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Review

Plant Genetics, Sustainable Agriculture and Global Food Security

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ABSTRACT

The United States and the world face serious societal challenges in the areas of food, environment, energy, and health. Historically, advances in plant genetics have provided new knowledge and technologies needed to address these challenges. Plant genetics remains a key component of global food security, peace, and prosperity for the foreseeable future. Millions of lives depend upon the extent to which crop genetic improvement can keep pace with the growing global population, changing climate, and shrinking environmental resources. While there is still much to be learned about the biology of plant–environment interactions, the fundamental technologies of plant genetic improvement, including crop genetic engineering, are in place, and are expected to play crucial roles in meeting the chronic demands of global food security. However, genetically improved seed is only part of the solution. Such seed must be integrated into ecologically based farming systems and evaluated in light of their environmental, economic, and social impacts—the three pillars of sustainable agriculture. In this review, I describe some lessons learned, over the last decade, of how genetically engineered crops have been integrated into agricultural practices around the world and discuss their current and future contribution to sustainable agricultural systems.

THE number of people on Earth is expected to increase from the current 6.7 billion to 9 billion by 2050. To accommodate the increased demand for food, world agricultural production needs to rise by 50% by 2030 (Royal Society 2009). Because the amount of arable land is limited and what is left is being lost to urbanization, salinization, desertification, and environmental degradation, it no longer possible to simply open up more undeveloped land for cultivation to meet production needs. Another challenge is that water systems are under severe strain in many parts of the world. The fresh water available per person has decreased fourfold in the past 60 years (United Nations Environmental Programme 2002). Of the water that is available for use, ~70% is already used for agriculture (Vorosmarty *et al.* 2000). Many rivers no longer flow all the way to the sea; 50% of the world's wetlands have disappeared, and major groundwater aquifers are being mined unsustainably, with water tables in parts of Mexico, India, China, and North Africa declining by as much as 1 m/year (Somerville and Briscoe 2001). Thus, increased food production must largely take place on the same land area while using less water.

Compounding the challenges facing agricultural production are the predicted effects of climate change (Lobell *et al.* 2008). As the sea level rises and glaciers melt, low-lying croplands will be submerged and river systems will experience shorter and more intense seasonal flows, as well as more flooding (Intergovernmental Panel on Climate Change 2007). Yields of our most important food, feed, and fiber crops decline precipitously at temperatures much >30°, so heat and drought will increasingly limit crop production (Schlenker and Roberts 2009). In addition to these environmental stresses, losses to pests and diseases are also expected to increase. Much of the losses caused by these abiotic and biotic stresses, which already result in 30–60% yield reductions globally each year, occur after the plants are fully grown: a point at which most or all of the land and water required to grow a crop has been invested (Dhlamini *et al.* 2005). For this reason, a reduction in losses to pests, pathogens, and environmental stresses is equivalent to creating more land and more water.

Thus, an important goal for genetic improvement of agricultural crops is to adapt our existing food crops to increasing temperatures, decreased water availability in some places and flooding in others, rising salinity, and changing pathogen and insect threats (World Bank 2007; Gregory *et al.* 2009; Royal Society 2009). Such improvements will require diverse approaches that will enhance the sustainability of our farms. These include more effective land and water use policies, integrated pest management approaches, reduction in harmful inputs, and the development of a new generation of agricultural

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crops tolerant of diverse stresses (Somerville and Briscoe 2001).

These strategies must be evaluated in light of their environmental, economic, and social impacts—the three pillars of sustainable agriculture (Committee on the Impact of Biotechnology on Farm-Level Economics and Sustainability and National Research Council 2010). This review discusses the current and future contribution of genetically engineered crops to sustainable agricultural systems.

WHAT ARE GENETICALLY ENGINEERED CROPS?

Genetic engineering differs from conventional methods of genetic modification in two major ways: (1) genetic engineering introduces one or a few well-characterized genes into a plant species and (2) genetic engineering can introduce genes from any species into a plant. In contrast, most conventional methods of genetic modification used to create new varieties (*e.g.*, artificial selection, forced interspecific transfer, random mutagenesis, marker-assisted selection, and grafting of two species, etc.) introduce many uncharacterized genes into the same species. Conventional modification can in some cases transfer genes between species, such as wheat and rye or barley and rye.

In 2008, the most recent year for which statistics are available, ~30 genetically engineered crops were grown on almost 300 million acres in 25 countries (nearly the size of the state of Alaska), 15 of which were developing countries (James 2009). By 2015, >120 genetically engineered crops (including potato and rice) are expected to be cultivated worldwide (Stein and Rodriguez-Cerezo 2009). Half of the increase will be crops designed for domestic markets from national technology providers in Asia and Latin America.

