Gene Flow and the Risk of Transgene Spread

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Somewhere in the world in 2006 the billionth acre of transgenic plants was planted. In this first decade of wide scale adoption of biotech crops, the vast majority of these plants have one or a few genes from other organisms (**transgenes**) inserted stably into their nuclear genomes, which naturally contain 10,000s of "ordinary" plant genes. *Transgene**s*** are genes that would never have been in their host plants if not for biotechnology. Once they are inserted, they behave like normal plant genes. To date most of these code for traits endowing plants with the ability to resist insect feeding and damage, and/or herbicide resistance that enables better weed control. Transgenes are subject to the usual biological processes, including gene flow, which is an ecological, regulatory, and economic concern for many people.

Question: What is gene flow?

Answer: ***Gene flow*** is simply the movement of genes from one organism to another. Gene flow is a natural process to which all genes are subject.

But transgenes, since they code for novel traits and come from other organisms, are often of special concern. Therefore, people ideally would like to minimize or prevent gene flow from transgenic organisms to undesirable hosts that are located nearby such as weedy wild relatives or to places where extensive crop breeding takes place.

Although gene flow through sexual means of ***hybridization*** (combining genes from two parents) is of most concern, horizontal gene flow also is discussed as a possible risk.

Q: What is horizontal gene flow?

A: There are two types of gene flow: horizontal and vertical. ***Horizontal gene flow*** is the movement of genes between disparate, unrelated species, such as between plants and microbes. Horizontal gene flow is discussed more theoretically than practically since it has never been shown to happen with transgenes in realistic experimental settings. Theoretically, transgenes, or more likely, pieces of transgenes could be transferred from decaying plant parts in the field to soil or aquatic microbes, or from transgenic food to bacteria in the gut or gut cells themselves. Entire transgenes with the regulatory portions of the DNA have never been found to be horizontally transferred.

But there is good evidence that genes have moved between species in evolutionary time. One well-characterized case is the movement of genes from the soil bacterium *Agrobacterium tumefaciens* to plants. *Agrobacterium* moves its genes from a plasmid (a circular piece of DNA outside the chromosome that only bacteria possess) to the plant's genome, thereby causing the plant to make food for it. In nature it causes crown gall disease in plants.

These days "disarmed" *Agrobacterium* is used by biotechnologists to transfer desirable traits into plants. The disease-causing genes have been deleted from *Agrobacterium* so that only the transgenes for desirable traits are transferred to plants under experimental conditions. *Agrobacterium* is considered to be nature's expert genetic engineer.

Q: What can be done to prevent potential horizontal gene flow?

A: Transgenes can be made to have the structure of plant genes by inserting pieces of DNA that bacteria do not process correctly. In the unlikely event that transgenes were transferred, they would not be functional in bacterial cells, and therefore not maintained. There is also a recent report of a plant gene that confers resistance to the antibiotic kanamycin, which is often used as a tool to produce transgenic plants. Presumably, this gene has been in plants all along, so there would be minimal new risk of moving it among organisms. It has been shown also to not function in bacterial cells, so that kanamycin resistance would not be endowed to bacteria if it happened to be transferred intact.

Scientists also have used selection genes other than those specific for antibiotics, such as selection genes coding for herbicide tolerance, or for the ability to metabolize certain sugars. There are a number of active research projects to find alternative selectable marker genes that do not originate from bacteria.

Scientists are devising ways to remove transgenes from plants once they have been inserted. One system uses DNA recombination systems to precisely remove pieces of DNA in genomes. A transgenic corn variety is now in farmer's fields in which such a system was used to remove marker genes prior to commercialization and field release. Even though marker genes have been considered safe, the political pressure to not have antibiotic resistance genes in food or agricultural products has prompted companies and researchers to find substitution genes and removal strategies.

Q: What is hybridization?

A: Hybridization (a type of vertical gene flow — gene exchange between closely related species) occurs when two different types of plants mate. For example, hybrid corn, which is the type most often grown, is produced by intermating two different varieties of corn to make a new variety that will not breed "true."

The progeny of hybrids often do not resemble the parent. Hybridization can occur between varieties or types of plants within the same species, or sometimes between species (certain kinds of plants even hybridize between genera, but that is rare). Most transgenic crops commercialized thus far, such as corn and soybean in the United States, have no wild relatives growing nearby so hybridization does not occur.

However, some people are still concerned about transgenic crops being hybridized with crops that are grown in organic farming (where transgenic plants are not permitted), or in other situations where transgenes might be undesirable. For instance, there was a report of transgenes being present in traditional landraces of corn in Mexico, where transgenic corn presumably was never grown. While this particular report was eventually found to be faulty and a follow-up study found no transgenes in Mexican landrace corn, this is a case where hybridization between transgenic and non-transgenic types could be undesirable.

Q: What is introgression?

A: Unlike hybridization, which can occur in only one generation, ***introgression*** is defined as the stable integration of a transgene into a related plant genome. Once again, this can occur within or between species. The ability of plants to hybridize is generally much greater than the likelihood of introgression. For hybridization to occur, plant types need to be growing near each other, flower at the same time, and be sexually compatible. The same is true for introgression, but requires several generations of crosses.

