GMOs Under Scrutiny

Engineered foods have withstood safety concerns, but haven't fulfilled big promises

By Rachel Ehrenberg

Arriving home after work a few summers ago, agricultural economist Matin Qaim found several disturbing messages on his home phone. A study by Qaim had shown that small-scale farmers in India who grew genetically modified cotton had larger harvests compared with conventional cotton growers. Those better yields resulted in greater profits for the mostly poor farmers and more disposable income to spend on basics like food and education.

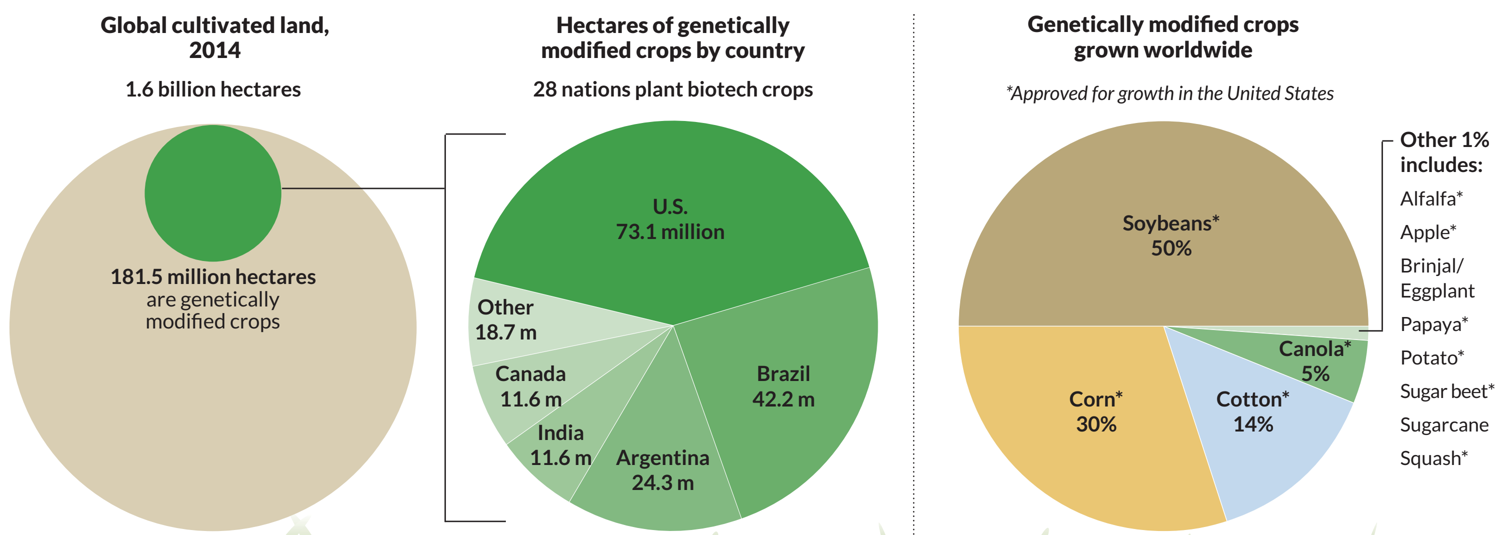
Several media outlets had covered the results, which had been published in the *Proceedings of the National Academy of Sciences*. But journalists weren't the only people contacting Qaim about the research. "Don't support this irresponsible destruction to the environment," implored one caller on Qaim's answering machine. "Think of your children, think of the world's children," a woman pleaded.

Qaim, of the University of Göttingen in Germany, has been studying the social and financial impacts of genetically modified organisms for years. Yet he is not blindly pro-GMO and his interpretation of his own study's results was nuanced. The GM cotton planted by the farmers was Bt cotton, which contains genes from *Bacillus thuringiensis*, a soil bacterium often used by organic farmers. Adding the Bt genes gives the cotton a built-in pesticide against the cotton bollworm, a scourge that can decimate crops.

Among the farmers Qaim studied, those who switched to the Bt cotton lost fewer plants and saw their profits increase by 50 percent. But the adoption of Bt cotton in that part of India was relatively recent and the positive impacts wouldn't necessarily last. Area bollworms might become resistant to Bt toxins, Qaim noted both in his paper and in interviews.

