

Transgenic organisms—time for conceptual diversification?

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Recent advances in genetic engineering have made it possible to effect previously unattainable genetic changes in most organisms subjected to breeding¹. The altered organisms into which hereditary (that is, genetic) material from another organism has been introduced are referred to as transgenic or genetically modified organisms (GMOs)². Wide use of these process-based terms has resulted in little appreciation for the sources, extent, and novelty of the genetic modifications made in GMOs. Not surprisingly, indiscriminate scientific, public, and regulatory scrutiny based on misleading conceptual assumptions have developed into negative perceptions of GMOs, particularly among European citizens^{3,4}. I hypothesize that the failure to establish, from the onset, explicit terminology to categorize the various applications of gene technology in breeding have contributed to this skepticism and to rejection of the technology by many consumers.

The current practice of process-based categorization of GMOs is biologically imprecise and does not accurately reflect the nature of the introduced genotypic changes. As the terms enforce focus on the process, rather than the product, of the technology, they obstruct the potential to subdivide and conceptually expand the categories of products derived through gene technology-based breeding (see below). We propose the adoption of alternative categories that would shift focus to a product-based perception of gene technology, allowing conscious differentiation in the perception of GMOs based on the sources of the genetic changes introduced.

The extent to which transgenic organisms differ from traditionally bred organisms underlies much of the controversy surrounding the use of GMOs⁵. In seeking a scientifically sound resolution, the key factor is a clear, accurate understanding of the context of the specific genetic changes introduced. Generally, the release and use of

Table 1. Proposed categories for organisms currently designated 'transgenic' or 'genetically modified'

Categories	Source of genetic modifications	Genetic variability via conventional breeding	Genetic distance
Intragenic	Within genome ^a	Possible	Low
Famigenic	Species in the same family ^b	Possible	↓
Linegenic	Species in the same lineage ^c	Impossible	
Transgenic	Unrelated species ^d	Impossible	↓
Xenogenic	Laboratory-designed genes ^e	Impossible	

^aFrom directed mutations or recombinations; the extent of modification also reflects those arising in classical, selection-based breeding.

^bTaxonomic family; the extent of modification also reflects those arising from applying cellular techniques in classical breeding.

^cPhylogenetic lineage; recombination of genetic material beyond what can be achieved by classical breeding methods.

^dContains recombinant DNA from unrelated organisms. Reflects the genetic composition of most GMOs commercialized today.

^eFor which no naturally evolved genetic counterpart can be found or expected (for example, synthetic genes and novel combinations of protein domains from various species).

GMOs with simple nucleotide changes are likely to generate few ecological concerns beyond those faced by the organisms' traditionally bred counterparts. However, species-foreign genes, synthetic genes, and other genetic changes have been introduced into GMOs, and some deviate substantially (genetically, biochemically, and physiologically as well as in ethical, regulatory, and public perceptions) from what classical, selection-based breeding has achieved^{6,7}. These organisms have genetic compositions that do not reflect evolutionary processes occurring under natural conditions^{8–10}.

Consider, for instance, the genome of a representative transgenic variety of corn carrying the gene encoding *Bacillus thuringiensis* toxin (*Bt*), which contains functional recombinations and synthetic modifications of DNA fragments from four different bacterial species (from the genera *Agrobacterium*, *Streptomyces*, *Bacillus*, and *Escherichia*), additional prokaryotic mobile elements (bacterial plasmid), and regulatory sequences from a virus (cauliflower mosaic virus) and a rice plant¹¹. The known natural mechanisms generating genetic variability in higher eukaryotes cannot combine, functionally enhance, and propagate DNA sequences derived from several unrelated organisms within the time scale achieved by genetic engineering. Therefore, genotypes achieved by genetic engineering can be conceptually different from those arising naturally or from classi-

cal selective breeding, thus warranting further classification.

The genetic distance between the engineered organism and the source of the new genetic variation would be a functional criterion for assessing the novelty of the introduced genetic changes. A more precise and explicit nomenclature based on the genetic distance associated with the introduced genetic modifications is illustrated in Table 1.

The five categories of GMOs 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 spontaneously¹². The focus of most current engineering has been on adding or altering phenotypic traits conferred by single genes, often with little understanding of the biochemical and cellular interactions of the gene product within the new genetic background^{13–15}. The proposed divisions implicitly consider the biochemical networks through their evolutionary distance from the introduced trait. The categorizations address many of the ethical, religious, and public concerns raised, by allowing a conscious and conceptual diversification of current and future developments in gene technology assisted breeding.

At the center of many objections to GMOs is concern about the introduction of genetic material from distantly related organisms, such as the insertion of animal DNA into crop plants. To meet such concerns, relevant

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product categorization, for instance 'fami-genic' or 'linegenic' (Table 1), would clarify that the engineered organisms contain recombined genetic material limited to the same taxonomic family or higher-order phylogenetic lineage, respectively.

The proposed categories (and further-refined taxonomy-based nomenclature) will help to maintain the cultural values, perception, and traditional identity of products derived from GMOs¹⁶—for instance, rendering molecular breeding efforts undertaken within the organism (intragenic) easily distinguishable from those relying on the introduction of evolutionarily distant (transgenic) or novel, synthetic genetic changes (xenogenic). The latter modifications are currently less palatable from biological, ethical, and religious perspectives. I contend that such a scheme to extend existing consumer familiarity with conventional products to the genetically modified counterpart, by limiting the novelty of the perceived changes, may ultimately lead to increased public acceptance^{17,18}.

Current approaches to gene technology-assisted breeding have been called 'brute-force' in their use of distantly related genes with little consideration for the multiple evolutionary changes that have occurred in

the biochemical networks separating species¹⁹. It is expected that an improved understanding of genetic structure, including positional effects, regulation, and interconnectedness of biochemical networks^{20,21}, will allow many commercially desired traits to be obtained through precise genetic modifications within the organisms' own genomes rather than through reliance on genetic variation evolved in unrelated species. Similarly, regulatory sequences are likely to be identified within the target genome that will allow precise expression of the desired trait. The generation of a more precise classification system thus provides an incentive for genetic engineers to explicitly consider and justify their choices of genetic resources.

In conclusion, the proposed terms permit a more precise communication of the sources of genetic variability used in gene technology based breeding. Openly considering and acknowledging the sources of the genetic material introduced may prove 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.

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