Transgenic plants and biosafety: science, misconceptions, and public perceptions

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C. Neal Stewart, Jr[+]
Harold A. Richards, IV[*]
Matthew D. Halfhill[+]

[+]Department of Biology
[*]Department of Nutrition
University of North Carolina-Greensboro

Address correspondence to Neal Stewart
nstewart@uncg.edu
336 334 4980
Department of Biology
University of North Carolina
Greensboro, NC 27402-6174

ABSTRACT

One usually thinks of plant biology as a non-controversial topic, but the concerns raised over the biosafety of genetically modified (GM) plants have reached disproportionate levels relative to the actual risks. While the technology of changing the genome of plants has been gradually refined and increasingly implemented, the commercialization of GM crops has exploded. Concerns of ecological and food biosafety have escalated beyond scientific rationality. While several risks associated with GM crops and foods have been identified, the popular press, spurred by colorful protest groups, has left the general public with a sense of imminent danger. An estimated 2.5×10^{12} transgenic plants have been grown in the US in the past 12 years, with over one trillion being grown in 1999 alone. These large numbers and the absence of any negative reports of compromised biosafety indicate that genetic modification by biotechnology poses no immediate risks and that resulting food products from GM crops are as safe as foods from conventional varieties. We are increasingly convinced that scientists have a duty to not only conduct objective research, but also effectively communicate the results especially pertaining to relative risks and potential benefits.

THE ANATOMY OF A CONTROVERSY

Until 1999, the controversy surrounding genetically modified (GM) crops existed obscurely among the fringe element of the environmental movement—at least in the USA. Until that time the production and commercialization of GM crops in the USA and other countries was quietly progressing to the point that close to half of soybean and cotton and over one-third of corn and canola in the USA was GM (Fig 1). Since 1992, the USDA has deregulated sixty transgenic crop varieties for commercial field release (APHIS Permits April 2000: http://www.isb.vt.edu/, Fig. 2). The adoption of GM varieties by farmers has taken place at record speed. During this period, academic and government scientists were actively performing experiments and publishing research on plant transformation and biosafety. The silence on all fronts was abruptly interrupted in 1998 by publicity surrounding scientific research findings. The first blow came when Armand Putztai, an immunologist in Scotland, appeared on UK television to announce that GM potatoes transgenic for snowdrop lectin were toxic to rats and compromised their immune systems. His television interview focused media attention on GM crops and was the catalyst for erupted furor in Europe against GM crops and food. By the time his study was published (11), the controversy had jumped the pond to the USA. In addition to the lectin study that concluded that the plant transformation process itself caused food to be toxic, a lightning rod paper from the USA was published in the British journal Nature in May 1999 (40). In this correspondence, the authors reported that pollen from corn transgenic with an insect resistance-coding gene from *Bacillus thuringienisis* (Bt) was hazardous to the Monarch butterfly. Subsequently, in various public forums environmental activists have dramatically reenacted the death of Monarchs as they approach an ear-of-corn that also happens to have on it a giant X. While on the surface such stunts can be viewed as sophomoric and inanely silly, the impact of agbiotech's detractors has been extensive. A near trade-war has been started between the EU and USA, companies such as Heinz and Gerber have banished ingredients from GM crops in their products, and Greenpeace has had a banner fund-raising year fueled by their "True Foods" campaign. However, the Monarch butterfly study did serve to point out that perhaps the risks to non-target insects had not been thoroughly studied prior to commercial release of transgenic plants. Perhaps there were other detrimental side-effects that would be observed during the lifetime of a transgenic product.

It can be argued that the distortion of science is at the root of the GM controversy, and even that scientists played an active role in its start and propagation. Research on the risks and benefits of biotechnology have not been clearly presented to the public in a manner that allows for informed conclusions to be drawn as to the value. The purpose of this paper is to review the science that underlies plant transformation and genetic modification, the ecology of transgenic plants, and the biosafety of GM food. Finally, we would like to offer some insights about the role of scientists in this controversy.

PLANT TRANSFORMATION

Plant tissue culture

Plant transformation generally relies on the introduction of plasmid constructs or segments of plasmid constructs into the genome of a plant cell. Entire transgenic plants must be regenerated from transformed cells, not a trivial task. Many plant cells are totipotent, i.e., they possess the ability to regenerate an entire plant from a single cell. However, tissue culture is slow, laborious, special skill-requiring, and has the propensity to cause mutations in the DNA within plant cells. Some crops such as soybean and sunflower have very difficult plant tissue culture systems. In addition, in a molecular breeding sense, premier varieties that have the most desirable innate

traits are seldom most amenable to tissue culture. That said, commercial GM crops have largely been produced using plant-transformation systems utilizing tissue culture. Therefore, we will briefly review the evolution of transformation technology and speculate on how innovations might impact the GM crop landscape.

