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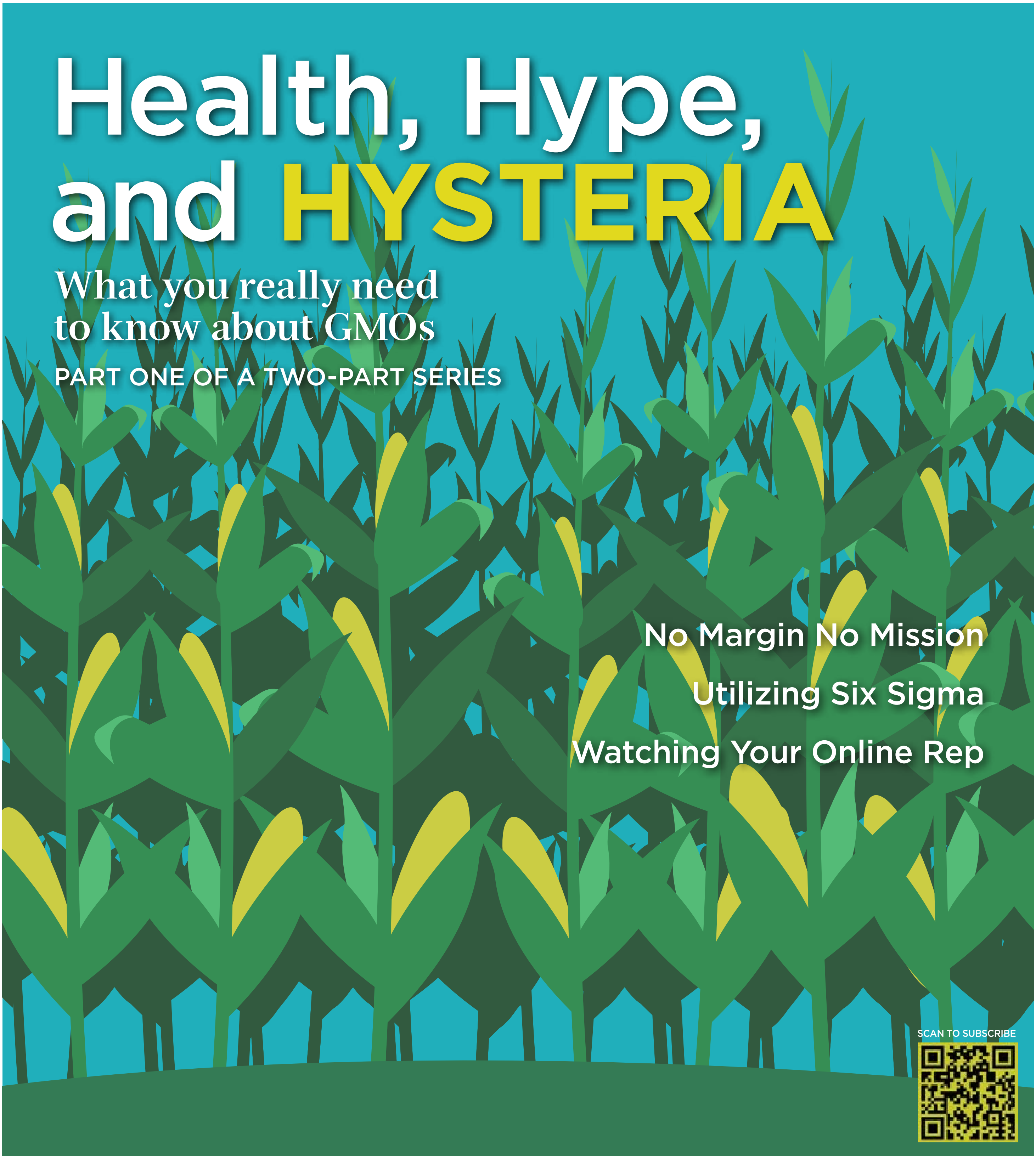

By **Claudia S. Copeland, PhD**

HEALTH, HYPE, AND HYSTERIA

Part one in a two-part series on GMOs

Every year, an estimated 250,000 to 500,000 children go blind due to vitamin A deficiency. According to the World Health Organization, half of these children will die within 12 months of losing their sight. This is because rice is the staple food for many impoverished people without access to high-quality, varied produce, and conventional rice does not provide vitamin A. Despite decades of global public health efforts, vitamin A deficiency continues to be a public health problem in more than half of all countries, especially in Africa and South-East Asia. What if it were possible to create a new strain of rice that was rich in vitamin A? In the late 1980s, a team of molecular biologists supported by the Rockefeller Foundation set to work using the new techniques they were developing in the lab to address this global challenge. Over a decade later, in 2005, a new strain of vitamin A-rich rice, dubbed Golden Rice, was being field tested right here in Louisiana.