Such caveats didn't matter to the hostile callers, Qaim says. He has learned to keep quiet about his work in his casual conversations with parents at his daughters' school. In the heated debate over genetically modified organisms, there's little room for nuance.

Lay of the land Since their introduction in the mid-1990s, genetically modified crops are gaining ground on their conventional counterparts. Of the 28 countries planting GM crops today, 20 are developing nations. SOURCES: INTERNATIONAL SERVICE FOR THE ACQUISITION OF AGRI-BIOTECH APPLICATIONS, FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS



Good breeding Over time, plant breeding has gained speed and precision. Traditional crossbreeding mixes entire plant genomes and can take decades to yield a new variety. Transgenics and RNA interference breeding influence a handful of genes and can bring new products within a few years. SOURCES: FAO/IAEA MUTANT VARIETY DATABASE, A.E. RICROCH AND M.-C. HÉNARD-DAMAVE/*CRITICAL REVIEWS IN BIOTECH* 2015, ISAAA

Plant modifications throughout history

What?	Date developed	How?	Safety testing required?	Examples
Traditional crossbreeding	1700s	Cross closely related plants and select offspring with desirable traits	No	Myriad, including Burbank russet potato, Santa Rosa plum, sugar beets, corn, strawberries, peas, tobacco, peaches
Mutation breeding	1930s	Expose seeds or young plants to radiation or chemicals and select desirable mutants	No	Myriad, including Star Ruby grapefruit, Rio Red grapefruit, Golden Promise brewer's barley, varieties of cocoa, cotton, green pepper, sunflower, tomato, plum, peppermint, sugarcane, kale
Transgenics	1980s	Transfer specific genes by nonsexual means from one organism into another	Yes	Herbicide- and pest-resistant crops. In development: drought-tolerant peanut, wilt-resistant banana, bacteria-resistant orange, fungus-resistant chestnut, biofortified rice (includes Golden Rice), barley, corn and potato
RNA interference	1990s	Using RNA to turn off specific genes	Yes	Nonbrowning potato and apple. In development: decaffeinated coffee, tearless onion, higher-nutrition tomato, peanut and corn

"We are in a world that's painted black and white," Qaim says. "In Europe in particular, people are deeply convinced that GM crops are bad for the world. If you say anything in favor of GM crops, you are talking in favor of evil."

That designation of evil is one of the two prevailing narratives concerning genetically engineered foods. GMO opponents tell the story that "Franken" organisms are a new technology that poses known and unknowable dangers to human health, the environment and society at large. On the other side, proponents argue that GMOs are a harmless and necessary tool for saving a world threatened by overpopulation and a changing climate. The loudest voices on the proponent side are typically cast as shills for Big Agriculture (some of them are), while the loudest on the anti-GMO side are typically cast as fear-mongering luddites (some of them are).

This broad brush is problematic for several reasons, Qaim and others argue. The term GMO itself is a catchall that encompasses a wide range of products developed through a variety of means, each with its own risks and benefits. There are GMOs that have led to large reductions in the use of pesticides, for example, and there are GMOs that have made herbicide use skyrocket. The broad brush also fails when labeling the developers of GM technology: Commercial giants of the agrochemical pesticide industry have developed GMOs, but so have academic scientists funded by nonprofits or the public sector.

"A technology like GM crops is neither good nor bad," Qaim says. "Talking about *the* impact of GMOs is way too broad."

The diversity of engineering processes and the products that result will probably continue to grow. For example, the relatively new CRISPR technology, which allows for superprecise gene editing (*SN: 12/26/15, p. 18*), may soon become a GMO tool of choice. But generally speaking, the technologies behind GMOs are decades old. And despite fears of unknown risks, GMOs have been studied extensively.