Conventional transformation technologies

The first plants were transformed in the mid-1980s using *Agrobacterium*-mediated transformation (26). This method exploits the natural propensity of the crown gall disease-causing agent, *Agrobacterium tumefaciens*, to transfer genes into a plant genome. Many plant species such as tobacco and *Arabidopsis* can be routinely transformed using this method. Most crop plants are not amenable to *Agrobacterium* for routine transformation (19). In 1987 this problem was addressed by the invention of the gene gun, also known as microprojectile bombardment (31, 32). Microprojectile bombardment uses micrometer-sized particles coated with DNA that are accelerated to randomly pierce plant cells. The scope of the efficacy of this method is broader than that of *Agrobacterium*, but is less precise in its transgene integration patterns (12). Nearly all of the commercial transgenic plants in current existence and most of those that will be produced in the next few years will be all produced using *Agrobacterium*- or gene gun-mediated transformation of cells followed by regeneration using tissue culture.

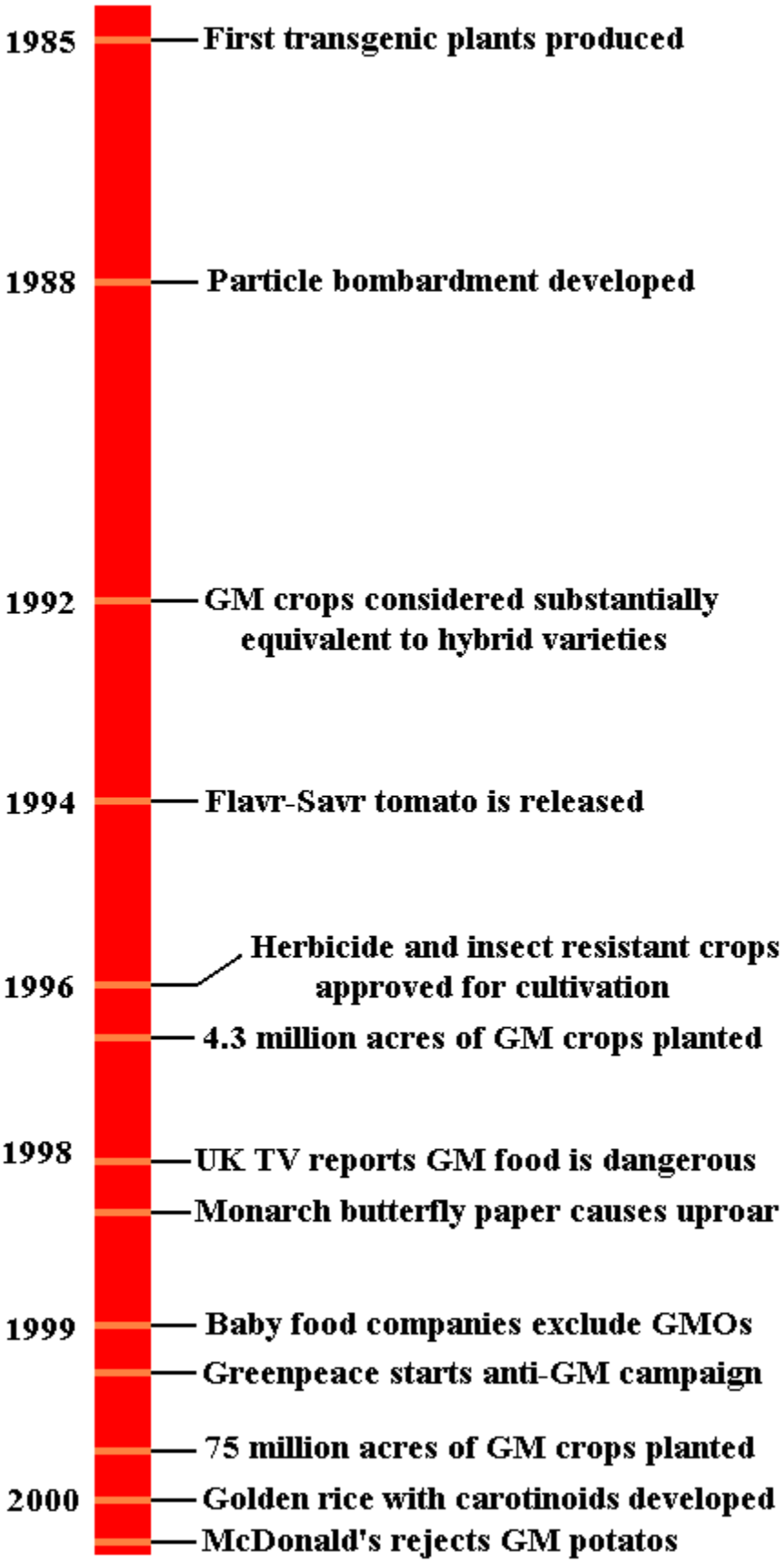
1985
First transgenic plants produced
1988
Particle bombardment developed
1992
GM crops considered substantially equivalent to hybrid varieties
1994
Flavr-Savr tomato is released
1996
Herbicide and insect resistant crops approved for cultivation
4.3 million acres of GM crops planted
1998
UK TV reports GM food is dangerous
Monarch butterfly paper causes uproar
1999
Baby food companies exclude GMOs
Greenpeace starts anti-GM campaign
75 million acres of GM crops planted
2000
Golden rice with carotinoids developed
McDonald's rejects GM potatos

Figure 1. Timeline of important events in the use of genetically modified crops.