Golden Rice grain compared to white rice grain in screenhouse of Golden Rice plants.

IMAGE BY INTERNATIONAL RICE RESEARCH INSTITUTE (IRRI)

Using bioengineering techniques, they introduced genes from daffodil and the bacterium Pantoea ananatis into a commercial rice genome, and then spent years optimizing the rich golden-orange colored rice. One bowl now provides about half of a person's daily requirement for Vitamin A. For its work, the non-profit Golden Rice Project–in particular Drs. Ingo Potrykus, Peter Beyer, and Adrian Dubock–won a 2015 Patents for Humanity award.

According to the Golden Rice Project humanitarian board, "Once locally developed varieties containing the Golden trait have cleared the regulatory hurdles at the national level, they will be made available to subsistence farmers free of charge. The seed will become their property and they will also be able to use part of their harvest to sow their next crop, free of cost. Golden Rice is compatible with farmers using traditional farming systems, without the need for additional agronomic inputs. Therefore, no new dependencies are created."

In other words, this is a not-for-profit project that is committed to giving free nutrient–enhanced seeds to farmers in developing countries for the purpose of saving lives. A win-win project to be sure–what's not to love about this?

And yet, not everyone is happy, and some are downright furious. Greenpeace, opposed to all genetically modified organisms, claims that Golden Rice is an industry-sponsored ploy to introduce GMOs to the world; an agricultural trojan horse that "poses risks to human health, and could compromise food, nutrition, and financial security."

Though they present no solid evidence supporting their claims about human health risks, they have a point about Golden Rice promoting GMOs. Dr. Steve Linscombe, the LSU AgCenter's regional director and a key collaborator in the Golden Rice project through LSU's field testing, openly states, "We look at this as a good mechanism for informing the public that genetic engineering does have a lot of positive benefits. This is just one example of many things to come down the road. This is the first step of many different things that can be accomplished with genetic engineering–and not just in rice."

But is this a good thing? Peruse the internet and you'll hear plenty of voices decrying the danger of GMOs. There is unease about tinkering with nature, and this fear

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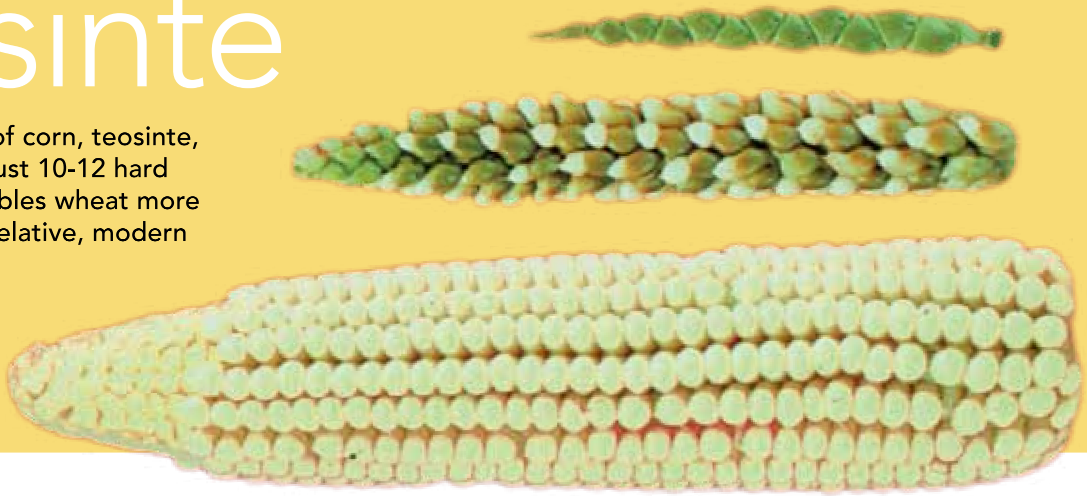


