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PERSPECTIVE

Intragenic Crop Improvement: Combining the Benefits of Traditional Breeding and Genetic Engineering

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New crop varieties are developed by applying traditional breeding methods that rely on random genome modifications. These varieties combine multiple traits that support farm efficiency and acceptable yields but also contain genes associated with the production of toxins, allergens, and/or antinutritional compounds that were not considered during the selection process. Furthermore, existing cultivars frequently lack the functional genes required for specific sensory traits and the formation of health-promoting antioxidants. One new method efficiently addresses some of these issues by either silencing undesirable genes or enhancing the expression of genes that are linked to dormant beneficial traits. Rather than incorporating foreign DNA into the plant's genome, these methods transform crops with plant-derived transfer (P-) DNAs that consist of only native genetic elements. The genetic modification can be characterized molecularly so that any inadvertent transfer of undesirable DNA, as may be the case with traditional methods, is excluded. A recently developed intragenic potato plant is silenced for the polyphenol oxidase, dikinase *R1*, and phosphorylase-L genes in a tuber-specific manner. French fries derived from these tubers lack discolorations, display an enhanced potato flavor, and produce greatly reduced amounts of the suspected carcinogen acrylamide. It is argued that intragenic modification is unlikely to trigger phenotypic, biochemical, or physiological variation that is new to the species. Similarly, the targeted traits are similar to those that breeders select for and often have a history of domestication and reduced fitness. For these reasons, an updated regulatory system is proposed whereby intragenic crops are considered as low risk and should be cleared for commercial release in a timely and cost-effective manner. By using modern techniques to modify the same genetic material that is used by breeders, intragenic approaches may be perceived as an acceptable extension of traditional methods in crop improvement.

INTRODUCTION

The transformation of wild species into domesticated crops, a process that started about 10 millennia ago, may be considered one of the greatest accomplishments of mankind. Numerous cultivars displaying an astonishing variety of agronomically and nutritionally important traits are currently available for the production of food and food ingredients. Realizing that today's crops are still a "work in progress", breeders continue developing new varieties that support lower input costs while providing higher yields (*1*). They also attempt to enrich vegetables and fruits with new sensory and health-promoting attributes that are requested by an increasingly quality-conscious consumer (*2*).

One of the methods employed by traditional plant breeding to enhance crop performance assesses numerous lines for hundreds of traits in multisite replicated plot field trials. A second more cumbersome and time-consuming approach captures or creates new traits and transfers them into existing varieties. This Mendelian aspect of plant breeding crosses varieties with wild relatives to produce F1 hybrids or, alternatively, self-fertilizes plants that were subjected to chemical mutagens to generate segregating M2 families. Individual plants that contain the new trait are extensively backcrossed to remove unlinked wild or mutated DNA. Although initially considered as artificial (*3*), trait introgression and mutation breeding are currently perceived as acceptable methods in crop improvement. An additional method that dramatically affects the integrity of crop genomes but is accepted as one of the tools of traditional plant breeding is based on the fusion of somatic cells from related but sexually incompatible plant species. Such interspecies fusions result in the development of amphiploid hybrids, and considerable backcrossing and ploidy reductions are needed to develop varieties suitable for release (*4*).

An important issue associated with traditional plant breeding arises from the fact that genetic variation, although randomly

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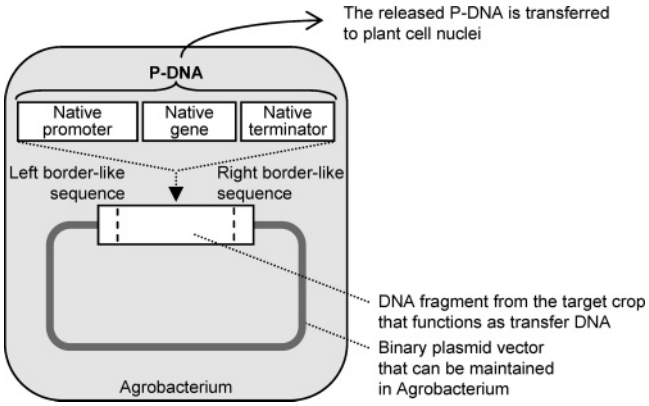