New technologies for genetic modification

Tissue culture-free transformation

Beginning in the late 1980s successful experiments were performed to diminish the need for tissue culture in plant transformation. In one clever application, a novel gene gun was used to bombard genes into soybean seedling meristems (6, 42). After bombardment, the meristems were placed on cytokinin-containing medium to obtain multiple shoot formation. This method did not employ any selectable marker but stable transformation that was detected using the presence of beta-glucuronidase (GUS) in putatively transformed tissues. However, this system required destructive tissue sampling and an expensive substrate (X-GLUC) in order to detect gene expression and transgenic status (27).

Vacuum infiltration of *Arabidopsis* was developed as the first method to bypass tissue culture entirely (3). In this method developing floral meristems/flowers are placed in an *Agrobacterium* solution under vacuum and germ cells are transformed. The plant is grown out and allowed to set seed. Potentially, each new seed that is collected represents and independent transformant. This method has been used recently to produce large numbers of T-DNA insertion mutagenized *Arabidopsis* plants (34). More recently it has been demonstrated that the vacuum step is not necessary and that simply dipping flowers in *Agrobacterium* solution is sufficient to transform cells (7). While there have been attempts to use this methodology on other plants species, there are no published are no published successes to date.

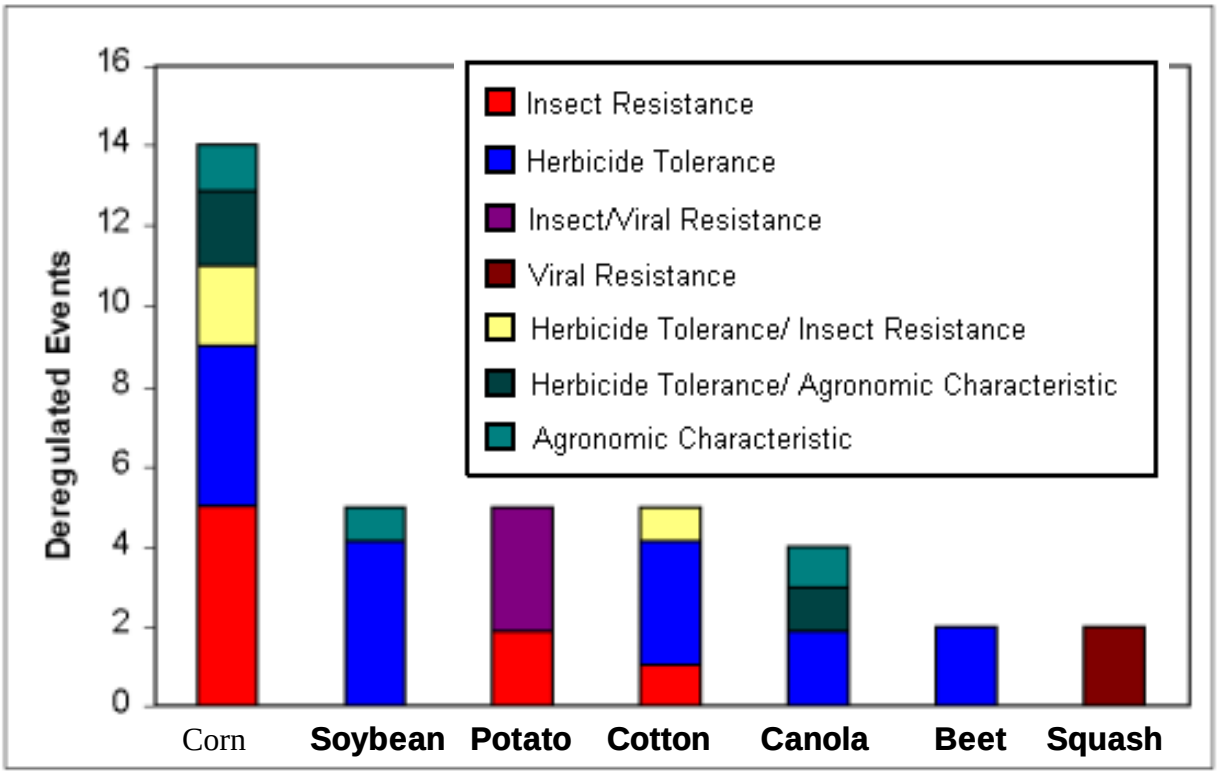

Figure 2. Deregulated transgenic events for crop species with two or more deregulated phenotypes (www.bio.vt.edu).