SAFETY ASSESSMENT OF GENETICALLY ENGINEERED CROPS

There is broad scientific consensus that genetically engineered crops currently on the market are safe to eat. After 14 years of cultivation and a cumulative total of 2 billion acres planted, no adverse health or environmental effects have resulted from commercialization of genetically engineered crops (Board on Agriculture and Natural Resources, Committee on Environmental Impacts Associated with Commercialization of Transgenic Plants, National Research Council and Division on Earth and Life Studies 2002). Both the U.S. National Research Council and the Joint Research Centre (the European Union's scientific and technical research laboratory and an integral part of the European Commission) have concluded that there is a comprehensive body of knowledge that adequately addresses the food safety issue of genetically engineered crops (Committee on Identifying and Assessing Unintended Effects of Genetically Engineered Foods on Human Health and National Research Council 2004; European Commission Joint Research Centre 2008). These and other recent reports conclude that the processes of genetic engineering and conventional breeding are no different in terms of unintended consequences to human health and the environment (European Commission Directorate-General for Research and Innovation 2010).

This is not to say that every new variety will be as benign as the crops currently on the market. This is because each new plant variety (whether it is developed through genetic engineering or conventional approaches of genetic modification) carries a risk of unintended consequences. Whereas each new genetically engineered crop variety is assessed on a case-by-case basis by three governmental agencies, conventional crops are not regulated by these agencies. Still, to date, compounds with harmful effects on humans or animals have been documented only in foods developed through conventional breeding approaches. For example, conventional breeders selected a celery variety with relatively high amounts of psoralens to deter insect predators that damage the plant. Some farm workers who harvested such celery developed a severe skin rash—an unintended consequence of this breeding strategy (Committee on Identifying and Assessing Unintended Effects of Genetically Engineered Foods on Human Health and National Research Council 2004).

INSECT-RESISTANT CROPS

> A truly extraordinary variety of alternatives to the chemical control of insects is available. Some are already in use and have achieved brilliant success. Others are in the stage of laboratory testing. Still others are little more than ideas in the minds of imaginative scientists, waiting for the opportunity to put them to the test. All have this in common: they are *biological* solutions, based on the understanding of the living organisms they seek to control and of the whole fabric of life to which these organisms belong. Specialists representing various areas of the vast field of biology are contributing—entomologists, pathologists, geneticists, physiologists, biochemists, ecologists—all pouring their knowledge and their creative inspirations into the formation of a new science of biotic controls. (Carson 1962, p. 278)

In the 1960s the biologist Rachel Carson brought the detrimental environmental and human health impacts resulting from overuse or misuse of some insecticides to the attention of the wider public. Even today, thousands of pesticide poisonings are reported each year (300,000 deaths globally, ~1200 each year in California alone). This is one reason some of the first genetically engineered crops were designed to reduce reliance on sprays of broad-spectrum insecticides for pest control.

Corn and cotton have been genetically engineered to produce proteins from the soil bacteria *Bacillus*

thuringiensis (*Bt*) that kill some key caterpillar and beetle pests of these crops. *Bt* toxins cause little or no harm to most nontarget organisms including beneficial insects, wildlife, and people (Mendelsohn *et al.* 2003). *Bt* crops produce *Bt* toxins in most of their tissues. These *Bt* toxins kill susceptible insects when they eat *Bt* crops. This means that *Bt* crops are especially useful for controlling pests that feed inside plants and that cannot be killed readily by sprays, such as the European corn borer (*Ostrinia nubilalis*), which bores into stems, and the pink bollworm (*Pectinophora gossypiella*), which bores into bolls of cotton.

First commercialized in 1996, *Bt* crops are the second most widely planted type of transgenic crop. In 2009, *Bt* crops covered >50 million hectares worldwide (James 2009). The genes encoding hundreds of *Bt* toxins have been sequenced (Crickmore 2011). Most of the *Bt* toxins used in transgenic crops are called Cry toxins because they occur as crytalline proteins in nature (Carriere *et al.* 2010; Deacon, http://www.biology.ed.ac.uk/research/groups/jdeacon/microbes/bt.htm). More recently, some *Bt* crops also produce a second type of *Bt* toxin called a vegetative insecticidal protein (Carriere *et al.* 2010; Crickmore 2011).