Figure 1. All-native DNA transformation. Genetic elements from a target crop, often comprising a gene that is operably linked to specific regulatory elements, are inserted within native border-like sequences to create a P-DNA. Advances in genomics research accelerate the identification of valuable native genes (*79*), and numerous promoters from a variety of plant species are currently availalbe, or can be efficiently isolated, to drive either near-constitutive or tissue-specific gene expression (*80*). *Agrobacterium* cleavage and secretion enzymes release the P-DNA from a binary vector for processing and transfer to plant cell nuclei. Upon transfer, the P-DNA integrates into double-stranded chromosome breaks. Various marker-free methods are available to obtain intragenic plants (*5*, *6*).

induced at the DNA level, is screened for phenotypically. Cultivars resulting from this practice will not only display most of the traits that the breeder selected for but also contain undesirable features and lack positive attributes that were not considered during the selection process. Here, we will discuss these issues and indicate how some of them can be addressed by applying intragenic methods. Instead or relying on unpredictable genome modifications, these new methods specifically recombine native genetic elements in vitro and insert the linked DNA back into the plant using marker-free transformation (*5*, *6*). One of the elements, the plant-derived transfer (P-) DNA, replaces the *Agrobacterium* T-DNA by functioning as vehicle for DNA delivery into the plant cell (*7*). Thus, intragenic modification incorporates neither uncharacterized DNA (as is the case with traditional breeding) nor foreign DNA (as is typical for transgenic modification; see **Figure 1**) into a plant's genome. We argue that intragenic applications produce GM crops that are inherently "low risk" and should be cleared through the regulatory process in a timely and cost-effective manner. Furthermore, we believe that intragenic crops may be considered more acceptable to consumers than transgenic plants.

ISSUES ASSOCIATED WITH TRADITIONAL PLANT BREEDING

Inadvertent Transfer of Undesirable Genes. In their efforts to accommodate the evolving needs of growers and consumers, plant breeders employ any available tool to identify the strongest possible traits. In one application, some of the genetic diversity that is offered within a sexual compatibility group is captured by crossing cultivated varieties with wild relatives and screening the resulting F1 hybrids for a new trait. Through extensive backcross programs, a segment of wild DNA, representing at least ~1% of the total genome (assuming six backcrosses and random recombination) and comprising the selected trait, is introgressed into existing varieties. Importantly, the introgressed DNA segment may contain one or several genes that are associated with undesirable characteristics. In addition to frequently observed linkage yield drag (*8*), introgression can result in obscure alterations linked to reduced food quality. For instance, transfer of "high starch" and "crisp chip" traits from *Solanum chacoense* to cultivated potato (*Solanum tuberosum*) increased glycoalkaloid levels in the resulting variety Lenape to almost twice the maximum allowed concentration (354 μg kg^{-1}) (*9*, *10*).

Lingering Presence of Plant-Produced Toxins or Allergens. It has been estimated that >99% of the total dietary intake of toxins is produced by food crops themselves (*11*). Symptoms of acute poisoning are induced by the occasionally high intake levels of natural pesticides such as glycoalkaloids (up to 665 mg day^{-1}) (*12*, *13*) and furocoumarins (up to 100 mg day^{-1}) (*14*). Furthermore, even low intake levels of genistein and other plant-produced compounds may trigger adverse long-term effects on human health (*15*). Many plant-derived toxins are effective against plant pathogens and insects, and breeders may have unknowingly selected for the presence of such genes by seeking to enhance disease tolerance levels. Given the advances in integrated strategies to control diseases and pests, it may be possible now to start lowering toxin levels, at least in the edible parts of food crops.

At temperatures exceeding 120 °C, amino acids and proteins react with sugars to produce Maillard products. Some of these products, such as acrylamide, display toxic and carcinogenic properties and accumulate in, for instance, bread crusts and the surface of potato chips and French fries (*16*). The average dietary intake level of acrylamide is 28 μg day^{-1} (*17*) and could be reduced to negligible amounts by using wheat and potato varieties accumulating low levels of asparagine. Unfortunately, breeders have not yet selected for low asparagine, and there are currently no acceptable varieties available that fortuitously display this trait. Thus, efforts to produce low-asparagine potato or wheat would require both source identification and trait introgression, a process that may take 20 years.

