollination between cultivated rye and a local weedy relative (wild rye) has produced populations of the weed species which are impossible to control by herbicides in the presence of the cultivated rye crop.

One area where cross pollination involving GM crops will cause potentially serious problems is in the area of organic crops. Cross pollination of an organic crop of, say, maize by a GM maize crop could result in the organic crop losing its organic certification. For naturally cross pollinated crops, much wider separation distances (at least 400 m) are necessary than previously thought to prevent such cross pollination. Fortunately, most organic crops in Europe harvested for seed are self pollinated (e.g. wheat, barley) and would not suffer this problem; maize is probably the only organic crop in this country under such risk.

Effects on Biodiversity

The two principal classes of GM crop (herbicide resistance and insect resistant) have been accused of reducing biodiversity in crops already low in wildlife as a result of intensive agriculture. The use of crop applications of glyphosate could eliminate all weeds from the crop, removing food plants for insects and subsequently food for insectivorous birds, while there have been reports that the Bt protein in insect resistant GM crops can damage insects other than the target organisms, crop-eating caterpillars.

The elimination of all weeds would have a detrimental effect on the natural biodiversity of the agroecosystem, but would also have a negative effect on the crop. In sugarbeet crops, for example, generalist herbivorous insects, feeding on many different plant species, feed on both weed and sugarbeet seedlings. When glyphosate was applied soon after sugarbeet seedling germination, it was found that insect damage to the growing sugarbeet crop increased, because the insects had only the sugarbeet on which to feed. Delaying application of the herbicide achieved greater survival of the sugarbeet seedlings, and increased biodiversity of insect and birdlife; the advantage of glyphosate on resistant crops is that the herbicide can be applied at any time and still control the weeds. GM crops could be incorporated into environmentally sustainable farming methods if suitable incentives for farmers, e.g. under an improved REPS scheme, were available.

There have been a number of reports suggesting that Bt GM crops reduce the populations of insects other than the targets, herbivorous insect pests. Most of these were due to errors in the experimental design; e.g. detrimental effects on beneficial insects such as lacewings fed on aphids from insect resistant crops were due to the poor nutritional quality of the aphids (after feeding on resistant plants) rather than to toxic effects of the GM gene on the beneficial insects. In one example, however, caterpillars of the monarch butterfly (a non-pest species) feeding on milkweed on which pollen from Bt maize had been dusted showed reduced survival. The point made was that the milkweed, the only food plant of the monarch, grows around maize fields so that Bt maize would cause a reduction in the monarch population. Even if this were a risk, the effect would be similar to that when Bt was applied by organic farmers and much less than when broad-spectrum insecticides were used. This is not to say that GM crops pose no potential threat to the environment. Unlike the natural protoxin found in the Bt bacteria used in organic farming, the toxin present in GM crops is not readily degraded in the soil (e.g. after decay of leaf tissue from GM plants); the consequence of this phenomenon is not known.

Potential Benefits of GM Crops

The vast majority of GM crops being developed are generated by multinational Life Science companies. As a consequence, the principal aim of GM varieties (as with conventionally bred varieties) is to maximise the profit for the company. In itself, this should not be a problem in a capitalist society, although the use of legal contracts preventing farmers from sowing farm-saved seed of GM crops (and the potential, but not realised biological barriers to keeping farm-saved seed, such as the Monsanto Terminator gene, which meant that seed of the next generation would not germinate) caused further outrage. Farm-saved seed in most developed countries is used as a way of reducing costs, whereas, in developing countries, it is also used as a way of developing locally adapted varieties.

Despite the financial goals of the companies, the first generation of GM crops (aimed primarily at the farmer, in terms of herbicide-and insect-resistant varieties) also had an element (deliberate or incidental) of improved environmental sustainability. Although toxic to all plants, glyphosate is not toxic towards non-target organisms such as insects, birds and mammals, including humans. Furthermore, it binds rapidly to soil particles and is degraded, meaning that there are no soil residues and no contamination of groundwater. In these terms, glyphosate is more environmentally protective than conventional herbicides. The development of RoundUp Ready GM varieties also opens up the use of glyphosate in reduced-tillage and no-till agriculture, designed to reduce soil erosion by wind and rain. In conventional agriculture, the stubble residue of the previous crop is usually ploughed in before the next crop is sown in order to destroy pathogens and weed seeds; the alternative of stubble burning has been largely banned. But deep ploughing leaves the soil surface exposed for several months, and, especially with the open-plan prairie–style farms of the US, China, the Ukraine and parts of France, rain and particularly wind act to remove vast quantities of topsoil by erosion. By sowing the next crop into slits cut into the residue of the previous crop (reduced tillage), the soil surface is not exposed, but weed and pathogens are not controlled. To eliminate the weeds, a broad-spectrum herbicide with a resistant crop should be used; the RoundUp Ready GM variety/glyphosate combination would be ideal for this situation.

With the Bt insect-resistant varieties, the farmer can dispense with the insecticides previously used to control caterpillar pests, although other sprays will be needed to control other pests as before. As the insecticides are less specific than Bt (even caterpillar-specific insecticides would kill caterpillars which did not feed on the crop, unlike the Bt varieties), the cultivation of Bt varieties would increase the biodiversity within the crop. One of the criticisms of the use of Bt in GM crops is that pests will develop resistance to the Bt over time (by selection for natural Bt-resistant mutants of the pest), resulting in ineffectiveness of Bt not only for GM but also for organic farmers. This is likely, as with most single-gene resistant varieties, GM or non-GM, but, ironically, the only well-documented field case of Bt-resistance in a pest population is in the diamond-back moth, as a result of Bt over-use by organic growers.