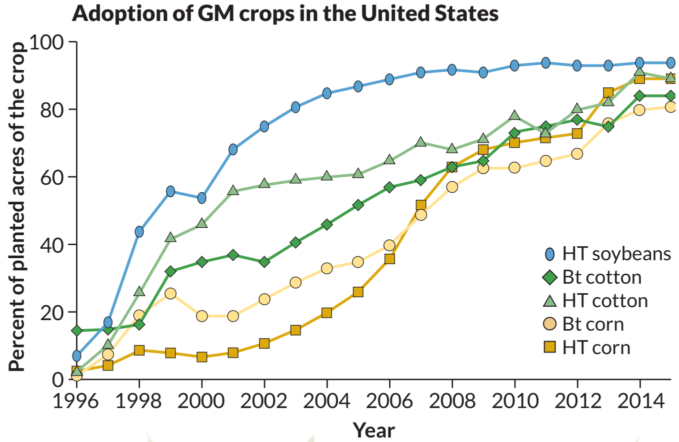
The picture drawn from decades of research is out of sync with many common public perceptions. While unforeseeable health issues are often at the forefront of public concern, foods containing GMOs have been on grocery shelves for more than 20 years. Piles of evidence suggest that eating GMOs is no riskier than eating conventional foods. Effects on the environment are more mixed. Some of the problems that have arisen, such as the uptick in the use of certain herbicides, are more about farming practices than about dangers inherent to GM technology; the same problems arise with conventional, non-GM crops.

The environmental consequences of engineered genes escaping into the wild are less clear. But while the fallout can be hard to predict, the odds of such escapes actually happening can often be evaluated. With the Food and Drug Administration's recent approval of GM salmon (*SN Online: 11/19/15*), for example, scientists agree that there is a slim possibility that escapees could harm native fish populations; that risk could be curtailed, however, with strict oversight about where and how such fish are farmed.

There's also a lot of unrealized promise. GMOs are often touted as a way to boost the nutrient content of foods to fight malnutrition. Yet GMOs that are on the market have largely

GM crop creep Crops engineered to be herbicide tolerant (HT) or toxic to specific insects (Bt), or both, have taken over U.S. farming acreage since their introduction in the 1990s. These modifications can reduce pesticide use and carbon emissions, but they can also lead to herbicide resistance if overused. SOURCE: USDA ECONOMIC RESEARCH SERVICE

Adoption of GM crops in the United States



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benefited those producing them — companies and farmers — rather than consumers. There are many health-boosting GMOs in development, including bananas with increased iron; plants that make omega-3 fish oils and rice, sorghum and cassava enriched with vitamin A. New crops, such as those engineered to tolerate drought or excess salt in the soil, could play a crucial role as shifts in climate threaten the farming status quo and in turn, food supplies.

2/3
Minimum fraction of foods sold in the United States that contain GMOs
SOURCE: GMA

80 percent
Estimated portion of hard cheeses sold in the U.S. that are made with enzymes created by genetically modified microbes
SOURCE: GMO COMPASS