An even more important issue of today's crops relates to the presence of allergen-encoding genes. A single peanut can be life-threatening to people predisposed to developing allergy reactions, and bread consumption often unknowingly damages the intestinal lining of 0.8% of Americans that suffer from gluten sensitivities (*18*). Allergen levels in foods from a variety of nuts, vegetables, and cereal crops often exceed the minimum threshold levels of about 30 μg that trigger allergic symptoms in an additional 2% of the population (*19*). Although some allergen-encoding genes have been inactivated through mutagenesis, it would be difficult to eliminate all 20−80 genes from crops such as soybean, rice, wheat, peanut, and apple that encode allergens or suspected allergens (*20*). Regulatory agencies oppose the intentional employment of genes that are known to produce allergens, toxins, or antinutritionals (*21*) but can do little to prevent the unchecked transfer of such genes through conventional breeding (*22*).

Issues in Activating Dormant Traits. Plants contain many different biosynthetic pathways associated with the production of important health-promoting compounds such as vitamins, carotenoids, and flavonoids. These pathways are often not active in the tissues of commercial varieties that are used for consumption. For instance, tomato plants accumulate antioxidant flavonols mainly in anthers, where they support the development of viable pollen (*23*). Specific accessions of wild species such as *Lycopersicon pennelii* that overexpress the chalcone isomerase (*Chi*) gene were found to also produce high-flavonol fruits (*24*). However, the subsequent introgression of loci governing this trait will take much time and may not solve the yield issues associated with constitutive *Chi* gene expression. Similar yield

penalties complicate efforts to develop crops that constitutively express other genes linked to the increased production of, for instance, flavonoids or carotenoids (*25*, *26*).

Another example illustrating the importance of modifying the expression levels of native genes in a tissue-specific manner relates to the starch degradation-associated *R1* and phosphorylase-L (*PhL*) genes. Global inactivation of these genes limits starch degradation in all plant tissues (*27*, *28*). This modification has a beneficial effect on sink tissues such as potato tubers because it reduces the cold-induced accumulation of glucose and fructose and, consequently, lowers the formation of Maillard reaction products. Unfortunately, this quality improvement is off-set by the reduced crop yield that results from the inability of source tissues to convert starch into sugars during the night (*27*, *28*). Similarly, constitutively reduced expression of the polyphenol oxidase (*Ppo*) gene in potato, apple, lettuce, and other crops not only enhances food quality by preventing black spot bruise but also lowers tolerance against microbial pathogens (*29*). Breeders have not yet been able to combine black spot bruise tolerance and disease tolerance through an inactivation of the *Ppo* gene in the edible parts of the plants only.

INTRAGENIC APPROACH AS AN EXTENSION OF TRADITIONAL PLANT BREEDING

Attempting To Address Public Perception. Some of the issues associated with traditional plant breeding may effectively be addressed by genetic engineering. However, support for genetically modified foods has remained at the same low levels as in 2001 (26−27%) (*30*). Hesitance to embrace the agricultural applications of genetic engineering has been linked to concerns about the stable introduction of foreign DNA into food crops rather than the modifications of plant genomes per se (*31*−*33*). This conclusion may explain why traditional methods such as somatic hybridization and mutation breeding, which dramatically affect the integrity of plant genomes, are generally perceived as acceptable.

Failure to respond to intrinsic consumer concerns by updating the regulatory process may have contributed to the continued disconnect between GM developer and consumer (*33*, *34*). In 2003, Nielsen proposed to bridge this gap by diversifying genetically modified crops on the basis of the genetic distance between DNA source and target crop (*34*). He was the first to define organisms transformed with native DNA as "intragenic", while using the term "famigenic" for plants containing DNA from the same family. One example of a famigenic plant is the tobacco cultivar Delfield, derived from a fusion of somatic cells from *Nicotiana tabacum* and *Nicotiana rustica* (*4*). Nielsen considered plants containing DNA from unrelated sources as transgenic, but would label most currently available GM crops as xenogenic because they contain synthetic genes that lack naturally evolved counterparts. The categories of modified organisms suggested are defined by their biological relevance, reflecting the level of genetic relatedness between the donor and the recipient organisms, and thereby indicate the broad potential for the engineered trait to evolve spontaneously.

Two preliminary surveys in the United States seem to confirm that much of the controversy surrounding the use of genetic engineering relates to the extent to which modified organisms differ from traditionally bred varieties (*35*, *36*). Whereas about 77−81% of respondents would accept a vegetable that contains an extra gene from that same vegetable, only 17−25% would be willing to consume a food that contains an extra gene from a bacterium. An independent unpublished study performed by Scott Smith (Brigham Young University) that is based on an e-mail survey of 779 consumers confirmed these findings, with 70% supporting intragenic modifications versus 26% support for transgenic plants. There is even more public support for genetic modification if the resulting products provide clear and transparent benefits to consumers (*37*).