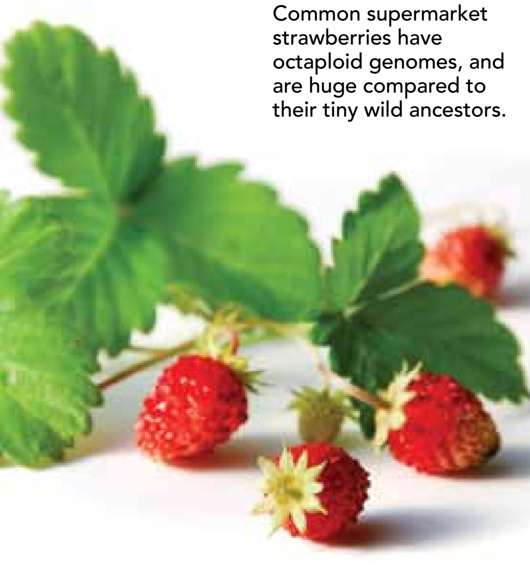
The wild ancestor of corn, teosinte, has tiny ears with just 10-12 hard kernels, and resembles wheat more than its succulent relative, modern commercial maize.

has been further increased by the lack of labeling of GMO food products. Concerned consumers feel like anything they eat could contain shadowy, unknown dangers. Dr. Shahla Wunderlich, in a recent publication in *Advances in Nutrition*, examined consumer knowledge and preference regarding GMOs. Awareness and understanding of GM foods was extremely low and subject to the way in which the investigators framed their questions. At the root of the issue is the newness of bioengineered food for humans—these products have not been around long enough for long-term epidemiological studies of humans. She believes that there "have not been enough research studies and evidence-based publications to confirm the health effects (positive or negative) of GM foods, as they have been only available commercially for purchase since the 1990s. Many consumers are, therefore, puzzled as they receive their information about GMO food products from the media, internet, and other news sources that may not be reliable. The scarcity of scientific research in this area leads to uncertainty among consumers about the direct health effects of GMO products."

This uncertainty has been fanned into public fear by anti-GMO activist groups and propagated in popular media outlets by non-scientist writers. It has also been compounded by serious social missteps and media naiveté by scientists. A study on the bioavailability of beta-carotene in Golden Rice fed to Chinese children was retracted for ethical reasons this September—the parents had been informed that the children in the study would receive beta-carotene, but not that the rice was genetically engineered. Quite understandably, they are worried and angry, even though there were no adverse health effects, believing that the rice must be dangerous if its nature was omitted in the consent forms. "If it's safe, why did they need to deceive us into this?" asked one angry father. It was not a simple oversight; according to *Nature* news, a Chinese Centers for Disease Control and Prevention official had changed the wording from the original consent forms to avoid mentioning Golden Rice because it was "too sensitive".

In this roiling social cauldron, getting a clear, objective picture of GM food is a formidable challenge, even for educated consumers. Are GMOs a better way to feed the world, or a threat to human health? And, what exactly are GMOs, anyway?

The term "GMO" is not a well-defined one. Virtually all food crops are genetically modified; organisms that have not been changed from their wild ancestors are few and far between, and in general not to be found in supermarkets. Unless you foraged your food from a forest, or hunted or fished it, you have been eating genetically modified organisms. Most crop plants, in fact, barely resemble their unmodified relatives. The wild ancestor of corn, teosinte, has tiny ears with just 10-12 hard kernels, and resembles wheat more than its succulent relative, modern commercial maize. Common supermarket strawberries have octaploid genomes, and are huge compared to their tiny wild ancestors. Wild almonds are bitter and filled with cyanide—a dozen could kill you. Genetic modification over thousands of years has given us food crops that are leaps and bounds above the natural fruits and vegetables our hunter-gatherer ancestors ate, in terms of size and nutrition.



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But wait, that is natural genetic modification; GMO refers to artificial genetic modification, right? Well, not really. Scratching the surface to try to discern what is and is not a GMO, it quickly becomes clear that there is no solid biological dividing line between legally natural and legally modified. (For example, many would be surprised to know that a crop plant produced through mutagenesis by nuclear radiation is not only considered natural, but can also be farmed organically and labeled as organic.) Organisms have traditionally been genetically modified through a number of means, from selective breeding of organisms with favorable traits to application of radiation or chemicals to produce mutations. According to European Union law, which is quite restrictive regarding GMOs, organisms produced through in vitro fertilization, conjugation, transduction, transformation, polyploidy induction, mutagenesis, and cell fusion (including protoplast fusion) of plant cells of organisms which can exchange genetic material through traditional breeding methods are all considered natural and not genetically modified. The GMO label is limited to organisms produced through recombinant DNA technology.