A mouthful

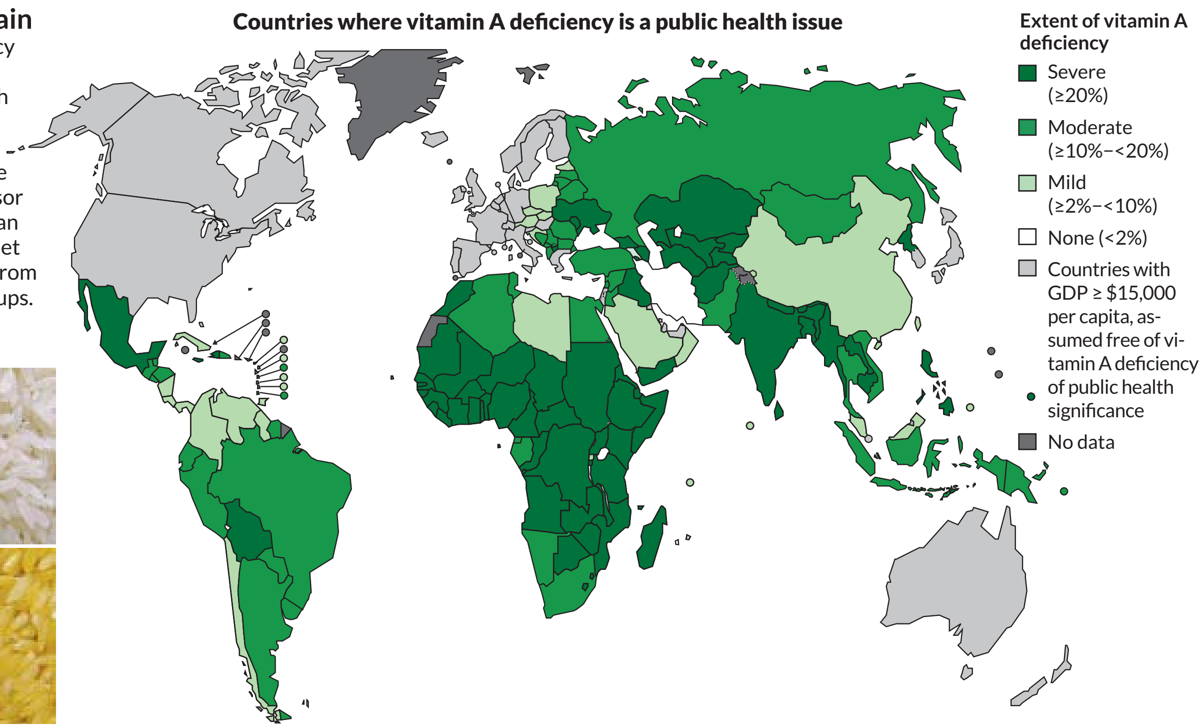
Foods containing GMOs have been on the market since the 1990s. Some are eaten as a whole organism — such as papaya engineered to resist the ringspot virus. Others end up as ingredients in processed foods, such as corn syrup. Genetic engineering is involved in more than two-thirds of foods sold in the United States, according to the Grocery Manufacturers Association. The processes that yield foods considered GM vary. Some contain genes from other organisms that impart a particular trait. Bt corn, for example, contains bacterial genes that make the crop toxic to soft-bodied caterpillars and some other insects. With other GMOs, the modifying entails dialing down the activity of genes that already exist in the plant, as with the just-approved Arctic apples and Innate potatoes that don't brown when cut. The genes responsible for the enzymes that brown the flesh are silenced.

Common GM ingredients, such as canola and soy oils, cornstarch and corn syrup, and sugar from beets, come from crops that have been modified to make farming them easier. Genetic engineering is also used to make minor ingredients that might be too complicated or expensive to produce via standard chemistry or too difficult or inefficient to harvest from their habitats in nature. Many microbes have been engineered to pump out vitamins, enzymes and other food additives, for example, a process that's typically much easier and more environmentally friendly than acquiring such ingredients from natural sources. The first genetically engineered food product approved by the FDA, in 1990, was a version of the bacterium *E. coli* engineered to make the enzyme chymosin, which prompts the ripening of cheese. Before the *E.coli* effort, chymosin was harvested from the stomachs of nursing calves as a by-product of the veal industry. Today, roughly 80 percent of hard cheeses sold in the United States are made with chymosin from engineered microbes.

These diverse products are all subject to testing before they can be sold. While there's always concern that genetic modifications could introduce a new allergen or a toxin into the food chain, that hasn't happened yet.

Testing is typically framed in terms of the notion of "substantial equivalence." The GMO is compared in substance and nutrition with its nonengineered version. The introduced genetic material, which yields a transgenic protein that causes some change to the organism, is also scrutinized for structural similarities with toxic proteins or other biologically active molecules, such as known allergens. The temperature and acidity level at which the transgenic protein breaks down is also assessed to see how it might fare in the body. Digestibility and

Against the grain
Vitamin A deficiency is a major cause of blindness and death in children. Golden Rice (bottom), engineered to make a vitamin A precursor in the grain, offers an antidote, but has met strong opposition from environmental groups.



RICE: THE GOLDEN RICE PROJECT; MAP: WHO "GLOBAL PREVALENCE OF VITAMIN A DEFICIENCY IN POPULATIONS AT RISK 1995–2005" potential toxicity are also evaluated.

While every new modification presents a new case for scrutiny, so far the GMO health track record is clean. And GMO products have been tested by more than their developers, who have a clear interest in their approval. Independent researchers have looked for red flags in numerous studies.

"So far, there is no reason for concern," says biotechnologist Alessandro Nicolia of the Italian National Agency for New Technologies, Energy and Sustainable Economic Development in Rome. He was a coauthor of a 2013 paper analyzing 10 years of GMO studies, 770 of which related to human and animal safety.