Bt toxins in sprayable formulations were used for insect control long before *Bt* crops were developed and are still used extensively by organic growers and others. The long-term history of the use of *Bt* sprays allowed the Environmental Protection Agency and the Food and Drug Administration to consider decades of human exposure in assessing human safety before approving *Bt* crops for commercial use. In addition, numerous toxicity and allergenicity tests were conducted on many different kinds of naturally occurring *Bt* toxins. These tests and the history of spraying *Bt* toxins on food crops led to the conclusion that *Bt* corn is as safe as its conventional counterpart and therefore would not adversely affect human and animal health or the environment (European Food Safety Authority 2004).

Planting of *Bt* crops has resulted in the application of fewer pounds of chemical insecticides and thereby has provided environmental and economic benefits that are key to sustainable agricultural production. Although the benefits vary depending on the crop and pest pressure, overall, the U.S. Department of Agriculture (USDA) Economic Research Service found that insecticide use in the United States was 8% lower per planted acre for adopters of *Bt* corn than for non-adopters (Fernandez-Cornejo and Caswell 2006). Fewer insecticide treatments, lower costs, and less insect damage led to significant profit increases when pest pressures were high (Fernandez-Cornejo and Caswell 2006). When pest pressures are low, farmers may not be able to make up for the increased cost of the genetically engineered seed by increased yields. In Arizona, where an integrated pest management program for *Bt* cotton continues to be effective, growers reduced insecticide use by 70% and saved >$200 million from 1996 to 2008 (Naranjo and Ellsworth 2009).

A recent study indicates that the economic benefits resulting from *Bt* corn are not limited to growers of the genetically engineered crop (Hutchison *et al.* 2010). In 2009, *Bt* corn was planted on >22.2 million hectares, constituting 63% of the U.S. crop. For growers of corn in Illinois, Minnesota, and Wisconsin, cumulative benefits over 14 years are an estimated $3.2 billion. Importantly, $2.4 billion of this total benefit accrued to non-*Bt* corn (Hutchison *et al.* 2010). This is because area-wide suppression of the primary pest, *O. nubilalis*, reduced damage to non-*Bt* corn. Comparable estimates for Iowa and Nebraska are $3.6 billion in total, with $1.9 billion for non-*Bt* corn. These data confirm the trend seen in some earlier studies indicating that communal benefits are sometimes associated with planting of *Bt* crops (Carriere *et al.* 2003; Wu *et al.* 2008; Tabashnik 2010).

Planting of *Bt* crops has also supported another important goal of sustainable agriculture: increased biological diversity. An analysis of 42 field experiments indicates that nontarget invertebrates (*i.e.*, insects, spiders, mites, and related species that are not pests targeted by *Bt* crops) were more abundant in *Bt* cotton and *Bt* corn fields than in conventional fields managed with insecticides (Marvier *et al.* 2007). The conclusion that growing *Bt* crops promotes biodiversity assumes a baseline condition of insecticide treatments, which applies to 23% of corn acreage and 71% of cotton acreage in the United States in 2005 (Marvier *et al.* 2007).

Benefits of *Bt* crops have also been well-documented in less-developed countries. For example, Chinese and Indian farmers growing genetically engineered cotton or rice were able to dramatically reduce their use of insecticides (Huang *et al.* 2002, 2005; Qaim and Zilberman 2003; Bennett *et al.* 2006). In a study of precommercialization use of genetically engineered rice in China, these reductions were accompanied by a decrease in insecticide-related injuries (Huang *et al.* 2005).

Despite initial declines in insecticide use associated with *Bt* cotton in China, a survey of 481 Chinese households in five major cotton-producing provinces indicates that insecticide use on *Bt* cotton increased from 1999 to 2004, resulting in only 17% fewer sprays on *Bt* cotton compared with non-*Bt* cotton in 2004 (Wang *et al.* 2008). A separate survey of 38 locations in six cotton-producing provinces in China showed that the number of sprays on all cotton fields dropped by ~20% from 1996 (before widepread cultivation of *Bt* cotton) to 1999 (2 years after widespread cultivation of *Bt* cotton) (Lu *et al.* 2010). This study also indicated a slight increase in insecticide use on all cotton fields from 1999 to 2008.

Although *Bt* cotton has effectively controlled its primary target pest in China (the cotton bollworm *Helicoverpa armigera*), reduced use of broad-spectrum insecticides has apparently increased the abundance of some pests that are not killed by *Bt* cotton (Wu

et al. 2008; Lu *et al.* 2010). In particular, mirids, which are hemipteran insects not targeted by *Bt* cotton, have become more serious pests in China (Lu *et al.* 2010). These results confirm the need to integrate *Bt* crops with other pest control tactics (Tabashnik *et al.* 2010). In Arizona, such an integrated pest management (IPM) approach has been implemented (Naranjo and Ellsworth 2009). In Arizona's cotton IPM system, key pests not controlled by *Bt* cotton are managed with limited use of narrow-spectrum insecticides that promote conservation of beneficial insects (Naranjo and Ellsworth 2009). Mirids such as the Lygus bug (*Lygus hesperus*) are controlled with a feeding inhibitor, and the sweet potato whitefly (*Bemisia tabaci*) is controlled with insect growth regulators (Naranjo and Ellsworth 2009).