Examples of Intragenic Applications. The intragenic approach is exemplified by quality-enhanced potato (*38*) (**Figure 2**). This modified potato contains fragments of the polyphenol oxidase (*Ppo*), dikinase *R1*, and phosphorylase-L (*PhL*) genes that are linked to a single tuber-specific promoter. The resulting tuber-specific silencing of the *Ppo* gene prevented the development of black spot bruise, whereas simultaneous silencing of the *R1* and *PhL* genes limited the cold-induced degradation of starch. The resulting lowered accumulation of reducing sugars was associated with increased starch levels, reduced fry darkening, enhanced flavor, and a strongly reduced formation of acrylamide during heat processing. These and other potential targets for intragenic modification are shown in **Table 1**. Some of the examples relate to experiments that are ongoing in various laboratories. Okanagan Specialty Fruits develops an intragenic bruise-tolerant apple by silencing *Ppo* (*39*), and Pastoral Genomics works on a drought-tolerant ryegrass (*Lolium perenne*) overexpressing a native *Avp1*-like salt tolerance gene (*40*). One application does not modify the expression of native genes but simply transfers them from wild germplasm into elite varieties. This approach, which is also referred to as cisgenesis, is particulary suitable as an alternative to the introgression breeding of disease resistance genes. Research groups headed by Jonathan Jones (Sainsbury, U.K.), Evert Jacobsen (Wageningen University, The Netherlands), and William Belknap (USDA, Albany, CA) have already initiated independent efforts to transfer various broad-spectrum late blight resistance genes such as *RB* from the wild potato species *Solanum bulbocastanum* to cultivated potato using intragenic/cisgenic technologies.

Additional examples of intragenic modification are theoretical, with efficacy demonstrated by transgenic experiments. For instance, vitamin, flavonoid, and carotenoid levels can be increased by overexpressing biosynthetic genes in a tissue-specific manner. Furthermore, silencing approaches can be employed to down-regulate the expression of undesirable genes. Such methods may be used not just to eliminate single allergens from foods but to actually remove many or even all known allergens. Most allergen proteins in plants are present as isoforms encoded by genes that are members of multigene families. Therefore, silencing constructs carrying fragments of genes that each represent a different family could be used to simultaneously down-regulate the expression of multiple allergen-encoding genes (*41*).

Low-Risk Regulatory Process for Traditionally Bred and Intragenic Crops. To clear a genetically engineered crop through the regulatory process, developers must first show that it poses no significant risks to the environment by, for instance, affecting nontarget organisms, causing resistance in pest populations, or altering the fitness of either the crop or native species (*42*, *43*). Furthermore, the inserted DNA should not contain allergen- or toxin-encoding genes and neither inactivate important genes nor produce new gene fusions. A third requirement for a GM crop is that its nutritional profile falls within the range established for untransformed plants that belong to the same sexual compatibility group (*44*). Any increases in the amount of important toxins that exceed the biochemical variability of a species and/or recommended maximum concentrations would require further assessments. Similarly, decreases in the concentration of valuable compounds including vitamin C and essential