Despite numerous studies finding that eating GMOs is no riskier than eating conventional foods, claims of adverse effects persist. GMOs are sometimes a scapegoat for allergies, including the uptick in gluten intolerance — digestive problems caused by a protein found in wheat and some other grains. But no such link is supported by the research, says Nicolia. He points out that, although GM wheat exists, it is not on the market anywhere in the world. And correlations can be easily conjured: The rise in gluten intolerance also coincides with a rise in the availability of organic foods, for instance.

The few cases in which a transgenic protein has acted as an allergen were identified via testing well before the products reached consumers. One, for example, involved transferring Brazil nut proteins, which contain an important dietary amino acid, into soybeans for animal feed. Testing revealed that the transgenic Brazil nut protein provoked an immune response in people; the study reporting the findings made headlines in 1996 when it appeared in the *New England Journal of Medicine*. Development of those soybeans was abandoned.

Of course, because evaluations look primarily for molecules that resemble known allergens, there is always a risk that something novel could spur an immune response. Absolute certainty doesn't exist, for GMOs or conventional foods. In fact, because the testing is fairly extensive and the quantities of transgenic proteins in an engineered organism are typically so low, many scientists argue that it's easier to detect a potential allergen in a GM crop than in a conventional crop. Not long after the kiwifruit's arrival in the United Kingdom, several adverse reactions revealed that some people were allergic to the fruit, according to the United Kingdom's 2003 GM Science Review Panel.

Several scientific bodies, including the U.S. National Academy of Sciences, the American Medical Association and the World Health Organization, have reviewed the existing evidence and concluded that eating GM foods is no riskier than eating conventional foods. Numerous studies, and reviews of those studies, have come to similar conclusions. Plant geneticist Agnès Ricroch coauthored several review papers assessing GMO safety, including a 2012 paper examining the long-term health of animals fed GM corn, potatoes, soybeans, rice and the grain triticale, a cross between wheat and rye.

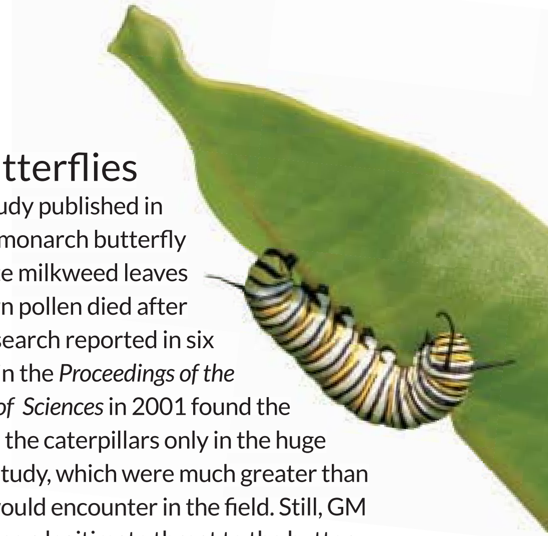
"In all of the studies published, of all GM crops authorized to be marketed, we have seen no adverse effects," says Ricroch, of France's Academy of Agriculture and AgroParisTech in Paris. "There is no risk to health for humans or animals."

Still, fears that genetically modified organisms cause health problems — from cancer to autism — linger. Such concerns have been fueled by a now thoroughly debunked but high-profile 2012 study by French researchers purporting to show that GM corn caused cancer in rats. The work was almost immediately discredited on multiple accounts, including faulty statistics and the fact that the researchers used rats from a strain that is naturally prone to tumors. The paper was widely criticized and later retracted. But the initial media campaign by the scientists, which included images of rats with enormous tumors and offers of early access only to journalists who agreed not to talk to other scientists about the results, had lasting effects. The paper, which was recently republished in a different journal, is still cited in some anti-GMO camps as evidence for a lack of consensus concerning health effects.

Discourse about the health hazards of eating GMOs is frustrating on multiple levels, says Ricroch. Controversy has slowed GMO progress in the area of enhancing foods' nutritional value. The poster child for such a crop is Golden Rice, which has been engineered to produce a vitamin A precursor, beta-carotene, in the grain (the plant normally produces the stuff in its green tissues but not in the edible endosperm).