One limitation of using any insecticide, whether it is organic, synthetic, or genetically engineered, is that insects can evolve resistance to it. For example, one crop pest, the diamondback moth (*Plutella xylostella*), has evolved resistance to *Bt* toxins under open field conditions. This resistance occurred in response to repeated sprays of *Bt* toxins to control this pest on conventional (nongenetically engineered) vegetable crops (Tabashnik 1994).

Partly on the basis of the experience with the diamondback moth and because *Bt* crops cause a season-long exposure of target insects to *Bt* toxins, some scientists predicted that pest resistance to *Bt* crops would occur in a few years. However, global pest monitoring data suggest that *Bt* crops have remained effective against most pests for more than a decade (Tabashnik *et al.* 2008; Carriere *et al.* 2010). Nonetheless, after more than a dozen years of widespread *Bt* crop use, resistance to *Bt* crops has been reported in some field populations of at least four major species of target pests (Bagla 2010; Carriere *et al.* 2010; Storer *et al.* 2010).

Retrospective analyses suggest that the "refuge strategy"—*i.e.*, creating refuges of crop plants that do not make *Bt* toxins to promote survival of susceptible insects—has helped to delay evolution of pest resistance to *Bt* crops (Carriere *et al.* 2010). The theory underlying the refuge strategy is that most of the rare resistant pests surviving on *Bt* crops will mate with abundant susceptible pests from refuges of host plants without *Bt* toxins. If inheritance of resistance is recessive, the hybrid offspring produced by such matings will be killed by *Bt* crops, markedly slowing the evolution of resistance.

In cases where resistance to *Bt* crops has evolved quickly, one or more conditions of the refuge strategy have not been met. For example, resistance occurred rapidly to the *Bt* toxin Cry1Ac in transgenic cotton in U.S. populations of *Helicoverpa zea*, which is consistent with the theory underlying the refuge strategy because this resistance is not recessive (Tabashnik *et al.* 2008). In other words, the concentration of Cry1Ac in *Bt* cotton was not high enough to kill the hybrid offspring produced by matings between susceptible and resistant *H. zea*. Thus, the so-called "high dose" requirement was not met (Tabashnik *et al.* 2008). In a related case, failure to provide adequate refuges of non-*Bt* cotton appears to have hastened resistance to this same type of *Bt* cotton by pink bollworm in India (Bagla 2010). In contrast, Arizona cotton growers complied with this strategy from 1996 to 2005, and no increase in pink bollworm resistance occurred (Tabashnik *et al.* 2010).

In the United States, *Bt* cotton producing only Cry1Ac is no longer registered and has been replaced primarily by *Bt* cotton that produces two toxins (Carriere *et al.* 2010). More generally, most newer cultivars of *Bt* cotton and *Bt* corn produce two or more toxins. These multitoxin *Bt* crops are designed to help delay resistance and to kill a broader spectrum of insect pests (Carriere *et al.* 2010). For example, a new type of *Bt* corn produces five *Bt* toxins—three that kill caterpillars and two that kill beetles (Dow Agrosciences 2009).

Despite the success of the refuge strategy in delaying insect resistance to *Bt* crops, this approach has limitations, including variable compliance by farmers with the requirement to plant refuges of non-*Bt* host plants. An alternative strategy, where refuges are scarce or absent, entails release of sterile insects to mate with resistant insects (Tabashnik *et al.* 2010). Incorporation of this strategy in a multi-tactic eradication program in Arizona from 2006 to 2009 reduced pink bollworm abundance by >99%, while eliminating insecticide sprays against this pest. The success of such creative multidisciplinary integrated approaches, involving entomologists, geneticists, physiologists, biochemists, and ecologists, provides a roadmap for the future of agricultural production and attests to the foresight of Rachel Carson.

HERBICIDE-TOLERANT CROPS

Weeds are a major limitation of crop production globally because they compete for nutrients and sunlight. One method to control weeds is to spray herbicides that kill them. Many of the herbicides used over the past 50 years are classified as toxic or slightly toxic to animals and humans (classes I, II, and III). Some newer herbicides, however, are considered nontoxic (class IV). An example of the latter, the herbicide glyphosate (trade name Roundup), is essentially a modified amino acid that blocks a chloroplast enzyme [called 5-enolpyruvoyl-shikimate-3-phosphate synthetase (EPSPS)] that is required for plant, but not animal, production of tryptophan. Glyphosate has a very low acute toxicity, is not carcinogenic, and breaks down quickly in the environment and thus does not persist in groundwater.