Visual selection

Once cells are transformed they are usually selected using antibiotics or herbicide, which kills untransformed cells (negative selection). Research has made strides toward developing positive selection systems. For example, cells transformed with a gene that allows them to metabolize mannose (28, 64) or to be more responsive to cytokinin (36) allow transformation to take place in the absence of antibiotic or herbicide resistance genes. Another approach would be selection based on a visible marker gene, such as the one encoding the green fluorescent protein (GFP). GFP has the unique characteristic of fluorescing green when exposed to UV or blue light. Transformed cells can be visibly selected on the basis of green fluorescence (Fig 3). Such an approach has had the added benefit of increasing the efficiency of transformation (15) and might aid in tissue culture-free transformation. For example, by using the meristem method described above in soybean, one might be able to process more samples and troubleshoot the methodology more rapidly. The ability to see, in real time, which cells and tissues are transformed could enable faster and more efficient transformation technologies to be developed.

Chimeraplasty

It is clear that plant transformation technologies have become more efficient and have enabled large number of transgenic plants to be produced, and the subsequent commercialization of a wide variety of transgenic crops. A technology called chimeraplasty has been developed that allows precise genetic modification to a plant without transformation. Point or frameshift mutations can be introduced using chimeric DNA/RNA (8). This approach has proven to be successful on tobacco and corn, but should hold great promise for making precise but small genomic changes in virtually any crop (4, 67). For example, chimeraplasty could be utilized to frameshift a gene coding for a known allergen in peanut or other allergen-ladened crop, and therefore halt its expression. Such a genetic modification would be both precise and substantial improvement in food safety, and could foreseeably only be accomplished using such a technique.

Improved methods to more precisely genetically modify plants such as transformation and chimeraplasty have great potential to accelerate the development of genetic modification. While some fear that technology is moving too quickly, scientists are just now beginning to understand precise genetic modification, and the results have been promising. Great strides have been made in better understanding how genes are integrated (19, 33, 50) and silenced (29, 41, 61, 63). Such knowledge will greatly assist in the precision and predictability of transgene expression in plants. Soon, the metabolic engineering of crops will be accomplished to make significant changes in crop output traits, such as altered physiology resulting in more nutritious food, alternative fuels, and facilitated pharmaceutical delivery. Such recent success has been the creation of “golden rice” rich in vitamin A (66). In the next twenty years we believe most row crops will be genetically modified, and perhaps nearly all non-wild plants will be genetically modified by the year 2100. The ubiquity of the technology does cause one to pause and consider the safety and risks of wide implementation of the technology.

ENVIRONMENTAL AND HEALTH BIOSAFETY

Risk assessment of agricultural and food technologies is not a new concept. Each innovation in food production has come with its own set of potential risks. These have ranged from increased pesticide exposure in conventional agriculture to higher pathogen exposure from organic farming. The risks associated with GM are similar to those of crop hybridization, the keystone of the first green revolution. Whereas hybridization leads to the transfer of thousands

of genes from one plant (often from different species) to another that leads to multiple effects, GM transfers one to a few genes, resulting in more predictable effects. Therefore, a priori, GM should result in fewer unintended risks. This, unfortunately, is not the message the general public receives.

Any attempt to create a better crop plant will be accompanied by potential consequences. Risk assessments of biotechnology do consider potential effects to environmental and human health. In general, these risk assessments have been an order of magnitude more stringent than for conventionally produced crops and food. Ecological concerns that are currently debated are increased invasiveness and volunteerism of the crop itself, intraspecific hybridization, interspecific hybridization, damage to non-target organisms, and resistance management. Food safety issues fall primarily into two categories: product toxicity and the introduction of novel antigens. The key is to determine the importance of thee risks as weighed against the benefits.