Because of vitamin A deficiency, more than 250,000 children become blind every year, and half of them die within a year of losing their sight. By adding a gene from a bacterium and one from corn (swapped for a daffodil gene used in earlier versions), the rice makes beta-carotene that is converted to vitamin A when eaten.

The Golden Rice project was never a commercial one. When



SF PHOTO/SHUTTERSTOCK

Bye-bye butterflies

In 1999, a small study published in *Nature* found that monarch butterfly caterpillars that ate milkweed leaves dusted with Bt corn pollen died after a few days. But research reported in six studies published in the *Proceedings of the National Academy of Sciences* in 2001 found the pollen was toxic to the caterpillars only in the huge doses used in the study, which were much greater than what the insects would encounter in the field. Still, GM crops appear to pose a legitimate threat to the butterflies: Heavy use of the herbicide glyphosate, thanks to the widespread planting of crops engineered to resist it, has wiped out much of the milkweed the butterflies rely on for food. Farmland in the Midwest lost 80 percent of its milkweed from 1999 to 2010; the decline was mirrored in monarch populations, scientists reported in 2013 in *Insect Conservation and Diversity*. *— Rachel Ehrenberg* its creators launched the project more than 20 years ago, the intention was to combat malnutrition in developing countries. Yet the crop has met serious resistance. In August 2013, fields of trial plants in the Philippines were trampled and destroyed by anti-GMO protestors. The destruction prompted thousands to sign a statement condemning the destruction of the rice fields, which was echoed in an editorial in *Science*.

The herbicide treadmill

Science has repeatedly laid to rest claims about GMOs' adverse effects on human health. But some environmental impacts have surfaced. The primary problem, though — weed resistance to particular herbicides — is not unique to GM crops.

Engineered crops typically have traits that help farmers tackle very old foes. Weeds are one such headache, and they were among the earliest targets of genetic engineers. While chemical weed killers were in use before the advent of GM crops, the use of the herbicide glyphosate, marketed as Roundup, has skyrocketed since the introduction in the 1990s of crops engineered to withstand it. Glyphosate meddles with an essential plant enzyme; the engineered crops have a bacterial version of the enzyme, so the plants persist while neighboring weeds perish. "Roundup ready" plants, which now dominate U.S. fields, include soybeans, corn, canola, cotton and sugar beets.

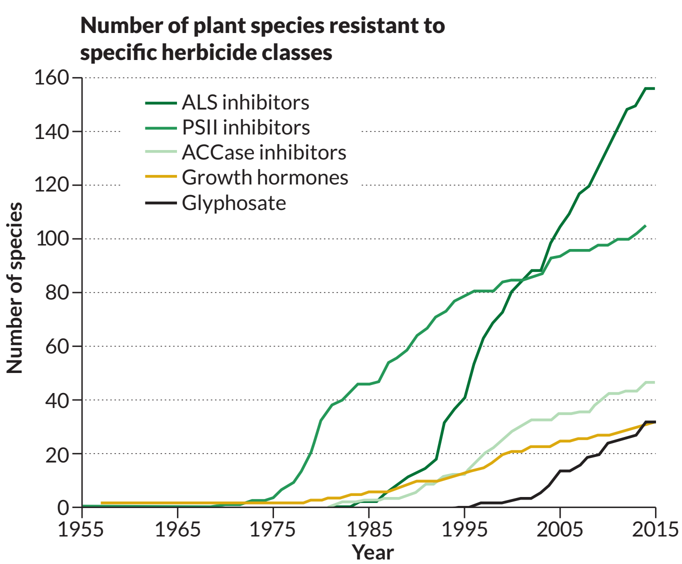
> "We've had [herbicide] resistance problems for more than 50 years. It results from overuse and mismanagement."
>
> CAROL MALLORY-SMITH

GM crops that tolerate herbicides deserve some praise: They help minimize mechanical weed removal, which means less soil erosion, more carbon stored in the soil and fewer carbon emissions from tilling equipment making trips across fields, scientists noted in 2012 in a special issue of *Weed Science* focused on herbicide-resistance management. And compared with many of the herbicides it replaced, glyphosate is less toxic; it also offered ease and flexibility to farmers who previously had to carefully navigate the timing and selection of applying various herbicides.