The first step (called a “backcross”) involves transgenic hybrids crossing with the non-transgenic host. Typically, for effective gene escape the non-transgenic host would need to be the female parent and the transgenic male parent would produce the pollen. So, scientists often study how pollen moves from transgenic plants to non-transgenic plants and how many transgenic seeds are produced from the non-transgenic parent.

Since hybrids are often sexually nonviable, introgression is relatively rare. For example, one of the few transgenic crops grown extensively in North America is canola (*Brassica napus*). Field mustard or wild turnip (*Brassica rapa*), a weed, is canola’s most closely related wild relative. Hybridization rates of transgenic canola with field mustard in the field potentially can occur up to 10 percent of the time, but the rates are usually much lower.

Backcrossing from the field mustard-canola hybrid to field mustard is 100 to 1,000 times less frequent. For introgression to occur, backcrossing must occur several consecutive times for the transgene to be stably integrated into the weed genome. While this scenario might seem unlikely at first, with the large numbers of transgenic individuals grown every year, a rare event could conceivably occur.

Q: Has hybridization and introgression occurred?

A: In non-transgenic plants it has been documented many times in certain crops. Non-transgenic sunflower, sorghum, alfalfa, and canola are known to hybridize and introgress with their wild relatives in some places. Transgenic introgression to wild relatives from commercial plantings has never been documented, but transgenic hybridization has occurred at least once. Concerns exist about plants whose pollen can move long distances. Experimental transgenic creeping bentgrass plants were found 21 km (13 miles) away from source plots and this is an example of long distance gene flow by pollen. Perennial plants that are in the field for many years might have more gene flow concerns compared with annual crop plants that are planted and harvested every year.

Herbicide-tolerant transgenic canola has produced fertile hybrids with field mustard in Canada, where the two kinds of plants are frequently grown grow together. Thus, it is conceivable in this system that many transgenic hybrids are produced, and could be selected to survive when the herbicide to which the transgenic plant is resistant is sprayed (*note: the transgenic hybrids would still be susceptible to other herbicides)*.

Q: What are the possible consequences of hybridization and introgression if it were to occur with transgenic plants?

A: That depends on the plant, gene, trait, and ecological factors. In crop-to-crop gene flow, transgenes might go someplace unexpected, such as when several different herbicide-tolerance genes ended up in the same canola plants. This is termed ***adventitious presence*** or ***admixture***. Admixture is of special concern in cases where pharmaceuticals are being produced in transgenic plants near fields where crops are produced for food, or for export markets in which transgenic products are not desired. *(Also, see how this applies especially to biofuels and biotechnology in my article on biofuels.)*

In the case where transgenes might be introgressed into ***weedy wild relatives***, there are concerns about exacerbating weediness traits or even the disruption of natural ecosystems. However, controlled field tests to deliberately encourage disease resistance or insect resistance in wild relatives through introgression resulted in recipient plants that were less fit and less competitive, compared with the original weed. Therefore, to assess the risk of gene flow one needs to examine not only the probability of genes moving between plants, but whether the new plants will be able to survive. Research has recently been performed to assess the ability to cripple the effect of transgenes. The goal here is for the transgenic effect to not be as strong if it went to a wild relative. In one case, the genetic background of the crop weakened the weedy relative. In another case, the weakness was built in to the genetic construct, called ***transgenic mitigation***, in which an herbicide resistance gene was paired with a dwarfing gene. In either case, transgenic weeds were less competitive than their non-transgenic parent weeds.

Q: Is there a special concern about gene flow and antibiotic resistance?

A: The possibility of horizontal gene flow makes some people worry that transgenes, especially transgenes that code for antibiotic resistance, will move into bacteria, thereby causing new antibiotic resistance problems for humans. In fact, a large majority of transgenic plants are produced by using a bacterial antibiotic selection gene that confers resistance to a specific antibiotic, such as kanamycin. In this way, transgenic plant tissue can be recovered from non-transgenic plant tissue that is being killed by the antibiotic.

Performing meaningful experiments to assess horizontal gene transfer is difficult because of the large sample sizes needed for potential detection. Many scientists believe that it will be much easier for horizontal gene flow to occur between bacteria or from bacteria to plants than from plants to bacteria. (*Also, see the other article on antibiotic resistance by Chassy.*)

Q: What's the bottom line?

A: Gene flow is a natural process and transgenes will inevitably move around in many species. Gene flow is not itself a risk or hazard. Advocating "zero tolerance" for gene flow is unrealistic for all plants and other organisms, including transgenic and non-transgenic. Many countries now allow 0.09 percent admixture in food plants if the transgene has been safe for consumption.

The real question is: exactly what are the risks? Risks of gene flow should be weighed against benefits, and perhaps certain crops with certain traits should not be commercialized, or not grown where wild relatives are present.

Physical containment, which most often consists of growing crops in laboratories, greenhouses or even modified caverns (a common method for mushrooms), can prevent gene flow. There are methods already available to contain gene flow and they are commonly used in plant breeding where only specific crosses are desired. As mentioned previously, novel biological means to control gene flow are under development.

References and further reading

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