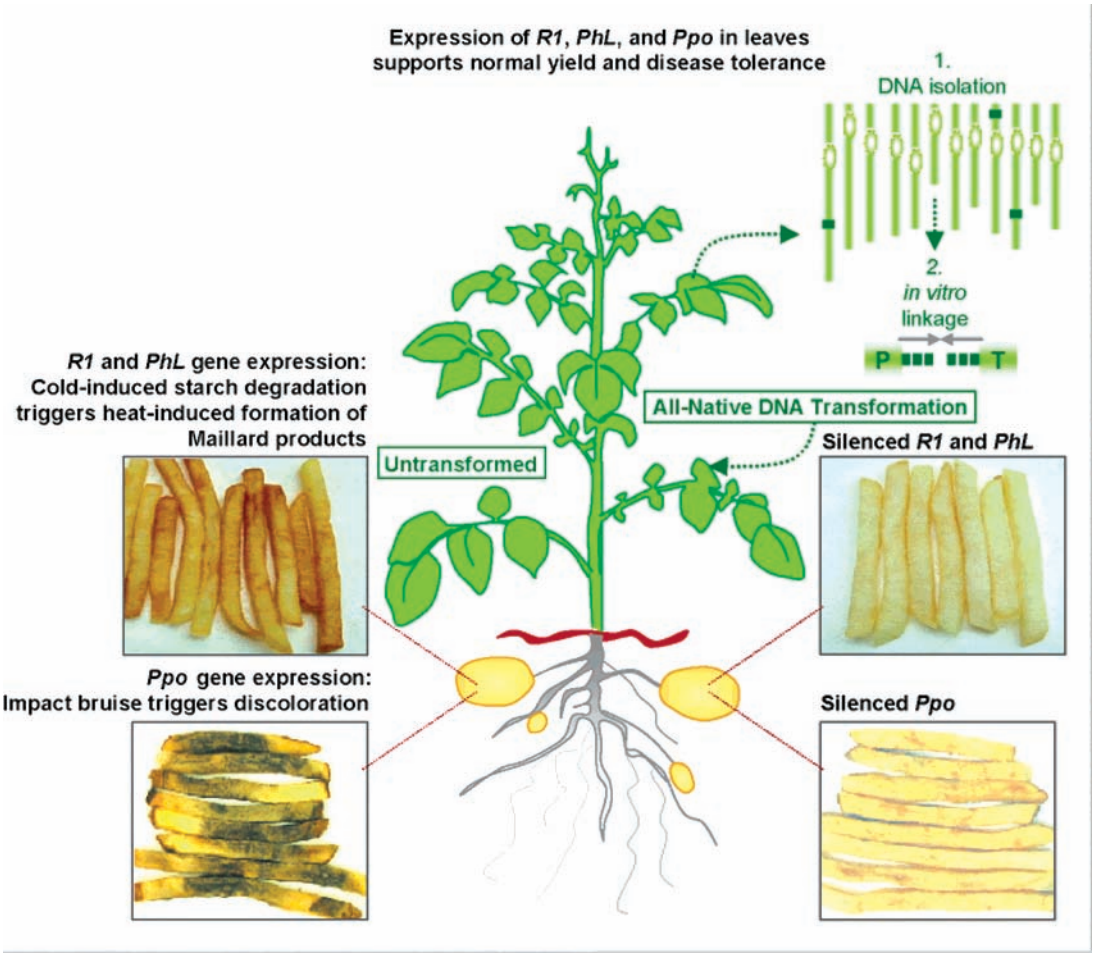

Figure 2. Example of a quality-enhanced intragenic crop. The tuber-specific promoter (P) of the granule-bound starch synthase (Gbss) gene was linked to DNA fragments from the three "undesirable" R1, phosphorylase-L (PhL), and polyphenol oxidase (Ppo) genes. Introduction of the resulting DNA fragment through all-native DNA transformation resulted in silencing of these genes that was restricted to the flesh of potato tubers. Consequently, the intragenic plants produced higher quality tubers without being compromised in disease tolerance or yield. T, terminator of the potato ubiquitin-3 gene.

amino acids would trigger studies on the potential impact of these changes on the nutritional value of the crop.

Regulatory agencies in the United States are currently working with universities, non-governmental organizations, and the private sector to revamp the regulatory approval process. They consider assigning GM crops into risk categories, whereby lower risk products would require less data and information. Those in higher tiers, whether because of novelty or other scientific uncertainty, would require more information to fill gaps in knowledge (*45*). The updated system would also represent a more efficient, transparent, predictable, and science-based regulatory process for small-market biotechnology-derived crops. Furthermore, a new public organization that resembles the USDA Interregional Research Project No. 4 (IR-4), which assists in obtaining minor-use pesticide registrations, would provide advice and data necessary for a detailed regulatory evaluation of genetically modified specialty crops (*46*).

Arguments for categorizing intragenic crops as low risk are described below and summarized in **Table 2**. First, these plants lack selectable marker genes, powerful insecticidal genes, or any other foreign genes that are new to agriculture and pose a potential threat to the environment. They differ from their untransformed counterparts only in expressing specific genes at modified levels to display valuable traits. Such traits include dwarfing, seedless fruits, or extended shelf life, or any other phenotype with a long history of domestication and consequently reduced fitness. Even modifications that result in enhanced farm yields are predicted to be neutral or detrimental in the wild (*47*).

