The History and Future of GMOs in Food and Agriculture

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Anthropologists tell us that early humans lived a hunter-gatherer lifestyle and that around 10,000 years ago they started to transition into an agricultural lifestyle that was to last until modern times and the industrial revolution (18). Over the millennia agriculturalists domesticated crops and animals to suit the needs of improved production, resistance to diseases and pests, and to serve human preferences (see for example www.foodtimeline.org/). In the process of domestication of crop plants, desirable traits were selected from the numerous random genetic modifications that occur in each crop generation. This domestication led to improved crops from a human perspective, although it could also be called counter-Darwinian selection since it was invariably accompanied by a loss of fitness of the plant—most of our crops never existed in the wild and can, in fact, no longer survive without human intervention and care (31). Plants such as strawberries, wheat, cabbage, corn, and almost all the rest of our crops descended from ancestors that are not recognizably similar to the plants we grow today.

In slightly more than a century an array of remarkable changes has occurred in human society—many of them based on the emergence of modern high productivity methods in industry and agriculture (18). The industrial revolution sparked a migration from the farm to the city. In 1875, 80% of Americans lived in rural areas and farms, while today that number stands at less than 1.5% (U.S. Census Bureau). The migration was made possible by the introduction of machinery that reduced the need for labor, improved seeds, mineral and synthetic fertilizers (and later chemical protectants), and improved techniques of farming, as well as better land and water stewardship. These advancements were extended globally by the Green Revolution, initiated by the work of Nobel Peace Prize winner Norman Borlaug. The resultant agricultural revolution his work supported literally lifted China, India, and a host of other nations out of a cycle of starvation and recurrent famine.

During the century in which modern agriculture emerged, crop plants were strikingly improved through the application of modern scientific breeding methods that drew heavily on seminal research in genetics—Darwin, who characterized hybridization between plant species, and Mendel, who is well-known for establishing the laws governing the heritability of traits, come to mind as founders of the modern era of plant breeding (21). Increases in productivity of corn from about 10 bushels/acre to more than 200 bushels per acre in less than 125 years at the historic Morrow Plots located on the campus of the University of Illinois in Urbana-Champaign is but one example of dramatic increases in agricultural productivity (http://agronomyday.cropsci.uiuc.edu/2001/morrow-plots/).

From early on researchers understood that there must be a class of cellular molecules responsible for coding all the traits that make up an organism. They postulated that each specific trait was encoded by a gene and they deduced that the genes or traits were inseparable from chromosomes. In a hallmark paper, Avery demonstrated that the bacteria *Pneumococcus* could be transformed by DNA isolated from another bacterium—that is to say traits could be transferred through transfer of DNA from a donor to a recipient cell (6). Avery had proven that DNA was the genetic material. By 1954 Watson and Crick had described the DNA double helix and the central dogma emerged: DNA encoded genes, which were then transcribed into messenger RNA (mRNA) that were then translated by ribosomes into proteins—each gene encoding one unique protein.

Thus, the modern science of molecular biology was born. Researchers added rapidly to the understanding of how genes function; how DNA, RNA, and protein are synthesized; and how the proteins themselves are encoded. In 1963, Nobel Laureate Marshall Nirenberg and his collaborators at the National Institutes of Health (NIH) deciphered the genetic code itself (29). It was subsequently shown that all living cells used essentially the identical code that must therefore have evolved very early in evolution. Enzymes that could cut and paste DNA were subsequently described, and in 1973 these were used, along with the principles of transformation described by Avery, to transform the bacterium *Escherchia coli* with recombinant DNA (e.g., rDNA is DNA spliced together in a test tube—albeit with enzymes and DNA pieces isolated from living organisms; 16). The process of inserting rDNA into a living cell became known as genetic engineering and it catalyzed the foundation of a new industry that with great hubris called itself the biotechnology industry. This use of the name biotechnology somehow overlooked millennia of experience in the use of living systems for useful purposes (bread, beer, wine, cheese, industrial chemicals, antibiotics, and so forth) that are also part of what must be more broadly called biotechnology.