But glyphosate-tolerant GM crops made things too easy. "Everyone started growing them and then everyone started using glyphosate," says weed scientist Carol Mallory-Smith of Oregon State University, an expert in herbicide resistance.

When the same herbicide is applied to the same area year after year, overuse can lead to evolved resistance, as it does with antibiotics, says William Vencill of the University of Georgia, coauthor with Mallory-Smith of a paper in the *Weed Science* special issue. There are now major weeds, such as Palmer amaranth (*Amaranthus palmeri*), that have developed resistance to glyphosate, leaving farmers scrambling for new solutions, including use of chemical controls that are more toxic than glyphosate. These weeds are not "superweeds," Mallory-Smith says. "There's nothing super about them and they can still be controlled with other herbicides." She emphasizes that this cycle, known as the herbicide treadmill, isn't unique to GM crops. "We've had resistance problems for more than 50 years," she says. "It results from overuse and mismanagement."

Rising resistance Many herbicides interfere with a specific aspect of plant metabolism. Repeated use (across acres and time) leads to weeds resistant to the herbicides' action. A growing number of weeds are resistant to several herbicide classes (listed below), including glyphosate (black). SOURCE: IAN HEAP, WEEDSCIENCE.ORG 2015



Into the wild

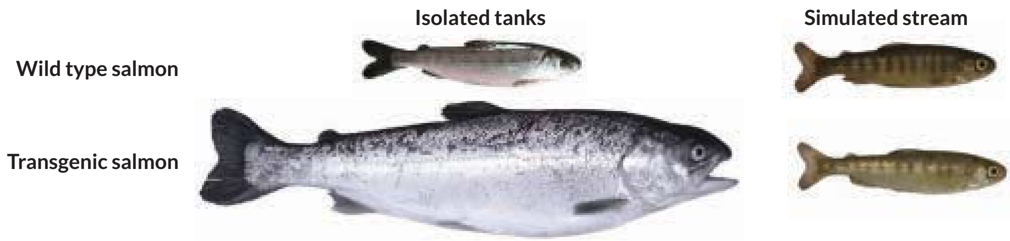
Herbicide resistance is predictable — that's Evolution 101. And the chances that genes from GM crops will spread to wild relatives is similarly predictable. It depends on basic biology, says Mallory-Smith. "The bottom line is if you have a species with compatible relatives that occur in the same area, gene flow will occur," she says.

And it has. While corn and soy don't have close wild relatives in the United States, canola, another widely planted GM crop, does. Herbicide-resistance genes from GM canola have turned up in wild, weedy mustard plants on roadsides in the United States, Canada and elsewhere. Mallory-Smith and colleagues have documented another escapee: a GM version of creeping bentgrass, a turf species that was being tested in Oregon. The grass has established itself in patches near the test site, and it has hybridized with a local weed called rabbitfootgrass.

"It's always good to ask where will the genes go and what difference will it make," says ecologist Allison Snow of Ohio State University, also an expert in transgenic gene flow. And while the documented cases of escapees suggest that regulatory agencies need to apply more caution regarding where GM plants can be grown, there haven't been any catastrophic outcomes, she says. "The things we worried about 10 years ago haven't yet happened," she says. "I can't point to anything dire."

GM escapees present legitimate legal and cultural conundrums, Snow notes. For example, an organic farmer can no

Fish out of water What would happen if GM fish escaped and bred in the wild is a big question. In experiments with GM coho salmon, the transgenic fish grow rapidly in a hatchery tank, but not in a simulated natural stream. It's unknown if the same would happen for newly approved GM Atlantic salmon.



longer call crops organic if they get contaminated by nearby GM crops. "But that's not an ecological problem," she says. "It has nothing to do with a GM species taking over."

The potential environmental implications of an escaped GM Atlantic salmon, the first GM animal to garner regulatory approval, are a little harder to predict. But there are multiple safeguards in place to prevent the fast-growing fish from escaping and breeding in the wild. There are biological precautionary measures: The fish are engineered to be all female and to have three sets of chromosomes so they can't breed with wild fish. But error rates in the sterilization process are inevitable and roughly 1 percent will probably be able to breed successfully. There are also physical hurdles: The current approved arrangement for farming the fish entails producing the eggs in an indoor facility in Canada and then shipping them to inland covered tanks in the highlands of Panama.