The second requirement for regulatory approval reveals a key issue in traditional plant breeding but is effectively addressed by intragenic modifications. By transforming plants with specific well-characterized elements only, the intragenic approach avoids the transfer of functional genes associated with the production of known allergens and toxins. Furthermore, any undesirable P-DNA integration event that either creates new gene fusions or disrupts the expression of an existing gene can easily be sequence-identified and discarded during the line selection process that precedes commercial production. This option to exclude undesirable integration events is not available to traditional plant breeding where unpredictable excision and integration events of transposable elements may damage important genes.

By modifying the expression of one or several native genes, intragenic modification enhances the agronomic performance or nutritional characteristics of the original cultivar. However, there are three reasons to assume that these changes do not create expression levels and/or secondary metabolite profiles that are new to the sexual compatibility group. First, any modification accomplished through all-native DNA transformation can, at least theoretically, be recreated by traditional methods. Whereas single translocation events produce cisgenic plants (*48*), intragenic modifications would require multiple translocations. Second, plants evolved extensive allele-specific differences in

Table 1. Examples of Traits That Can Be Incorporated into a Plant by either Transferring or Modifying the Expression of Native Genes

trait	target plant	target gene	approach	ref
increased flavonol content	potato	*Chi*	tuber-specific overexpression	*54*
increased carotenoid and flavonoid content	tomato	*Det1*	fruit-specific silencing	*55*
increased anthocyanin content	tomato	*Ant1*	fruit-specific overexpression	*56*
increased β-carotene content	potato	*Lcy-e*	tuber-specific silencing	*57*
increased xanthophyll content	tomato	*Lcy + Chy*	fruit-specific overexpression	*58*
increased zeaxanthin content	potato	*Zep*	tuber-specific silencing	*59*
increased vitamin C content	strawberry[a]	*GalUR*	constitutive overexpression[b]	*60*
increased vitamin E content	*Arabidopsis*	*gmt*	seed-specific overexpression	*61*
increased vitamin E content	soybean	*Vte3 + Vte4*	seed-specific overexpression[c]	*62*
increased folate content	tomato	*Acds*	fruit-specific overexpression	*63*
reduced glycemic index	potato	*Sbe I + Sbe II*	tuber-specific silencing	*64*
heat-stable vegetable oil	soybean	*Fad3*	seed-specific silencing	*65*
heat-stable vegetable oil	cottonseed	*Fad2*	seed-specific silencing	*66*
extended shelf life	tomato	*Pg*	fruit-specific silencing	*67*
extended shelf life	tomato	*Acc oxidase*	fruit-specific silencing	*68*
extended shelf life	tomato	*Acc synthase*	fruit-specific silencing	*69*
extended shelf life	tomato	*Dhs*	constitutive silencing[b]	*70*
enhanced aroma	tomato	*Aadc1A*	constitutive overexpression[b]	*71*
enhanced aroma	potato	*Cgs*[b]	constitutive overexpression[b]	*72*
enhanced flavor	potato	*R1 + PhL*	tuber-specific silencing	*38*
reduced heat-induced acrylamide content	potato	*R1 + PhL*	tuber-specific silencing	*38*
reduced heat-induced acrylamide content	potato	*Asn1 + Asn2*	tuber-specific silencing	*73*
reduced heat-induced acrylamide content	potato	*Apg1*	tuber-specific overexpression	*73*
bruise tolerance	potato	*Ppo*	tuber-specific silencing	*6*
reduced lignin content	alfalfa/feed	*C3H*	silencing in vascular tissues	*74*
reduced allergen content	tomato	*Ltpg1 or Ltpg2*	constitutive silencing[d]	*75*
reduced allergen content	apple	*Mal d 1*	constitutive silencing[d]	*76*
reduced allergen content	peanut	*Ara h 2*	constitutive silencing[d]	*41*
reduced allergen content	soybean	*Gly m Bd 30 K*	constitutive silencing[d]	*77*
late blight resistance	potato	*RB*	use of original promoter	*78*

[a] Concept demonstrated in *Arabidopsis*. [b] Molecular strategies may be improved upon by employing tissue-specific promoters. [c] Gene isolated from *Arabidopsis*. [d] Multigene silencing constructs may be used to simultaneously inactivate various allergen-encoding genes.