Since the products of these different methods are not substantially different, this has caused problems for bodies like the European Union, which has had working groups bogged down for years in the task of trying to define which organisms are GMOs. Fundamentally, GMOs are defined by legal bodies, not scientists, and are designated according to the processes used to create them, rather than the products that they are. Since the same product can be created using different means, this has led to a frustratingly irrational framework for biologists. Giovanni Tagliabue of the National Research Council in Rome, puts it this way: "The basic concept boils down to the following: there is no such thing as 'GMOs' (it's not a significant category), and therefore any question regarding 'them' as a supposed whole is nonsensical." He has a point, but at the same time, world governing bodies have made GMOs into a legal category, and therefore GMOs do exist in human society, biologically nonsensical or not.

Two plants with the same genetic change being labeled and regulated differently because of how that change was induced may seem absurd. However, there are clear examples of crop plants produced through recombinant DNA technology that could not have been produced by conventional techniques, such as strawberries made cold-resistant through the insertion of a gene from arctic flounder. The idea of inserting a gene from one organism into a very different organism is unsettling to many, especially those who are either religious ("the world should be as God created it") or uncomfortable with the idea of the artificial ("food products should be natural"). Certainly, we all should live according to our own values, but, objectively, is there reason to believe that engineered foods are more dangerous or less healthy than "non-GMO" foods?

Ironically, genetically modified foods may in fact be safer than non-GM foods, for two reasons. First, all foods produced through recombinant DNA technology require extensive testing for toxicity, allergenicity, and nutritional content prior to allowing them to be introduced as food or animal feed. Non-GMOs do not require such testing, even if they are produced by high-tech modern breeding techniques. Second, genetic engineering is a more targeted approach than traditional methods, which are quite

random—either chance, or a "shotgun"-type treatment, e.g. dousing the plant with mutagens—followed by selection of plants with positive traits. Traits are the outward expression of genes via the proteins they encode. Genetic engineers know exactly what genes they introduced into the plant, and therefore what proteins are being expressed in the phenotypic trait. Traditional plant breeders do not; they see the final trait, but they do not know what mutations underlie it, nor do they know about other genes that may have changed alongside the new trait. Fundamentally, the new organisms are not well-understood, and could be dangerous, especially since many plants produce toxic substances in order to defend themselves.

This has happened in the past on a number of occasions. For example, solanine is a natural toxin present in all potatoes in small amounts. The conventionally bred Lenape potato, however, had almost four times as much solanine as normal potatoes, resulting in severe gastrointestinal sickness in people who ate these potatoes before they were withdrawn from the market. The Solanaceae family includes potatoes, tomatoes, peppers, and eggplant, but also tobacco and the hallucinogenic and highly toxic mandrake, deadly nightshade, and Datura. With a little spontaneous mutation from nature or chemical mutagenesis, mild domesticated potatoes can regain traits more characteristic of their toxic cousins. Such mutations arise spontaneously, and can be selected by natural selection, since they protect plants from herbivores. Not only the Lenape, but other varieties of potatoes have spontaneously mutated to become toxic, such as a 1986 harvest of Magnum Bonum potatoes in Sweden.

Other examples of spontaneously toxic vegetables include zucchini, yellow squash, and celery. Outbreaks of celery-induced photodermatitis in grocery and farm workers were caused by psoralens, normally low-level toxins that were expressed at high levels in a strain of celery that had mutated under natural conditions. Natural toxins can even be deadly, as in the case of the cytotoxin curcurbitacin, responsible for killing an elderly man in Germany who ate zucchini grown by a neighbor. (The emergency department leader, Norbert Pfeuer, stated that the highest risk is in fact in small gardens, when gardeners use their own seeds each year to grow more zucchini. The development of a toxin is a natural evolutionary process to protect a plant.) Curcurbitacin has been found in the USA as well, arising from sources as divergent as home-gardened yellow squash from Alabama and conventionally farmed zucchini from California.

"spontaneously toxic vegetables..."

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Such poisonings have never happened with GMOs, because not only do biologists know exactly which genes are being modified, and how, but all transgenic plants must be rigorously tested before being approved for marketing. In contrast, the actual genetic change in conventionally modified foods is unknown, so toxicity (including carcinogenicity) will not be detected until after consumers become sickened.

