Commentary

Agricultural Biotechnology Is Much More Than Herbicide-Tolerant Crops

Henry I. Miller
is a physician and molecular biologist, and is the Robert Wesson Fellow in Scientific Philosophy and Public Policy at Stanford University's Hoover Institution. He was the founding director of the Office of Biotechnology at the Food and Drug Administration.

Robert Wager
is a faculty member in the biology department at Vancouver Island University in Nanaimo, British Columbia, Canada

ABSTRACT
Herbicide-tolerant genetically engineered (GE) plants have been a lightning rod for activists, who regularly attack them, citing a number of spurious objections. Contrary to their claims, the plants do not contain herbicides; rather they are resistant to the herbicides, in order to make weed control – an essential aspect of farming – more efficient and cost-effective. But molecular genetic engineering applied to crops has made monumental contributions in addition to herbicide-resistance, and these are discussed.

Journal of Commercial Biotechnology (2017) 23(1), 7–10. doi: 10.5912/jcb776
Keywords: genetic engineering; genetic modification; herbicide-resistance; Bt; pest-resistance;

Tomatoes offer an instructive story about genetic modification. Before plant breeder Alexander Livingston came along in the late 19th century, tomatoes were "small, hollow, tough [and] watery," according to his 1893 tome, Livingston and the Tomato. Since then, tomatoes have undergone astonishing improvements and after more than a century of breeding: Thousands of varieties are grown worldwide after having been modified for many climates and soils and to enhance a variety of desirable traits, including pest-resistance, abiotic stress tolerance, improved nutrition, better taste and delayed ripening. They are an important part of the human diet, supplying minerals, vitamins and phytochemicals, and are the fourth most important commercial crop in the world in terms of net production value, which is estimated at more than $50 billion.

In the 1990's, the techniques of molecular genetic engineering (GE) were first used to create tomatoes with delayed ripening for longer shelf-life (which means less wastage), and although the attempts were technically successful, overall the tomato, dubbed the Flavr Savr, wasn't very good and flopped commercially. Sometimes, however, technology has a way of taking us back to the future, and an article in the journal *Nature* in July 2015 suggests that long shelf-life tomatoes are making a comeback. A group of Anglo-American academic scientists employed genetic engineering techniques to achieve "targeted control of tomato softening, without affecting other aspects of ripening, by silencing a gene" that codes for a single enzyme. The project is still in the early stages but seems promising.

While the use of molecular techniques for the genetic engineering of tomatoes was in suspended animation for decades, there have been monumental breakthroughs in other plants. A subset of these – which have been modified to be herbicide-tolerant – have been a lightning rod for activists, who regularly attack them, citing a number of spurious objections. Contrary to their claims, the plants do not *contain* herbicides; rather they are resistant to the herbicides, in order to make weed control – an essential aspect of farming – more efficient and cost-effective. And although the total amount of herbicides applied may have increased as the result of these herbicide-tolerant, genetically-engineered crops, the overall environmental impact is *smaller* because the herbicides applied (most often glyphosate, or Round-Up), have less impact compared to the herbicides they replaced. See the table here for a comparison of the toxicity of glyphosate to other common chemicals.

In addition to the herbicide-tolerant plants that the activists deride and disparage, there are many crop plants that have been genetically engineered for

Correspondence:
Henry Miller, Hoover Institution, Stanford University, US. Email: henry.miller@stanford.edu

unrelated traits. They include both plants with improved agronomic properties — which directly benefit growers primarily – and those that boast properties attractive to consumers. Many of the latter are in the development pipeline, and they are becoming ever more prevalent.

BT-CROPS

Broad spectrum insecticide spraying is effective at controlling insect pests but it also kills beneficial insects. More than 20 years ago agricultural scientists found an ideal way to reduce or eliminate insecticide spraying. A soil bacterium called *Bacillus thuringiensis* (Bt) produces a variety of proteins that are selectively toxic to certain insects but non-toxic to all other animals. Inserting the genes that code for these Bt proteins into crops allows the crops to protect themselves from the insect pests. Over the past twenty years Bt crops have allowed farmers to reduce the amount of broad spectrum insecticide spraying by hundreds of millions of pounds.

Bt crops include corn, cotton and soy. The newest Bt crop, brinjal (eggplant), represents a major agricultural advance. Brinjal requires up to 100 applications of insecticide through the growing season to protect it from a voracious insect pest. Often, subsistence farmers in the developing world have little or no protective equipment. The GE version containing Bt proteins has been a tremendous success in Bangladesh. Growing Bt brinjal dramatically reduced insecticide applications, resulting in less environmental impact, reduced occupational exposure for farmers and improved yields. It is likely that India will soon follow Bangladesh's lead.