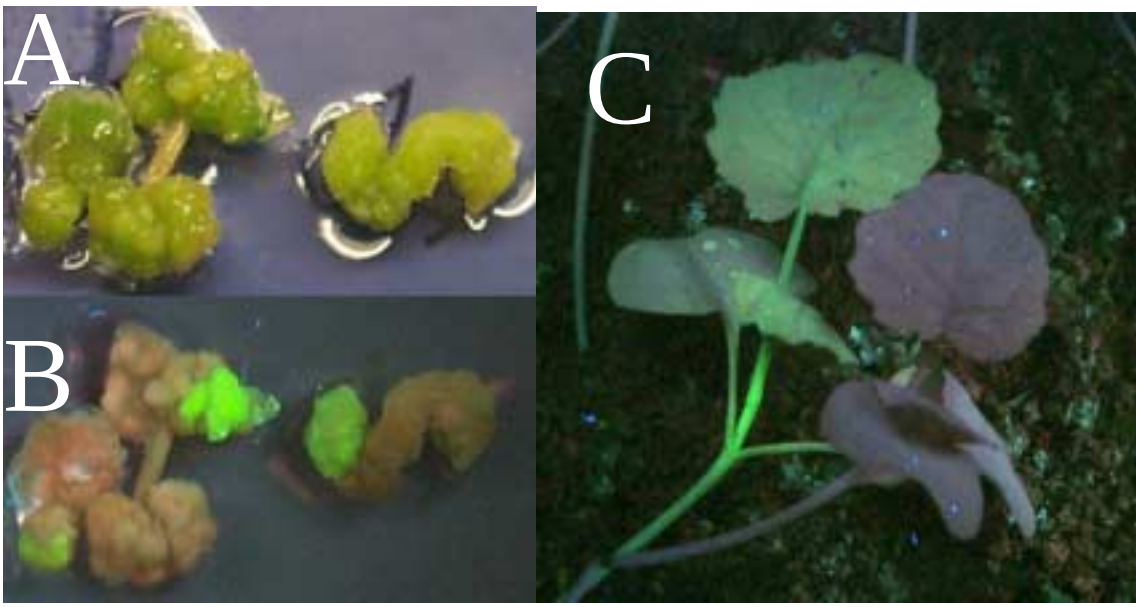

Figure 3. GFP selection of transgenic callus and GFP fluorescence of whole plants. (A) Canola hypocotyls five weeks post-incubation with *Agrobacterium tumefaciens* containing a GFP gene linked to a *Bacillus truringiensus* (Bt) gene under white light, and (B) the same canola sections under UV light. (C) GFP/Bt canola (left) and nontransformed canola (right) pictured under UV light.

ECOLOGICAL BIOSAFETY

Increased invasiveness and volunteerism of transgenic crops

As new genes are discovered and utilized by the biotechnology industry, crops will have suites of new abilities and will be grown in new geographic areas. In the case of crops such as alfalfa (*Medicago sativa*), canola (*Brassica napus and Brassica rapa*) sunflower (*Helianthus annuus*), and rice (*Oryza sativa*) that have some "weed-like" characteristics, some have argued that transgenic and novel traits contained could allow the crop itself to become weedier and invasive (51, 52). This would not be a problem in many crops that are highly domesticated and exotic to the regions in which they are grown, such as soybean and corn in the US and Canada, because they do not have the traits needed to allow survival outside agriculture (62). Volunteerism is an agriculture problem where uncollected seeds from the last year's crop

germinate and grow within the current crop. Canola has been genetically modified with at least three distinct herbicide resistance genes (two from transgenesis and one from mutagenesis), and volunteers of these varieties could become a particular nuisance to agriculture by requiring other herbicides for control (62). Special regulatory efforts have been applied to certain transgenic crops that have the potential for increased invasiveness and damaging volunteerism.

Intraspecific hybridization

Intraspecific hybridization could occur when transgenic crops are grown in close proximity to non-transgenic varieties. The agricultural practice of saving seed from the previous years harvest could allow transgenic material to be unintentionally persistent. Crops such as corn and other grain crops that are wind pollinated have a potential to pass genes to adjacent conspecifics independent of whether the crop is GM or a conventional variety. This is a particular problem for organic farmers, who ensure that their products are not genetically modified and could potentially suffer economic losses if transgenic material is found in their harvests. Fitness-enhancing genes could be dispersed within the same species with no hybridization barrier, which could lead to slightly higher numbers of GM individuals than are expected by regulatory agencies. Transgenic crops could rapidly accumulate fitness enhancing traits (transgene stacking) that could lead to new and potential unintended problems.

Interspecific hybridization and transgene persistence

Hybridization between closely related species can be a mode of transgene flow directly into wild populations (10, 51). Crop plants with weedy wild relatives are of particular concern. If expressed in the genetic background of a weed species, a transgene could increase the fitness of the weed in nature. In the worst-case, if perhaps unlikely scenario, the weed could become more invasive and competitive, and in a relatively short time cause damage to natural ecosystems.

Interspecific hybridization depends on several circumstances to allow gene flow between related species. The crop must have some naturally occurring wild relatives growing near cultivation. Crops such as corn and soybean have no relatives in the US and Canada; therefore, they represent no risk of interspecific gene flow. Alfalfa, *Brassica* crops, and rice are examples of crop species that do have wild relatives near cultivation (51, 62), and these species complexes should be the focus future gene flow studies. The two species must share a degree of sexual compatibility, and distantly related species sometimes share enough genome homology to produce viable progeny (54). The species must occur sympatrically, or at close enough distances to allow the transfer of viable pollen. Flowering time must occur concurrently, in order for the two species to be fertile at similar periods throughout the year. Many weeds have complex patterns of dormancy, asynchronous germination, and germination signaling that have been lost in crops by artificial selection (1, 39).