It was obvious that there were many very useful applications of this new technology, and that many of these could be very profitable. In the ensuing years the biotechnology industry succeeded in producing pharmaceuticals, chemicals, enzymes, and a list of other products that have made it a multi-billion dollar industry. By 1988, genes had been successfully inserted into soybeans (22), paving the way for what is now the world's leading genetically engineered crop, glyphosate-tolerant soybeans. Through the insertion of a single gene that encodes an

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alternative form of a key enzyme involved in aromatic amino acid biosynthesis, the soybean is made tolerant to the herbicide glyphosate, which affords farmers inexpensive, labor and energy efficient, and environmentally sound weed control (3,4,9,10). Today more than 70% of the world's soybeans are genetically engineered, or transgenic, varieties (26).

Over the last decade, transgenic crops bred using modern biotechnology have been planted on more than a billion acres across the globe (26). More than 10.3 million farmers, 8.5 million of them in developing countries, will plant more than 250 million acres of biotech corn, canola, cotton, and soybeans along with small amounts of bioengineered papaya, sugarbeets, sweetcorn, and squash (26). Farmers elect to pay more for seeds that will produce higher yields, require less chemical inputs, reduce labor, and shrink the environmental footprint of agriculture—poor smallholders in developing countries are especially eager to realize greater yields at lower cost with less danger of exposure to toxic pesticides. It has been estimated that this technology has brought farmers around the world $27 billion in additional profits, reduced pesticide application by 224 million kg, reduced the environmental impact associated with pesticide use by 14%, and reduced greenhouse gas emissions from agriculture by the equivalent of removing 4 million cars from the road (9). It has been a remarkable success story—in fact, transgenic crop technology has been adopted faster than any other technology in the history of agriculture. All of this has been realized without any adverse effect to agriculture or the environment and with no additional risk to the food system or the consumer. There is an excellent textbook on this topic, *Plants, genes, and crop biotechnology,* which explains the challenges facing world agriculture and how plant breeders use modern molecular methods to solve agricultural challenges (15). Another excellent book that explains the science and risks of GMOs is *Mendel in the Kitchen: A Scientist's View of Genetically Modified Foods* (19).

How can we conclude that there has been no risk to the consumer? Risk in the food system is, of course, relative or comparative. We can only compare the safety of one food, crop, or technology to another on a case-by-case basis. No food is 100% safe and no technology for processing a food is 100% safe. In the 1980s the U.S. National Academy of Science (NAS) was asked by the White House to look at the potential hazards posed by transgenic crops. The NAS concluded (28), and they have reiterated this position several times, that in spite of many imagined hazards, transgenic plants pose no new or unusual risks to agriculture, the environment, or consumers. The National Research Council (NRC) followed with the conclusion that crops produced through biotechnology should be as safe or safer than those produced by other methods (30); NRC pointed to the need to assess the safety of the product per se, rather than the plant-breeding technology used in its development. Paradoxically—for reasons that we will discuss shortly—the U.S. government agencies did not heed the NAS and NRC. While avowing advocacy to the statement that transgenic crops pose no new or different risks and that we should judge the product and not the process, the FDA, USDA, and EPA set in place a coordinated interagency framework for regulation and premarket safety evaluation that is reserved exclusively for transgenic products of biotechnology (14). If they pose no new or different risks, why did governments choose to regulate these crops?

The answer to that question is complex, but can probably be reduced to two key factors: 1) government regulators were asked to address the issue of transgenic crop safety, and they did what regulators do: they developed a regulatory paradigm, and 2) industry and environmental NGOs—an odd combination indeed—wanted transgenic crops regulated. NGOs wanted the regulation because of their concerns about safety, and industry sought it because they wanted a process that would give their new products a government stamp of approval.

The brief history of transgenic crops written thus far in this article has been deliberately incomplete. An important part of the story has not been told. As it happens, when recombinant DNA was first inserted into living cells to launch the biotechnology industry, it was not without criticism and concern—indeed scientists themselves were concerned that they might open Pandora's box and convened what is now called the Asilomar conference to develop guidelines for safe experimentation and use of recombinant DNA (7). NIH was ultimately tasked with the responsibility to establish the RAC (Recombinant Advisory Committee) that developed and oversaw safe use of rDNA. The scientists acted in the most precautionary and responsible manner, but in so doing they sent the message that rDNA was powerful and potentially dangerous stuff. Ultimately, the NIH guidelines were relaxed to a more reasonable standard of safety. Today, recombinant DNA experiments are performed in high schools across the United States.