In addition to potential environmental benefits, the GM crops benefit the farmer by reducing the number of pesticide applications necessary (saving the costs of chemicals, diesel and labour), and reducing crop losses due to insect damage, for example. The commercial benefits to farmers have varied; in some areas of the southern US, RoundUp Ready soyabean was unsuccessful. Such negativeinteractions between variety performance and environment are meant to be eliminated during the trials process before a new variety (GM or conventional) is released, although this does not always happen. In the 1980s, a conventionally bred winter wheat variety, Moulin, outperformed all other varieties until one year when a cold wet May affected pollen formation, resulting in drastically lower grain yields. Overall, the continued high proportion of crops grown to GM crops indicates a commercial success for the farmers, although the EU embargo has encouraged many US farmers to grow non-GM crops to supply the European market

The next generation of GM varieties will exhibit traits aimed to benefit the consumer rather than the producer, such as high-starch potatoes (which absorb less fat during frying), and sugarbeet suitable for diet-conscious consumers (with the fattening sucrose replaced by fructans). In addition, new products such as biodegradable PHA plastics (by cloning a gene from a bacterium, *Ralstonia*, into maize) will be available.

GM and Developing Countries

Some of the early Monsanto promotional literature focused on the potential of GM varieties to prevent world hunger; this was rightly dismissed as gross exaggeration. Most famines have been more to do with an inability of poor people to access, buy or grow sufficient food rather than with a shortage of food *per se,* but there are situations where genetically improved crops (not necessarily GM) could dramatically improve food security and improve health conditions in developing countries, such as the development of crop varieties able to tolerate stresses such as heat, drought and salinity.

Although the Bt GM crops were developed with the farmers in developed countries in mind, an interesting recent development has been the discovery that yield improvements resulting from the cultivation of such crops were highest in developing countries, where insecticides are too expensive for most farmers. The high cost of GM seed (mirroring the negative effects of high-input agriculture of the first Green Revolution in the 1960s) and the legal obligation not to sow farm-saved seed would appear to prevent the widespread uptake of commercial GM crops in developing countries. Some of the GM companies are entering into agreements with developing countries; whether these will prove to be beneficial to the countries in question remains to be seen.

On the other hand, there are quality traits of value to developing countries which can be introduced into crops only by GM techniques. Many health problems in these countries are readily treatable but high cost can prevent widespread adoption of these treatments. Vaccination against diseases such as hepatitis B and cholera, in which part of a protein of the infectious agent is injected into the patient to elicit an immune response, is of limited use in many countries because of the need for refrigeration and for skilled medical personnel. To overcome this, edible vaccines have been developed by cloning the DNA sequence for the protein into banana, so that the transgenic fruit acts as the vaccine; consumption of a banana will vaccinate a child.

In south-east Asia, insufficient vitamin A in the diet (based primarily on rice which lacks the vitamin A precursor, beta-carotene) causes blindness (120 million at risk) and even death (1-2 million children per year). A publicly-funded research programme based in Switzerland has introduced three genes (one from daffodil, two from bacteria) into rice so that the GM rice synthesises beta-carotene ("golden rice"). This GM rice, when fully developed, would not solve the problem of vitamin A deficiency but could contribute to an improved diet and future for many millions.

On the other hand, the developing countries are also at risk from certain GM developments, such as import substitution; for example, there have been proposals to use GM technology to generate a cocoa butter-like oil from linseed which can be grown in western Europe, instead of importing cocoa butter from developing countries.

Conclusions

The general public consensus regarding GMs in the EU is that there should be a ban on the cultivation of GM crops and importation of GM food into the EU. There has been a 5-year moratorium, but signs are that, under pressure from the WTO, EU governments are accepting applications to grow GM crops from 2004. Is this right?

Medicine, particularly in the supply of human proteins which are deficient or defective in certain genetic diseases, already depends heavily on GM products, e.g. clotting factor VIII for the treatment of haemophilia, insulin/diabetes, plasminogen activator/strokes, dornase alpha/cystic fibrosis. Here, though, there are clear benefits for the use of GM products and the GM organisms are constrained in laboratories. For GM crops, the benefits are less clear, while the release into the environment of the GM organisms opens up new avenues of concern.

Part of the problem in making a personal decision is the difficulty in finding objective information. The GM countries and some governments have clear vested interests, but so do many of the environmental movement; sales of organic food have been stimulated by the GM debate.

Are GM crops vital for our well being in Ireland? Probably not. Can they be used to improve the quality of life. Possibly. Is there a serious risk of damage if GM crops are introduced into Ireland?

In my opinion, decisions should be made on a case-by-case basis, as the current regulations allow, rather than by a blanket acceptance/rejection of GM technology ***per se***; we need to evaluate each product, not the technology which produced it. What is the rationale behind permitting the cultivation and sale of potatoes bred conventionally and incorporating insect resistance genes from wild potato species while banning insect-resistant Bt GM potatoes, or allowing the importation into the EU of rapeseed oil from Australia but not Canada, because the former is from conventional varieties, and the latter from GM varieties? With a case-by-case assessment in Ireland, GM varieties of non-food crops (e.g. flax) or of crops where there are no close relatives in the country (e.g. potato), would be more likely to be acceptable, in contrast to GM varieties of oilseed rape. GM crops have fallen foul of a public increasingly wary of multinationals, monopoly and globalisation, yet this is surely not a good reason for banning a technology with such potential.

(This lecture was delivered at the UCC Science Faculty Public Lecture Series 2002-2003, on November 14, 2002.)