The variable homology of the genomes between related species leads to a wide range of possibilities for the rate of introgression of a transgene, or any other gene, after the F_1 hybrid generation. Meiotic abnormalities caused by the distant relation between parental genomes can lead to decreased rates of introgression into new genotypes (30, 54). Chromosomes can be lost or disrupted due to unequal pairing at metaphase, which results in higher rates of infertility and decreased rates of seed production. Recombination, an important process in the incorporation of foreign DNA, is diminished in the unstable chromosome configurations of hybrids from distant relatives. In contrast, hybrids produced by closely related species have been shown to combine

fitness indices (seed production, pollen fertility, biomass, etc) that parallel the parental species (22, 23, 44). In this situation, the hybridization barrier between these species can be very low, and the introgression of a transgene is likely. The reproductive fitness of interspecific hybrids affects the ability of a transgene to be lost in the genetic background of a wild relative.

The possibility for increased fitness of transgenic hybrids and backcrosses depends on the nature of the transgene and the environment (10). For example, weeds containing a transgene that confers resistance to an herbicide would be a nuisance to agriculture, but would have little affect in a non-agricultural environment where the herbicide is absent. In contrast, an insecticidal *Bacillus thuringiensis* (Bt) transgene in a weed host could alter natural ecology by giving transgenic weeds a selective advantage as the result of natural insect pressure (58) if that specific insect was critical to limiting the survival of the weed. Transgenes that provide fitness enhancing characteristics under natural conditions have the greatest potential to disrupt the balance of established ecosystems. How much weed fitness increase from transgenes should be tolerated? Ellstrand et al (10) have suggested a threshold of 5% fitness increase for practical purposes, at which point they propose that significant economic results might occur that may outweigh potential benefits from the transgenic crop.

Transgenic interspecific hybrids have been produced involving transgenic canola modified with herbicide resistance genes with wild *B. rapa* (44, 45). After one backcross generation, many of the progeny were morphologically and cytologically similar to the *B. rapa* parent (44). After successive backcrosses into the weedy parent, it was found that, as expected, up to 50% of the subsequent BC3 and BC4 hybrids had resistance to the herbicide (44). This illustrates that a transgene can be passed between species and expressed in successive generations.

Effects to non-target organisms

Transgenic crops that express insecticidal transgenes to control agricultural pests may also affect non-target organisms (24, 40, 53). Three studies using corn transformed with a *Bacillus thuringiensis* (Bt) insecticidal transgene have generated evidence of possible non-target effects. Lacewings (*Chrystoperla carnea*), an insect predator, suffered from higher mortality rates by feeding on European corn borers (*Ostrinia nubilalis*) reared on Bt corn compared to corn borers raised on isogenic (non Bt producing) plants (24). Monarch butterfly larvae (*Danaus plexippus*) that consumed milkweed (*Asclepias curassavica*) leaves dusted with Bt containing corn pollen had decreased feeding, growth, and survival rates compared to larvae that consumed leaves with non-transgenic corn pollen (40). The authors concluded that Bt corn posed a danger to non-target monarch populations that feed on milkweed near Bt cornfields. Several independent authors have questioned the validity of this paper by arguing that the methods of the study were non-reproducible, the "non-choice" based feeding strategy for the larvae was inappropriate, and that the levels of pollen used were artificially high (5, 25, 46). More recently field experiments have shown that Bt corn have no effects on swallowtail butterflies (65). Genetically modified Bt corn was shown to exude active Bt toxin from the roots that could potentially accumulate in the soil (53). In this experiment, transgenic corn was grown in an agar medium, and protein was extracted from the medium and fed to tobacco hornworm (*Manduca sexta*) larvae. These larvae suffered higher mortality rates than larvae that fed on non-Bt corn protein extracts. However, using more realistic conditions with soil, others have shown rapid degradation of plant-expressed Bt proteins that were comparable to the rate of degradation of Bt proteins in microbial products (48, 49, 57). Clearly there will be a need to further analyze

possible non-target effects caused by genetically modified crops. However, such research needs to be placed in the context relevant to current practices in agricultural systems.

Possible deleterious side effects, must be weighed against the positive effects of an insect control regime that utilizes insecticidal transgenic plants. The decreased use of broad-spectrum insecticides benefits both human and non-target insect populations. For example, Bt cotton requires three or fewer insecticide treatments per year. This is a dramatic reduction compared to the 5-12 insecticide sprays needed to control pests in non-transgenic cotton fields (56). It has been recently reported that growing Bt cotton reduced pesticide use by over 900,000 kg during 1997 (16). The overall reduction of pesticides results in more profits to the farmer and the decrease of chemicals added to the environment. Insect biodiversity could also be enhanced by the reduction of broad-spectrum insecticides, and would allow natural predator versus prey interactions to occur enhancing pest control. Insect behavior studies utilizing "choice" feeding experiments have shown that a parasitic wasp (*Cotesia plutellae*) preferentially selected canola leaves damaged by Bt-resistant diamondback moth (*Plutella zylostella*) (55). The parasitic wasp experienced no reduction of reproductive success as the result of Bt toxicity when it attacked Bt resistant larvae, and could help constrain the spread of Bt resistant pests through natural predation. Using fewer insecticides in a pest control regime utilizing transgenic crops demonstrates many advantages to the environment and to farm worker safety.