Consumers also directly benefit from Bt crops. Every year, scores of packaged food products are recalled from the U.S. market because of the presence of contaminants such as insect parts, toxic molds, bacteria and viruses. Because farming takes place out of doors and in dirt, such contamination is a fact of life. Over the centuries, the main culprits in mass food poisoning have often been mycotoxins, such as ergotamine from ergot or fumonisin from the mold Fusarium. These come from the fungal contamination of unprocessed crops, which is exacerbated when insects attack food crops, opening wounds in the plant that provide an opportunity for pathogen invasion. Once the molds gain a foothold, poor storage conditions also promote their post-harvest growth on grain.

Fumonisin and some other mycotoxins are highly toxic, causing fatal diseases in livestock that eat infected corn and esophageal cancer and neural tube defects in humans. Regulatory agencies such as the U.S. FDA and UK Food Safety Agency have established recommended maximum fumonisin levels in food and feed products made from corn. Unprocessed or lightly processed corn (e.g., corn meal) can have fumonisin levels that exceed recommended levels. In 2003, the UK Food Safety Agency tested six organic corn meal products and 20 conventional (non-organic) corn meal products for fumonisin contamination. All six organic corn meals had elevated levels—from nine to 40 times greater than the recommended levels for human health—and they were voluntarily withdrawn from grocery stores. By contrast, the 20 conventional (i.e., non-organic) products averaged about a quarter of the recommended maximum levels. Research has shown that there is more than 90% reduction of this toxin in Bt corn, so it is difficult to understand how environmental NGO's like Greenpeace actively and relentlessly campaign against these Bt crops.

VIRUS-RESISTANT PAPAYAS

Papaya ring spot virus (PRSV) has caused massive crop damage around the world. The virus was first detected in Hawaii in the 1940's, and by the 1950's, infestations forced farmers to stop growing papayas on Oahu, so production moved to the Puna district of the big island. Soon 95% of all Hawaiian papayas were grown there. In 1992 the virus arrived in Puna and in only a couple years was decimating the $64 million a year industry. By 1991, scientists had developed virus-resistant papaya varieties using molecular genetic engineering techniques that spliced a gene coding for the virus's coat protein into the papaya genome, and today more than 80% of the state's papayas are those varieties.

A dramatic photograph of the unmodified, virus-susceptible papaya trees and the genetically engineered virus-resistant ones growing side by side may be found here. The ones on the left have a marketable yield of approximately nil, while the ones on the right have normal yields.

Papaya-growing countries around the world are developing GE papaya to resist their own specific PRSV strains.

INNATE POTATO AND ARCTIC APPLE

Potatoes are one of the most consumed foods on earth but they suffer from significant losses due to post-harvest bruising. By down-regulating (i.e., turning off) the genes for the enzymes that mediate bruising, at least two companies have developed GE potato varietiesthat resists bruising, potentially saving over a billion pounds from being wasted annually. "Innate" potatoes from the J.R. Simplot Company are bruise-resistant and contain 50%-70% less asparagine, a chemical that when heated to high temperatures is converted to acrylamide, a presumptive carcinogen. The advantage of lower levels of a carcinogen is obvious, but the resistance to bruising is important to sustainability because of the potential to decrease waste. Second-generation Innate potatoes contain an additional trait: resistance to the destructive fungus called late blight, which caused the Irish potato famine of the mid-19th century and is still a problem.

Environmentalists take note: Potatoes resistant to bruising and late blight represent major advances in sustainability, because every serving of french fries and every potato chip made from them represents less farmland and water consumption.

Arctic apples are conceptually similar. Using molecular genetic engineering to reduce the level of the enzymes involved in "enzymatic browning"—the unappetizing discoloration that occurs when an apple is cut or bruised–the fruit is highly resistant to browning. The ingenious biology that made this possible – the insertion of genes in the reverse of their normal orientation (antisense) such that the genes that meditate browning are not expressed — is far more precise and predictable than conventional, older techniques that have been employed to create virtually our entire food supply (including even "heirloom" varieties and the overpriced organic stuff). The beauty of this technology is that it can be transferred to any apple variety relatively quickly. Approximately 40 percent of all apples are wasted, so this technology will increase sustainability and should put downward pressure on prices.