Some crop plants have been genetically engineered for tolerance to glyphosate. In these herbicide-tolerant crops,

a gene, isolated from the bacterium Agrobacterium encoding an EPSPS protein resistant to glyphosate, is engineered into the plant. Growers of herbicide-tolerant crops can spray glyphosate to control weeds without harming their crop.

Although herbicide-tolerant crops do not directly benefit organic farmers, who are prohibited from using herbicides, or poor farmers in developing countries, who often cannot afford to buy the herbicides, there are clear advantages to conventional growers and to the environment in developed countries. One important environmental benefit is that the use of glyphosate has displaced the use of more toxic (classes I, II, and III) herbicides (Fernandez-Cornejo and Caswell 2006). For example, in Argentina, soybean farmers using herbicide-tolerant crops were able to reduce their use of toxicity class II and III herbicides by 83–100%. In North Carolina, the pesticide leaching was 25% lower in herbicide-tolerant cotton fields compared with those having conventional cotton (Carpenter 2010).

Before the advent of genetically engineered soybean, conventional soybean growers in the United States applied the more toxic herbicide, metolachlor (class III), to control weeds. Metolachlor, known to contaminate groundwater, is included in a class of herbicides with suspected toxicological problems. Switching from metolachlor to glyphosate in soybean production has had large environmental benefits and likely health benefits for farmworkers (Fernandez-Cornejo and McBride 2002).

In the Central Valley of California, most conventional alfalfa farmers use diuron (class III) to control weeds. Diuron, which also persists in groundwater, is toxic to aquatic invertebrates (U.S. Environmental Protection Agency 1983, 1988). Planting of herbicide-tolerant alfalfa varieties is therefore expected to improve water quality in the valley and enhance biodiversity (Strandberg and Pederson 2002). The USDA Animal and Plant Health Inspection Service recently prepared a final environmental impact statement evaluating the potential environmental effects of planting this crop (Usda Animal and Plant Health Inspection Service 2010).

Another benefit in terms of sustainable agriculture is that herbicide-tolerant corn and soybean have helped foster use of low-till and no-till agriculture, which leaves the fertile topsoil intact and protects it from being removed by wind or rain. Thus, no-till methods can improve water quality and reduce soil erosion. Also, because tractor tilling is minimized, less fuel is consumed and greenhouse gas emissions are reduced (Farrell *et al.* 2006; Committee on the Impact of Biotechnology on Farm-Level Economics and Sustainability and National Research Council 2010). In Argentina and the United States, the use of herbicide-tolerant soybeans was associated with a 25–58% decrease in the number of tillage operations (Carpenter 2010). Such reduced tillage practices correlate with a significant reduction in greenhouse gas emissions which, in 2005, was equivalent to removing 4 million cars from the roads (Brookes and Barfoot 2006).

One drawback to the application of herbicides is that overuse of a single herbicide can lead to the evolution of weeds that are resistant to that herbicide. The evolution of resistant weeds has been documented for herbicide-tolerant traits developed through selective breeding, mutagenesis, and genetic engineering. To mitigate the evolution of weed resistance and prolong the usefulness of herbicide-tolerant crops, a sustainable management system is needed. Such approaches require switching to another herbicide or mixtures of herbicides or employing alternative weed control methods (Committee on the Impact of Biotechnology on Farm-Level Economics and Sustainability and National Research Council 2010). Implementation of a mandatory crop diversity strategy would also greatly reduce weed resistance. Newer herbicide-tolerant varieties will have tolerance to more than one herbicide, which will allow easier herbicide rotation or mixing, and, in theory, help to improve the durability of the effectiveness of particular herbicides.

In addition to environmental issues, economic issues related to pollen flow between genetically engineered, nongenetically engineered, and organic crops and to compatible wild relatives are also important to discussions of herbicide tolerance due to possible gene flow. These issues are addressed in the USDA report on genetically engineered alfalfa and are also discussed in other reviews (Ronald and Adamchak 2008; McHughen and Wager 2010; Usda Animal and Plant Health Inspection Service 2010).