There was a willing audience for scientists' dire precautionary incantations. Anti-rDNA activists cautioned that we should not play God with nature, that we did not understand the complexities of nature, and that we invariably cause havoc when we interfere with nature (23). In my opinion, there were strong undercurrents of anti-capitalist and anti-corporate politics to the opposition—somewhat difficult to understand since socialist thought traditionally views science and technology as the potential salvation of the working class. Concerns about genetic engineering of organisms resonated with environmental NGOs who were looking for new causes. Pesticides had been vanquished, nuclear testing had stopped, and whaling appeared to have been curbed; the environmental movement needed a new cause that could mobilize followers and attract contributions. The movement learned early on that nothing motivates like fear—a point to which we will return. In a masterstroke, anti-GMO activists seized on a term that regulatory scientists sometimes used in reference to transgenic plants: genetically modified organisms (GMOs). Never mind that plant breeders had been genetically modifying plants for years, the term GMOs stuck to transgenic plants. They told us that these GMO plants never existed in nature, that they were unnatural because genes had been inserted into them from other species, that we did not evolve with these plants and would be unable to metabolize them, that these plants would be dangerous for the environment, that they would create genetic pollution, and that they would ultimately fail at their intended purpose.

Quite literally thousands of consumer, environmental, and charitable NGOs have participated in a well-organized, well-financed, and professionally managed global campaign against GMOs. They have been supported by governments, the organic food industry, the chemical industry, food manufacturing industry, and food retailers among others. Why would food manufacturers and retailers fight GMOs? Simple, it helps them sell more expensive GMO-free products (20). The anti-GMO movement has managed to spread a long list of hypothetical risks and fears to consumers across the globe by getting their stories placed on TV, radio, and in print. Global coverage of GMOs in the media has been 90–95% negative (1,2). Not surprisingly, the mere mention of GMO has a negative connotation with consumers. Nobody wants their food to be "genetically modified!" The anti-GMO campaign has had a larger impact in some countries than others, and consumer opinion varies around the globe. One fact is clear: the anti-GMO campaign has defined what a GMO is in the minds of consumers around the world—

they have quite literally framed the debate and the issues. Governments have responded with strict regulation of GMOs in order to assure consumers that the products are safe.

Of course one must be careful in interpreting the poorly designed studies about consumer attitudes toward GMOs. If a study asks "are you concerned about eating GMOs?" "are you afraid of GMOs?" or "do you think GMOs are safe to eat?" you can throw it out—those leading questions are not good social science research methodology. The International Food Information Council in Washington, DC, does frequent surveys of consumer attitudes in the United States about GMOs, and they find consumers in the United States are not concerned about GMO safety (25).

The anti-GMO campaign must be considered to have been successful in spite of the billions of acres of GMOs that will be planted in 2008 and beyond. GMO potatoes were taken off the market because processors and McDonald's feared consumer rejection, and other products have been kept from entering the market. Only 22 countries now grow GMO crops in spite of the spectacular results where they are grown. Zambia rejected GMO food aid in 2002 (12). The costs of regulation are unnecessarily high; a minimum estimate of costs is \$6–15 million, and the costs for some products are rumored to have been as high as \$50–100 million (27). Mandatory labels required in many localities mean that repetitive testing of lots must be done at each step in the food chain adding cost to both GMO-free and GMO-containing products. I would maintain that GMO testing buys a consumer exactly zero additional food safety. Trade in grain and food ingredients is made more complex and frustrating. Farmers who want to grow GMOs are as frustrated as neighboring organic farmers who are certain that GMO pollen will invade their fields and "pollute" their crops.

The question is where do we go from here. The best that can be said is that it will take a great deal of unbiased transparent information and dialog to resolve concerns about GMOs. Passion against GMOs runs deep in only a small percentage of the population, but many consumers, and certainly many organizations, have become fixed in their opposition—which is to say that they have formed an opinion and moved on to other issues. On the other hand, there are certain inescapable realities that may change opinions. In the following paragraphs several of these will be briefly described.