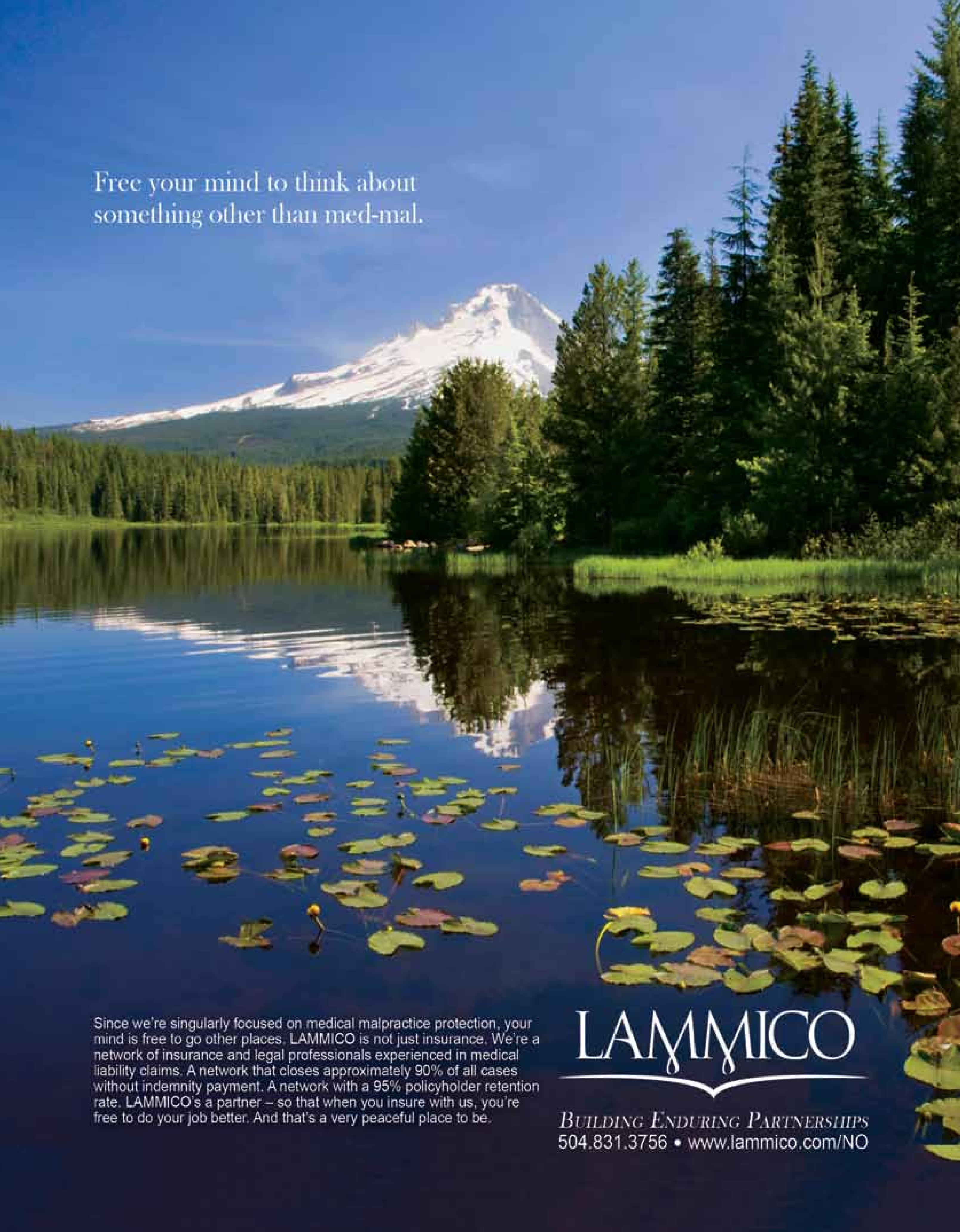
In addition to requiring testing for toxicity and allergenicity, the Food and Drug Administration requires testing for nutritional quality; newly engineered plants must provide the same nutrition as their conventional counterparts. Also, if a pest-resistance gene has been introduced, the plant requires EPA approval as well. The FDA maintains a public database of all genetically engineered plants with a summary of their testing results. The searchable database can be accessed at http://www.accessdata.fda.gov/scripts/fdcc/?set=Biocon.