VIRAL-RESISTANT CROPS

Although *Bt* and herbicide-tolerant crops are by far the largest acreage, genetically engineered crops on the market, other genetically engineered crops have also been commercialized and proven to be effective tools for sustainable agriculture. For example, in the 1950s, the entire papaya production on the Island of Oahu was decimated by papaya ringspot virus (PRSV), a potyvirus with single-stranded RNA. Because there was no way to control PRSV, farmers moved their papaya production to the island of Hawaii where the virus was not yet present. By the 1970s, however, PRSV was discovered in the town of Hilo, just 20 miles away from the papaya growing area where 95% of the state's papaya was grown. In 1992, PRSV had invaded the papaya orchards and by 1995 the disease was widespread, creating a crisis for Hawaiian papaya farmers.

In anticipation of disease spread, Dennis Gonsalves, a local Hawaiian, and co-workers initiated a genetic strategy to control the disease (Tripathi *et al.* 2006). This research was spurred by an earlier observation that

transgenic tobacco expressing the coat protein gene from tobacco mosaic virus showed a significant delay in disease symptoms caused by tobacco mosaic virus (Powell-Abel *et al.* 1986).

Gonsalves's group engineered papaya to carry a transgene from a mild strain of PRSV. The transgene was designed with a premature stop codon in the PRSV coat protein sequence to prevent expression of a functional coat protein because, at the time of engineering, it was thought that the protein itself was an important factor in resistance. RNA analysis later revealed that the plants with the best resistance exhibited the least detectable message, which was suggestive of the involvement of an RNA silencing mechanism (Tripathi *et al.* 2006).

Conceptually similar (although mechanistically different) to human vaccinations against polio or small pox, this treatment "immunized" the papaya plant against further infection. The genetically engineered papaya yielded 20 times more papaya than the nongenetically engineered variety after PRSV infection. By September 1999, 90% of the Hawaiian farmers had obtained genetically engineered seeds, and 76% of them had planted the seeds. After release of genetically engineered papaya to farmers, production rapidly increased from 26 million pounds in 1998 to a peak of 40 million pounds in 2001. Today, 80–90% of Hawaiian papaya is genetically engineered. There is still no conventional or organic method to control PRSV. Funded mostly by a grant from the USDA, the project cost ~$60,000, a small sum compared to the amount the papaya industry lost between 1997 and 1998, prior to the introduction of the genetically engineered papaya.

GENETICALLY ENGINEERED CROPS ON THE HORIZON

Peer-reviewed studies of the genetically engineered crops currently on the market indicate that such crops have contributed to enhancing global agricultural sustainability. As reviewed here, benefits include massive reductions in insecticides in the environment (Qaim and Zilberman 2003; Huang *et al.* 2005), improved soil quality and reduced erosion (Committee on the Impact of Biotechnology on Farm-Level Economics and Sustainability and National Research Council 2010), prevention of the destruction of the Hawaiian papaya industry (Tripathi *et al.* 2006), enhanced health benefits to farmers and families as a result of reduced exposure to harsh chemicals (Huang *et al.* 2002, 2005), economic benefits to local communities (Qaim *et al.* 2010), enhanced biodiversity of beneficial insects (Cattaneo *et al.* 2006), reduction in the number of pest outbreaks on neighboring farms growing nongenetically engineered crops (Hutchison *et al.* 2010), and increased profits to farmers (Tabashnik 2010). Genetically engineered crops have also dramatically increased crop yields—>30% in some farming communities (Qaim *et al.* 2010). As has been well-documented for *Bt* cotton in Arizona, the ability to combine innovations in farming practice with the planting of genetically engineered seed has had a huge positive benefit/cost ratio, far beyond what could be achieved by innovating farming practices or planting genetically engineered crops alone. The benefit/cost ratio of *Bt* crops is the highest for any agricultural innovation in the past 100 years.

There are dozens of useful genetically engineered traits in the pipeline, including nitrogen use efficiency (Arcadia Biosciences 2010). Success of crops enhanced for this efficiency would reduce water eutrophication caused by nitrogenous compounds in fertilizers and greenhouse gas emissions resulting from the energy required to chemically synthesize fertilizers.

The USDA Animal and Plant Health Inspection Service has developed a transgenic plum variety, the "HoneySweet," which is resistant to Plum Pox, a plant disease that infects plum and other stone fruit trees, including peach, nectarine, plum, apricot, and cherries. Although Plum Pox is very rare in the United States, and its outbreaks are immediately eradicated, the HoneySweet variety was developed as a precautionary measure to avoid a major disruption in the availability of plums, prunes, and other stone fruits should Plum Pox become widespread as is already the case in Europe Usda Animal and Plant Health Inspection Service 2009).