"There are a lot of redundant layers of strict confinement," says Virginia Tech fisheries expert Eric Hallerman. "That's why I'm comfortable with it."

The fast-growing fish contains a growth hormone gene from Chinook salmon and regulatory DNA from the eel-like ocean pout that keeps the salmon growing all year, enabling the fish to reach full size in a year and a half instead of the standard three years. And while the modified salmon look formidable next to slower-growing relatives, if they did escape and somehow managed to persist, it's not clear who would outcompete whom in the wild, says fisheries biologist Robert Devlin of Fisheries and Oceans Canada.

For several years, Devlin and his colleagues have been growing an equivalent transgenic Pacific salmon in land-bound caged tanks and mock streams. Experiments with these transgenics and wild fish present a mixed picture that plays out differently in different contexts. For example, the engineered salmon outcompete their wild relatives in the cushy tanks where food is plentiful. But they are at a disadvantage in the mock streams where there is less food and there are predators. Evidence from other studies, reviewed in June 2015 by Devlin and coauthors in *BioScience*, suggests that the GM fish take more risks than wild salmon, which makes them more likely to be eaten.

Yet different experiments, breeding GM Atlantic salmon with wild brown trout, suggest that in some contexts hybrid offspring can outcompete both their GM and wild parents, scientists reported in the *Proceedings of the Royal Society B* in 2013.

Devlin is reserved in his verdict. "I'm not against transgenic technology and I'm not for it," he says. "I'm neutral. There could be lots of benefits, but my view is we proceed with scientific information rather than speculation."

That view dominates in the scientific community, yet acceptance of GMOs by the public hinges on more than good science. Some critics take issue with GMOs, not out of misplaced fear, but because they see a yawning gap between the promise of GM foods — feeding the world's poor — and what's been realized: a handful of corporations making money selling both the GM seeds and the chemicals needed to grow them. That scenario doesn't inspire trust, Qaim notes. In the United States, a legacy of regulatory debacles, such as the delay in curtailing the use of the pesticide DDT, doesn't help either.

Yet while GMOs and profits for agribusiness seem cemented together in the public's mind, it's an inaccurate picture, Qaim says. Despite approved crops being created for markets in the developed world, farmers in developing countries have seen higher incomes, greater productivity and significant reductions in pesticide use, according to a 2014 analysis by Qaim and former Göttingen colleague Wilhelm Klümper. And the next generation of GMOs, many of which are stalled in regulatory limbo, increasingly have traits that benefit consumers, not just the producers of the crops.

90 percent
Fraction of biotech crop farmers who are in resource-poor nations

Whether the specter of Big Ag's role in developing and selling many of the existing GMOs will overshadow future developments remains to be seen. Currently, even when there's funding and momentum to develop a new GMO in the lab, public sector efforts often wilt in the face of the cost, time and political will needed to gain approval — leaving the successes to the giants, Qaim notes. If the tide turns, promising crops, such as a gluten-free wheat or GM green beans with added iron to fight anemia, might make their mark alongside the yield-improving GM crops.

Hallerman says the real significance of the GM-salmon approval is that it could be a step toward opening minds among the public, although that may take generations, he says. (Whole Foods and Costco have announced they will not sell the GM salmon.) "It's not about salmon for Western consumers," he says. "It's about food security in the developing world." ■

Explore more

- National Research Council. "Public engagement on genetically modified organisms: When science and citizens connect." 2015.

L.F. SUNDSTRÖM *ET AL*/PNAS 2007

Name: ____ Pd. _____ Date: _________________

GMOs under Scrutiny

1) What benefit did the farmers in India experience by planting GMO cotton containing the Bt gene? ____

2) What advantage do Bt cotton plants have over “normal” cotton plants? ____________________

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3) Why do some scientists think that this advantage won’t last? ______________________________

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4) Describe 3 ways that GMO plants have either benefited farmers or consumers (other than the Bt cotton), or are proposed to convey benefit.

a) ____

b) ____

c) ____

5) Aside from color, how is “golden rice” different than white rice, and why was it developed?

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6) How is transgenic salmon advantageous to fish farmers? _________________________________

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7) Why are some people afraid of “escapees”? ____

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8) What steps have been taken to minimize that possibility? _______________________________

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