This testing regimen appears to be working well, with respect to food safety. Undesirable traits have certainly been found, but they have been discovered during the pre-market testing. This testing process is not infallible, of course, and significant differences between GM plants and conventional plants have been noted, such as reduction in phytoestrogens in a strain of GM soy, which could have health effects in the form of reduced nutrition. The testing does, however, provide a level of protection against major health risks that is absent from conventionally bred crops.

While there is no solid evidence (accepted by the scientific community) of health dangers stemming from GMOs, several studies have been published in the past proposing GMO-associated health problems. All have failed to be replicated and some have been retracted. One of the most recent and well-known is a report in *Food and Chemical Toxicology* by Seralini et al. (2012) of cancer, liver necrosis, and increased mortality in rats fed genetically modified corn. The study was widely criticized due to small sample sizes, a lack of a dose-response effect, and other flaws, and Elsevier retracted the report in 2013. It has been republished in *Environmental Sciences Europe* without peer review.

Earlier, in 1999, Ewen and Pusztai reported abnormalities in development and immunity in rats fed transgenic potatoes. While the report was published in the *Lancet* and widely disseminated in popular media, it was only published alongside a letter from a committee of researchers from the Rowett Institute and the Royal Society questioning the study. Subsequently, several researchers tried and failed to replicate the findings. A number of other studies that were too methodologically flawed to be accepted in peer reviewed journals have nonetheless been widely circulated on the internet.

In contrast, a large body of widely respected, peer-reviewed literature documenting a lack of safety issues has failed to garner the media spotlight. Dr. Alison Van Eenennaam of the University of California at Davis recently reviewed hundreds of studies of the effects of GM feed on animals over the past 15 years. Since over 70% of GM biomass is fed to farm animals, this provides a very large population of animals in which to examine any possible health effects of GMOs. Several long-term studies, including multigenerational ones, have been conducted (the longest of which was a 10-generation study of quail fed 50% GM corn). Consistently, GM feed had fewer unintended effects than feed developed through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"The labeling of all GMO products would give consumers the choice to select their food as they wish. It would be like organic foods that are labeled now and consumers have freedom to choose."

conventional breeding techniques. None of the unintended effects were at the level to be considered health hazards.

This preponderance of scientific evidence, and the view of the scientific community at large, has not reached the majority of the population. Most consumers do not have a good understanding of genetics, and with strong media attention to flawed, alarmist studies alongside little coverage of solid, "boring" studies, many feel a sense of misgiving or even fear towards GMOs. One proposal to ease this fear is to allow labeling of GM foods. Dr. Wunderlich emphasizes that choice can help allay consumers' fears about engineered food. "The labeling of all GMO products would give consumers the choice to select their food as they wish. It would be like organic foods that are labeled now and consumers have freedom to choose. Organic products are by definition non-GMO and so they offer consumers at least one option if they are concerned about GMO foods."

GM growers tend to be against labeling, but it may in reality be in their best interest, since a lack of labeling feeds into a sense of GMOs as shadowy unknowns being imposed on concerned consumers. It does not facilitate understanding and rational comparison between foods developed through genetic modification vs. conventional breeding. Dr. Wunderlich understands the concerns of GM growers, but does not believe that labeling will result in the large-scale economic consequences the growers fear. "The GMO growers may have a fear that labeling their products may initially change the consumers' selections, but ultimately consumers will expand their knowledge and learn more about the differences in food production systems. Consumers with higher scientific knowledge may tend to have less negative attitudes towards GMOs. Our studies show that consumers' attitudes, however, impact purchasing behavior more than knowledge." A perhaps more palatable alternative might be an official "non-GMO" label, regulated like the USDA organic label.

Setting aside the issue of consumer attitudes, overwhelmingly, the evidence points to a lack of any significant direct negative health effects of GMOs. So, does this translate into a lack of any problems related to GMOs? Well... no. There are a host of indirect effects that could stem from GMOs, from natural pesticides killing "good" insects to increased herbicide use with engineered glyphosate-resistant crops. Such effects could stem from the way GMOs are farmed or from behavioral changes by consumers. For example, if people who have access to carrots and other orange vegetables stop eating them because they think they'll get plenty of vitamin A from Golden Rice, they will be ingesting fewer of the micronutrients and other macronutrients in those vegetables. Environmental effects could also impact human health. These indirect effects will be considered in the March/April issue of the *Healthcare Journal*, in the second part of this 2-part series on GMOs and health. ■