Resistance management

Resistance to transgenic proteins by insect pests could limit the duration that an insecticidal transgenic variety can be feasibly grown. The diamondback moth, an important pest to *Brassica* crops worldwide, was the first documented pest to develop resistance to Bt toxins, applied as microbial formulations, in open-field populations (59). Recently, Bt resistance has been documented to have arisen in at least two independent recessive loci with different modes of action (60). To this point, no dominantly inherited Bt resistance genes have been documented, but this finding would severely limit the effectiveness of future Bt crops. Various resistance management strategies have been proposed to delay the onset of resistance, and the method commonly used is the deployment of a high expressing transgenic event coupled with a nontransgenic refuge (56). The refuge allows Bt susceptible pests to survive on the nontransgenic material and mate with Bt resistant individuals. The goal of this strategy is to keep the recessive Bt resistance genes at low levels in the target populations, and thus limit the rate that the entire population will acquire Bt resistance. The effectiveness of this strategy depends on the refuge size, refuge design (mixed with transgenics or separate), rate of spraying the refuge with pesticides, and the rate of migration of insect pests (56). These factors must be analyzed to ensure that acquired resistance will not limit the use of this potentially beneficial technology.

FOOD BIOSAFETY

Toxicity

Any compound entering the food supply is subject to specific scrutiny for food safety. For example, a potentially toxic transgenic product, such as Bt toxin, must pass the same standards for safety that are applied to any biochemical pesticide products. Exceptions for this type of testing occurs when the gene product expressed in transgenic plants are substantially equivalent to an existing compound in the food supply. Examples of this would include expression of normal dietary products like vitamins A and E. However, these would have to be

tested for bioavailability and for any unexpected effects that could have occurred during the transformation process; e.g., to assess for substantial equivalence to conventional crop varieties.

Testing for toxicity of food becomes necessary when a plant is overproducing innate compounds or when the transgene product has a known level of toxicity. An example of one of these gene products that would require testing are plant pathogenesis-related proteins (13). This class of proteins is desirable for overexpression because they typically result in one or more forms of pest or disease resistance. However, because these compounds are natural antibiological agents, tests are needed to demonstrate safety for human consumption. Tests for toxicity must also be conducted for proteins that are not found in the human diet. Green fluorescent protein (GFP) has a number of potential uses, from transgene tracking to stress indication (37), but for these applications to be realized, GFP will enter the food supply, requiring that its potential toxicity be determined (Fig. 3).

Some scientists have argued that protein products are not the only potential source of toxicity in transgenic plants. They hypothesize that secondary, pleiotropic, or mutagenic effects resulting from gene expression or integration could cause unforeseen hazards, including toxicity and limited nutrient availability (9). These issues are addressed during the assessment of substantial equivalence for each product. The study that erupted the European backlash against GM foods initially was communicated in an interview granted by Armand Putztai on British television. Experimental evidence for this phenomenon (11) was published a later date. The researchers fed rats either wild-type, wild-type spiked with lectin, or transgenic potatoes expressing the lectin protein. Lectins are of commercial interest because of their pesticidal properties. They reported that only the transgenic potato fed group experienced intestinal damage, and they concluded that the genetic transformation process itself caused the observed complications. This study has been heavily criticized for, among other points, a lack of a control group fed transgenic potatoes not expressing the lectin gene and lack of balanced diets used for these studies (35). The diets were not balanced for protein or other components, which could explain the observed results. Other researchers have reported results that contradict the Ewan and Putztai's (11) conclusions. Hashimoto et al. (21) engineered potatoes that overexpressed soybean glycinins to elevate the content of leucine, lysine, and threonine. They hypothesize that increased intake of these amino acids will result in lowered serum cholesterol. In their analysis, they fed rats either a control diet, control diet with nontransgenic potatoes, or control diet with one of two transgenic lines of potatoes. They found no significant differences in the health status of the rats in each respective group. If genetic manipulation itself were responsible for health complications, as has been suggested, then the transgenic potato fed groups would have experienced some measurable complication. Interestingly, serum cholesterol of the rats did not change, but the authors note that the expected nutritional benefit should only be seen in animals with high levels of serum cholesterol. Similar results were obtained when toxicity studies were conducted on herbicide resistant soybeans (18, 20).