Other promising applications of genetic engineering are those that affect staple food crops. For example, rice is grown in >114 countries on six of the seven continents. In countries where rice is the staple food, it is frequently the basic ingredient of every meal. Thus, even modest changes in tolerance to environmental stress or enhanced nutrition in rice can have a large impact in the lives of the poor.

With regard to nutritional enhancements, some efforts have focused on vitamin deficiencies. Vitamin A deficiency is a public health problem in >100 countries, especially in Africa and Southeast Asia, affecting young children and pregnant women the most (Golden Rice Project 2010). Worldwide, >124 million children are estimated to be vitamin A-deficient. Many of these children go blind or become ill from diarrhea, and nearly 8 million preschool-age children die each year as the result of this deficiency. Researchers estimate that 6000 children and young mothers die every day from vitamin A deficiency-related problems (Potrykus 2010). The World Health Organization estimates that improved vitamin A nutritional status could prevent the deaths of 1.3–2.5 million late-infancy and preschool-age children each year (Humphrey *et al.* 1992).

To combat vitamin A deficiency, the World Health Organization has proposed an arsenal of nutritional "well-being weapons," including a combination of breastfeeding and vitamin A supplementation, coupled with long-term solutions, such as promoting vitamin A-rich diets and food fortification. In response to this challenge, a group of Rockefeller Foundation-

supported scientists decided to try to fortify rice plants with higher levels of carotenoids, which are precursors to vitamin A. Using genetic engineering, they introduced a gene from daffodils (which make carotenoids, the pigment that gives the flower its yellow color) and two genes from a bacterium into rice (Ye *et al.* 2000). The resulting geneticially engineered golden and carotenoid-rich rice plants were named "Golden Rice."

Results from human feeding studies indicate that the carotenoids in the second generation of Golden Rice (called Golden Rice-2) can be properly metabolized into the vitamin A that is needed by children (Tang *et al.* 2009). One 8-ounce cup of cooked Golden Rice-2 provides ~450 μg of retinol, which is equivalent to 50–60% of the adult Recommended Dietary Allowance of vitamin A. Other studies support the idea that widespread consumption of Golden Rice would reduce vitamin A deficiency, saving thousands of lives (Stein *et al.* 2006). The positive effects of Golden Rice are predicted to be most pronounced in the lowest income groups at a fraction of the cost of the current supplementation programs (Stein *et al.* 2006, 2008). If predictions prove accurate, this relatively low-tech, sustainable, publicly funded, people-centered effort will complement other approaches, such as the development of home gardens with vitamin A-rich crops, such as carrots and pumpkins.

In a sense, the resulting nutritionally enhanced rice is similar to vitamin D-enriched milk—except the process is different. Vitamin A fortification of rice is also similar to adding iodine to salt, a process credited with drastically reducing iodine-deficiency disorders in infants. Worldwide, iodine deficiency affects ~2 billion people and is the leading preventable cause of mental retardation. The benefits of iodized salt are particularly apparent in Kazakhstan where local food supplies seldom contain sufficient iodine and where fortified salt was initially viewed with suspicion. Campaigns by the government and nonprofit organizations to educate the public about fortified salt required both money and political leadership, but they eventually succeeded. Today, 94% of households in Kazakhstan use iodized salt, and the United Nations is expected to certify the country officially free of iodine-deficiency disorders (Ronald and Adamchak 2008).

The development of genetically engineered crops that are tolerant of environmental stresses is also predicted to be broadly beneficial. Such crops are expected to enhance local food security, an issue of importance especially for farmers in poorer nations that have limited access to markets and are now often dependent on others for their staple foods (Royal Society 2009).

The development of submergence tolerant rice (Sub1 rice), through a nongenetically engineered process that involved gene cloning and precision breeding, demonstrates the power of genetics to improve tolerance to environmental stresses such as flooding, which is a major constraint to rice production in South and Southeast Asia (Xu *et al.* 2006). In Bangladesh and India, 4 million tons of rice, enough to feed 30 million people, are lost each year to flooding. Planting of Sub1 rice has resulted in three- to fourfold yield increases in farmers' fields during floods compared to conventional varieties. Although the Sub1 rice varieties provided an excellent immediate solution for most of the submergence-prone areas, a higher and wider range of tolerance is required for severe conditions and longer periods of flooding. With increasing global warming, unusually heavy rainfall patterns are predicted for rain-fed as well as irrigated agricultural systems. For these reasons, we and others have identified additional genes that improve tolerance (Seo *et al.* 2011). Such genes may be useful for the development of "Sub1^{plus}" varieties.