There are tens of thousands of new uses of transgenic technology growing in greenhouses in government research laboratories, at universities, and in industry labs around the world. Some of these are nearing the market. In the immediate future we will see heart-healthy, plant-derived oils entering the market with low transfat, high mono-unsaturated, and omega-3 fatty acid–containing varieties leading the list. Soybeans that make better tasting products with improved color, solubility, and protein functionality are not far off. Wheat proteins that have been optimized for their processing characteristics are a laboratory reality. Crops grown without pesticides that can give good yields in moderate droughts are in the greenhouse. Blight resistant potatoes that would have averted the Irish Potato Famine are being test planted in Europe. Plants that do bioremediation of toxic chemical spills or that produce pharmaceutical proteins less expensively and more safely are already in the fields. The possibilities are simply endless. Transgenic technology is a powerful tool in the hands of plant breeders.

It is hard to believe that a technology can be misunderstood and inappropriately regulated forever. Over the last decade evidence has accumulated that demonstrates that conventional breeding produces large random mutations in DNA while biotech molecular methods are more precise and defined and much less disruptive at the DNA level. It has been shown that genes frequently cross species barriers in nature and that conventional plant breeding depends on the trans-species movement of genes. It has also been demonstrated that what are called GMOs are more similar to the crop from which they are derived at the DNA, protein, and metabolite level than are conventional varieties. It turns out that, based on the scientific evidence, it is conventional crops that should be called GMOs. Simply put, the perceived hazards of transgenic technology are fiction. If nothing else, this demonstrates the tremendous power that comes from framing the definition of this technology for the public eye by those who oppose it.

There are signs of hope in that an increasing number of scientists, including a few government regulators, are stepping forth and discussing the risks (or lack of risks?) of this technology. European food safety experts have openly suggested that GMOs should not be regulated any differently than other novel foods or crops produced by other breeding techniques (11), and American counterparts have suggested that it is time to ratchet back the regulatory stranglehold on GMOs and make regulation commensurate with real risk rather than perceived hazard (8). IFT published an expert report that explains in depth the safety and miniscule risks associated with GMOs (24).

Almost a billion people will go to bed hungry in the world tonight (see www.fao.org and www.unmillenniumproject.org/; 12). More than a billion live on less than a dollar a day and billions have one or more nutrient deficiencies. Draught, loss of water resources, and saline or infertile soils, along with the lack of resources to buy inputs such as seeds and fertilizers, challenge more than a billion people who subsist on small farms. World population will grow 50% in the next few decades (32); most of the growth will be in developing countries, yet land available for farming will continue to shrink by 1.5% per annum. The FAO tells us that we must double food production in the next 20–30 years or hunger will worsen significantly. For example, the world will experience at least a 400-million-tons-per-annum deficit in cereal grain production by 2025 (this is an estimate that was made before biofuels recently became fashionable). Will biotechnology solve these problems? Of course not, they are complex multifaceted problems that will require complex solutions. But that is not the right question; it is foolish to ask one technology to solve all of the world's ills, and it is equally foolish to reject a technology because it cannot solve all of the worlds' problems. Is there a role for biotechnology in solving the problems we face in agriculture? The answer to that question is a most emphatic yes. It is, in fact, hard to imagine how we could accomplish what we need to in agriculture without biotechnology!

There are those who tell us that we should abandon biotechnology and live in harmony with nature. Many who drive luxury cars, who fly jets to remote vacation destinations, who eat organic food (5), who live the healthiest, safest, and most comfortable lives in the history of our planet, are telling us that while they don't mind a little industrial technology, they simply deplore the industrialization of agriculture (see for example the movie *The Future of Food*, produced by D. Koons-Garcia; see also 13). They want their food produced in the old-fashioned, presumably more wholesome, traditional way—this from a consuming public that, for the most part, has never been on a farm and certainly not a farm, market, butcher shop, or slaughterhouse of the 1890s. Americans of the 1890s lived to age 40 or 45 and frequently died from starvation if food poisoning or tuberculosis didn't fell them first. Life then was not the romanticized existence fantasized by those who yearn for the "good old days" and the traditional means of production.

We live in a culture of fear. People are afraid of virtually everything and savvy operators of every stripe have learned to exploit that fear. Michael Crichton recently wrote in "State of Fear" about the culture of fear and the need to look at matters objectively and with the best available science (17). How does the food industry do on exploiting fear? "No MSG." "All Natural." "No Artificial Anything." "Our job is to give consumers what they want." Apparently it's okay to exploit ignorance and fear as long as you can claim that it's not your job to educate consumers. Let me close by asking you a question. Are you doing your part to resolve the great GMO controversy?

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