CASSAVA

Cassava is a potato-like tuber that is grown primarily in Africa and the Indian subcontinent, and more than 500 million people rely on it for food and income. It grows in poor soil and drought conditions, making it an important crop for millions in the developing world. But cassava has a few problems. It produces cyanide at levels that require extensive treatment before it can be consumed, and it is low in iron, zinc, beta-carotene (the precursor of vitamin A) and protein. Viral diseases have been known to destroy 100% of a farmer's crop. All of these challenges are being addresse with genetic engineering. Field trials in Africa are showing excellent viral resistance, and scientists have been successful at elevating micronutrients and protein content as well as reducing the cyanide levels by 99%. People in Africa will soon have access to genetically engineered varieties that will help to ensure abundant, healthy cassava crops.

BANANA

More than 90% of current varieties of bananas are derived from cuttings, or clones, of natural mutant bananas which were discovered over 10,000 years ago. Those mutations allow bananas to be sterile and to grow without seeds. For almost a hundred years North America and Europe enjoyed a banana variety called Gros Michel. That ended in the 1950's when fungus virtually wiped out this variety. A different variety, Cavendish, that was resistant to the fungus soon replaced Gros Michel, but it, too, is now threatened by a disease called *Black Sigatoka* that can only be treated by applying massive doses – as many as 50 applications a year — of fungicides. However, that remedy is rapidly losing effectiveness as the fungus becomes more resistant, and the banana could be extinct within the next decade. Current techniques such as conventional cross breeding are limited in scope and effectiveness, but the use of molecular genetic engineering techniques promises to be much more effective.

GOLDEN RICE

Billions of people worldwide get most of their calories and nutrients from rice – and therein lies a problem. Ordinary rice — which itself has been extensively genetically modified over centuries — produces β-carotene, a precursor of vitamin A, in the leaves but not in the grains, where the biosynthetic pathway is turned off during plant development. In "Golden Rice" (GR) — called that because of its golden color — two genes (one from corn, the other from a bacterium) have been inserted into the rice genome by precise molecular techniques of genetic engineering. That modification enables the carotenoid biosynthetic pathway to produce and accumulate β-carotene in the rice grains.

Since a prototype of GR was developed in the year 2000, new lines with ever-higher β-carotene content have been generated, and feeding studies in adult humans have demonstrated that GR is a good source of vitamin A. Why are vitamin A and its precursor, β-carotene, important? Vitamin A is critical for normal vision and also plays a central role in maintaining the integrity of the immune system. The World Health Organization estimates that 250 million preschool children are vitamin A deficient, which causes blindness in 250,000 to 500,000 of them every year. Within 12 months of losing their sight, half die, often from diarrheal diseases or measles.

This ongoing catastrophe is preventable. In theory, the most desirable remedy would be a varied and adequate diet, but this is not always achievable. The reasons are manifold, ranging from traditional preferences to geographical and economic limitations. GR varieties have the advantage of not creating new dependencies or displacing traditional foods. Moreover, they are sustainable because there is no need for public health infrastructure to provide repeated alternative interventions for fortification or supplementation. GR varieties will be given away at no cost to subsistence farmers in the developing world.

Unfortunately, intense lobbying by anti-genetic engineering environmental groups like Greenpeace has slowed the delivery of this humanitarian product. Recently, more than 110 Nobel Laureates published an open letter to Greenpeace asking them to stop their campaign against Golden Rice. The activists' response was to demean the expertise of the Nobelists.

THE PROMISE OF GENETIC ENGINEERING

Molecular genetic engineering of crop plants besides those engineered to be herbicide-tolerant has already made monumental contributions. A 2016 study by British economists Peter Barfoot and Graham Brookes concluded:

> *The insect-resistant (IR) technology used in cotton and corn has consistently delivered yield gains from reduced pest damage. The average yield gains over the 1996-2014 period across all users of this technology has been +13.1% for insect resistant corn and +17.3% for insect resistant cotton relative to conventional production systems. 2014 was also the second year IR soybeans were grown commercially in South America, where farmers have seen an average of +9.4% yield improvements;*

And as discussed above, genetic engineering of papayas has saved the papaya industry in Hawaii and the Innate potato and similar varieties will avoid wastage and be a huge boost to sustainability. As more products move through the pipeline, GE crops with healthy traits that benefit the consumer, reduce losses to pests and diseases, and lower pesticide use will become more common.

Or perhaps we should qualify that statement by saying that they will become more common *if* excessive, unscientific, technique-based government regulation and the relentless opposition of activists can be kept at bay. As University of California Berkeley agricultural economist David Zilberman has observed, excessive regulation "comes at a cost — it prevents the introduction of beneficial innovation, and eventually lack of innovation is a source of heightened risk" to human health and the environment.