In Africa, three-quarters of the world's severe droughts have occurred over the past 10 years. The introduction of genetically engineered drought-tolerant corn, the most important African staple food crop, is predicted to dramatically increase yields for poor farmers (African Agricultural Technology Foundation 2010). Drought-tolerant corn will be broadly beneficial across almost any non-irrigated agricultural situation and in any management system. Drought-tolerance technologies are likely to benefit other agricultural crops for both developed and developing countries.

In addition to environmental stresses, plant diseases also threaten global agricultural production (Borlaug 2008). For example, an epidemic of stem rust threatens wheat, a crop that provides 20% of the food calories for the world's people. Because fungal spores travel in the wind, the infection spreads quickly. Stem rust has caused major famines since the beginning of history. In North America, huge grain losses occurred in 1903 and 1905 and from 1950 to 1954. During the 1950s, Norman Borlaug and other scientists developed high-yielding wheat varieties that were resistant to stem rust and other diseases. These improved seeds not only enabled farmers around the world to hold stem rust at bay for >50 years but also allowed for greater and more dependable yields. However, new strains of stem rust, called Ug99 because they were discovered in Uganda in 1999, are much more dangerous than those that destroyed as much as 20% of the American wheat crop 50 years ago. Effective resistance does not exist in American wheat and barley varieties, but recently resistance was identified in African varieties and molecular markers mapped to facilitate introgression of the trait using marker-assisted selection (Steffenson 2011).

Bananas and plantains are the world's fourth most important food crop after rice, wheat, and maize. Approximately one-third of the bananas produced globally are grown in sub-Saharan Africa, where the crop provides >25% of the food energy requirements for >100 million people in East Africa alone. Banana Xanthomonas wilt disease, caused by the Gram-negative bacterium *Xanthomonas vasicola* pv. *musacearum*, is a

major threat to banana productivity in eastern Africa (Tripathi *et al.* 2009; Studholme *et al.* 2010). Cavendish banana, which represents 99% of export bananas, is threatened by a virulent form of the soil-borne fungus *Fusarium oxysporum* called Tropical Race Four (Peed 2011). The fungal leaf spot disease Black Sigatoka, caused by the ascomycete *Mycosphaerella fijiensis*, has spread to banana plantations throughout the tropics and is increasingly resistant to chemical control (Marin *et al.* 2003). Research to develop new methods to control these diseases of banana are underway in several laboratories.

CONCLUSION

For hundreds of years, farmers have relied on genetically improved seed to enhance agricultural production. Without the development of high-yielding crop varieties over recent decades, two to four times more land would have been needed in the United States, China, and India to produce the same amount of food. Looking ahead, without additional yield increases, maintaining current per capita food consumption will necessitate a near doubling of the world's cropland area by 2050. By comparison, raising global average yields to those currently achieved in North America could result in a very considerable *sparing* of land (Waggoner 1995; Green *et al.* 2005). Because substantial greenhouse gases are emitted from agricultural systems, and because the net effect of higher yields is a dramatic reduction in carbon emissions (Burney *et al.* 2010), development and deployment of high-yielding varieties will be a critical component of a future sustainable agriculture.

Thus, a key challenge is to raise global yields without further eroding the environment. Recent reports on food security emphasize the gains that can be made by bringing existing agronomic and food science technology and know-how to people who do not yet have it. These reports also highlight the need to explore the genetic variability in our existing food crops and to develop new genetic approaches that can be used to enhance more ecologically sound farming practices (Naylor *et al.* 2007; World Bank 2007; Royal Society 2009).

Despite the demonstrated importance of genetically improved seed, there are still agricultural problems that cannot be solved by improved seed alone, even in combination with innovative farming practices. A premise basic to almost every agricultural system (conventional, organic, and everything in between) is that seed can take us only so far. Ecologically based farming practices used to cultivate the seed, as well as other technological changes and modified government policies, clearly are also required.

In many parts of the world, such policies involve building local educational, technical, and research capacity, food processing capability, storage capacity, and other aspects of agribusiness, as well as rural transportation and water and communications infrastructure. The many trade, subsidy, intellectual property, and regulatory issues that interfere with trade and inhibit the use of technology must also be addressed to assure adequate food availability to all. Despite the complexity of many of these interrelated issues, it is hard to avoid the conclusion that ecological-farming practices using genetically engineered seed will play an increasingly important role in a future sustainable agriculture.

Fourteen years of extensive field studies (Carpenter 2010) have demonstrated that genetically engineered crops are tools that, when integrated with optimal management practices, help make food production more sustainable. The vast benefits accrued to farmers, the environment, and consumers explain the widespread popularity of the technology in many regions of the world. The path toward a future sustainable agriculture lies in harnessing the best of all agricultural technologies, including the use of genetically engineered seed, within the framework of ecological farming.

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