Allergenicity

Another concern related to food safety is the potential for genetically modified food to introduce allergens into the food supply. If the allergenicity of the compound is known, then the process of evaluation is simplified. Gene products that are not allergenic normally will not suddenly become allergenic when expressed in a transgenic plant. For instance, no known case of allergies to plant ferritin exist, therefore transgenic iron-enriched rice (17) poses no allergenicity risk. If the gene product is a known allergen, then it will also be an allergen in a transgenic plant. As an example, when a Brazil nut albumin was expressed in soybean to boost

methionine content, it was found that serum from Brazil nut allergic subjects reacted with the transgenic soybean extracts (47). Therefore, people with an allergy to Brazil nuts would now also be allergic to that line of soybeans, even though they were not allergic to native soybean before. As a safety precaution, this line of soybean was not commercialized.

Allergenicity assessment is considerably more complicated when the allergenicity of a transgenic protein is unknown. GFP is once again a good example. Although there are no known allergies to GFP, might it induce allergies when people begin to routinely ingest GM foods expressing GFP? Even though over 200 food allergens have been identified and sequenced (14), no common motif or consensus sequence has been discovered. However, a generalized protocol has been developed to examine potential allergenicity that is based on physico-chemical properties of known allergens (43).

Most known food allergens are stable to digestion (2). Therefore, testing a protein's stability during the digestive process is one way to identify potential allergens. If a protein is degraded in the stomach and small intestines, then it is unlikely to reach immune cells to cause a hypersensitivity response. Proteins that are stable should be examined further. These experiments can be coupled with comparison of sequence similarity to known allergens. Novel proteins with a significant sequence similarity can be tested for reactivity with serum from subjects allergic to the homologous allergen. Although these tests may not be comprehensive in identifying potential allergenicity, the limited variety of source foods (over 90% of the people who have food allergies are allergic to one or more of the following foods - cow's milk, wheat, nuts, legumes, eggs, or seafoods) suggests that the vast majority of transgene proteins will be safe for consumption (38).

CONCLUSIONS

The Biotechnology Industry Organization (BIO) estimates that 76.2 million acres of transgenic crops were grown in the US alone in 1999. Their estimate of worldwide production of transgenic crops from 1996 to 1998 was 101 million acres. If 80% of these were in the USA (a conservative estimate), then the 1999 production was about 48.5% of the cumulative pre-1999 US acreage of transgenic crops (BIO estimates:http://www.bio.org/food&ag/1999Acreage.html). It is interesting to note that the estimation of the total crop acreage under regulated test permits in (1987-1999) the US was approximately 0.4 million acres, or only 0.2% of the total acreage of transgenic crops grown during that period (Doug King, personal communication based on APHIS field permit data: http://www.isb.vt.edu). If we assume that approximately 16,000 individual plants are grown per acre (a conservative estimate for field corn), then since 1987, approximately 2.5 trillion transgenic plants have been grown in the field in the USA during the past dozen years! At this time, there has been no indication that this technology has resulted in environmental hazards or compromised human health.

Plant biotechnology offers tremendous promise for not only feeding the world's growing population, but for also improving the diets of people the world over. Although concerns over ecological and human health safety have led to mistrust over the application of this technology, many of these fears seem unsubstantiated or based on misinformation. A concerted effort must be made to identify valid concerns and risks, and to provide reliable and useful information to the public. Previously, genetically enhanced foods have focused on increased yield and other agronomic properties, which primarily benefits agribusiness corporations and farmers. The second generation of genetically modified foods will emphasize consumer health benefits. It is only with these new crops that the public will come to accept the uses of genetic modification of foods, and it is here that the overlap of nutrition science, ecology, and plant biotechnology will

become most evident. What is needed now is more collaboration between the nutrition and plant science fields to adequately evaluate the functionality of genetically modified foods and to develop new products that could significantly benefit the general population. In addition, biotechnologists need the objective participation of ecological researchers in helping to better determine ecological biosafety of transgenic plants.

In general, scientists must become more proactive in the public debate if agricultural biotechnology is to make a long-lasting and sustainable impact on improving food and fiber production, and human health. Currently, the most vocal group in the debate of GM crops has been environmental groups. Their arguments have primarily been based on fear of the unknown and technology plus misinformation based upon the misrepresentation of scientific data. The agricultural biotechnology industry is placed in a precarious position concerning their opinion in the public debate because of their obvious financial stake in the outcome. Academic and public scientists have tended to make two mistakes with regards to the current controversy. The first is their reticence to speak directly to the public and the media for fear of being misunderstood. The second is to assume that the public and the media will take their scientific data at face value. However, media sensationalism of single experiments can lead public opinion to make misinformed decisions. These mistakes have effectively removed the most objective and dispassionate parties (scientists) from the debate, which is unfortunate for public policy. For a scientific and technical society such as ours to properly function, public policy must be informed and shaped by the ideas of those who understand the science and technology best. Scientists need to reexamine their role and professions to include more public and media outreach as a part of their everyday work. Failure to do so will exacerbate the current vacuum of misunderstanding and fear surrounding the current controversy and those to come.

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