Table 2. Proposed Aspects of the Regulatory Process for Crops Developed through Various Genome Modification Methods

Regulatory aspect	modification within species boundaries			Introduction of foreign DNA			
	introgression breeding	mutation breeding	intragenic modification	famigenic alterations	interspecies somatic hybr.	transgenic alterations	xenogenic alterations
environmental impact assessment	not necessary			yes[a]			
molecular characterization of modification(s)	not possible[b]		yes		not possible[b]	yes	
basic assessment of nutritional profile[c]	yes						
risk assessment of foreign protein	no			yes	not possible[b]	yes	
public communication[d]	yes						
remaining risk of approved product	potential presence of existing *and new* allergens, toxins, and antinutritionals		potential presence of allergens, toxins, and antinutritionals from the original cultivar		Potential presence of existing *and new* allergens, toxins, and antinutritionals	potential presence of allergens, toxins, and antinutritionals from the original cultivar; possibility of long-term negative effect of foreign protein	

[a] Multiyear field trials to confirm that expression of a foreign gene has no negative impact on either agricultural productivity or the environment. [b] The inability to either molecularly characterize genome modifications or identify and analyze newly expressed proteins raises a potential safety risk for consumers. [c] Confirm that important beneficial compounds (such as vitamin C and essential amino acids) are not reduced and undesirable compounds (such as glycoalkaloids) are not increased. [d] Disclose the source of genetic variability to increase consumer familiarity and possibly improve the public response to engineered organisms and their products.

their gene expression levels that are likely to exceed any modification accomplished intragenically. For instance, 6−15% of *Arabidopsis* genes are differentially expressed by any tested pair of ecotypes (*49*). At one end of the spectrum are the knockouts that can be created for any non-essential gene using either natural or chemical mutagens. The maximal expression levels at the other end may result, in part, from the need of plants to respond to multiple environmental stresses (*50*). Third, a targeted analysis of important compounds and metabolites in transgenic potato tubers with modified primary carbohydrate metabolism,

polyamine biosynthesis, and glycoprotein processing demonstrated that there were no consistent differences with respect to appropriate controls (*51*). Broader scale metabolomics analyses reached a similar conclusion (*52*) as did proteomic analysis (*53*). Collectively, we believe that the risk of unexpected undesirable effects triggered through altered expression levels of a target gene is as small as that for plants developed through, for instance, introgression or mutation breeding.

A greater potential safety risk is linked to the expression of foreign genes that are naturally not expressed in crops, as is the case with famigenic, transgenic, and xenogenic plants. Expression of these genes can produce a new trait that affects fitness in ways new to the species. Additionally, foreign proteins represent a potential risk to consumers, either directly or through indirect inadvertent interactions with native proteins. In addition to addressing these potential risks, it may be important to also consider the distance between gene source and target crop as part of the regulatory process. Disclosure of the sources of the genetic material introduced may prove to be necessary to define further research directions, maintain product identity, and increase consumer familiarity through categorization and, thus, improve the response to engineered organisms and their products. We conclude that new varieties developed through intragenic/cisgenic modification, introgression breeding, and mutation breeding represent low-risk crops that should be cleared through the regulatory process in a timely and cost-effective manner.

CONCLUSION

Traditional methods in plant breeding rely on random genome modifications and are difficult to apply to either eliminate undesirable features or activate dormant traits. Furthermore, improvements of specific characteristics could be associated with inadvertent and unnoticed genetic changes that compromise food quality. These issues are effectively addressed by precisely recombining native elements in vitro and inserting the resulting expression cassettes into plants using marker-free and all-native DNA transformation. The intragenic method is exemplified by a potato variety displaying enhanced flavor while accumulating reduced amounts of the toxic compound acrylamide and represents a first example of this new approach. Potential new targets include, for instance, low allergenicity and high antioxidant content. By employing the plant's own DNA, excluding foreign DNA transfer, and molecularly analyzing insertion events, intragenic plants are at least as safe as those developed through traditional plant breeding. We propose to lower the regulatory burden for intragenic crops while increasing the requirements for crops developed through introgression breeding, mutation breeding, or somatic hybridization. An evaluation of these low-risk crops should be focused on any potential safety issues to the consumer. More stringent tests of famigenic, transgenic, and xenogenic crops also include careful studies on the potential impact of these plants on the environment.

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