

BIOTECHNOLOGY

are engineered foods

Evil?

Proponents of genetically modified crops say the technology is the only way to feed a warming, increasingly populous world. Critics say we tamper with nature at our peril. Who is right?

By David H. Freedman

R

OBERT GOLDBERG SAGS INTO HIS DESK CHAIR AND GESTURES AT THE air. "Frankenstein monsters, things crawling out of the lab," he says. "This the most depressing thing I've ever dealt with."

Goldberg, a plant molecular biologist at the University of California, Los Angeles, is not battling psychosis. He is expressing despair at the relentless need to confront what he sees as

bogus fears over the health risks of genetically modified (GM) crops. Particularly frustrating to him, he says, is that this debate should have ended decades ago, when researchers produced a stream of exonerating evidence: "Today we're facing the same objections we faced 40 years ago."

Across campus, David Williams, a cellular biologist who specializes in vision, has the opposite complaint. "A lot of naive science has been involved in pushing this technology," he says. "Thirty years ago we didn't know that when you throw any gene into a different genome, the genome reacts to it. But now anyone in this field knows the genome is not a static environment. Inserted genes can be transformed by several different means, and it can happen generations later." The result, he insists, could very well be potentially toxic plants slipping through testing.

Williams concedes that he is among a tiny minority of biologists raising sharp questions about the safety of GM crops. But he says this is only because

KEVIN VAN AELST



the field of plant molecular biology is protecting its interests. Funding, much of it from the companies that sell GM seeds, heavily favors researchers who are exploring ways to further the use of genetic modification in agriculture. He says that biologists who point out health or other risks associated with GM crops—who merely report or defend experimental findings that imply there may be risks—find themselves the focus of vicious attacks on their credibility, which leads scientists who see problems with GM foods to keep quiet.

Whether Williams is right or wrong, one thing is undeniable: despite overwhelming evidence that GM crops are safe to eat, the debate over their use continues to rage, and in some parts of the world, it is growing ever louder. Skeptics would argue that this contentiousness is a good thing—that we cannot be too cautious when tinkering with the genetic basis of the world's food supply. To researchers such as Goldberg, however, the persistence of fears about GM foods is nothing short of exasperating. "In spite of hundreds of millions of genetic experiments involving every type of organism on earth," he says, "and people eating billions of meals without a problem, we've gone back to being ignorant."

So who is right: advocates of GM or critics? When we look carefully at the evidence for both sides and weigh the risks and benefits, we find a surprisingly clear path out of this dilemma.

BENEFITS AND WORRIES

THE BULK OF THE SCIENCE ON GM safety points in one direction. Take it from David Zilberman, a U.C. Berkeley agricultural and environmental economist and one of the few researchers considered credible by both agricultural chemical companies and their critics. He argues that the benefits of GM crops greatly outweigh the health risks, which so far remain theoretical. The use of GM crops "has lowered the price of food," Zilberman says. "It has increased farmer safety by allowing them to use less pesticide. It has raised the output of corn, cotton and soy by 20 to 30 percent, allowing some people to survive who would not have without it. If it were more widely adopted around the world, the price [of food] would go lower, and fewer people would die of hunger."

In the future, Zilberman says, those advantages will become all the more significant. The United Nations Food and Agriculture Organization estimates that the world will have to grow 70 percent more food by 2050 just to keep up with population growth. Climate change will make much of the world's arable land more difficult to farm. GM crops, Zilberman says, could produce higher yields, grow in dry and salty land, withstand high and low temperatures, and tolerate insects, disease and herbicides.

Despite such promise, much of the world has been busy banning, restricting and otherwise shunning GM foods. Nearly all the corn and soybeans grown in the U.S. are genetically modified, but only two GM crops, Monsanto's MON810 maize and BASF's Amflora potato, are accepted in the European Union. Eight E.U. nations have banned GM crops outright. Throughout

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Asia, including in India and China, governments have yet to approve most GM crops, including an insect-resistant rice that produces higher yields with less pesticide. In Africa, where millions go hungry, several nations have refused to import GM foods in spite of their lower costs (the result of higher yields and a reduced need for water and pesticides). Kenya has banned them altogether amid widespread malnutrition. No country has definite plans to grow Golden Rice, a crop engineered to deliver more vitamin A than spinach (rice normally has no vitamin A), even though vitamin A deficiency causes more than one million deaths annually and half a million cases of irreversible blindness in the developing world.

Globally, only a tenth of the world's cropland includes GM plants. Four countries—the U.S., Canada, Brazil and Argentina—grow 90 percent of the planet's GM crops. Other Latin American countries are pushing away from the plants. And even in the U.S., voices decrying genetically modified foods are becoming louder. At press time, at least 20 states are considering GM-labeling bills.

The fear fueling all this activity has a long history. The public has been worried about the safety of GM foods since scientists at the University of Washington developed the first genetically modified tobacco plants in the 1970s. In the mid-1990s, when the first GM crops reached the market, Greenpeace, the Sierra Club, Ralph Nader, Prince Charles and a number of celebrity chefs took highly visible stands against them. Consumers in Europe became particularly alarmed: a survey conducted in 1997, for example, found that 69 percent of the Austrian public saw serious risks in GM foods, compared with only 14 percent of Americans.

In Europe, skepticism about GM foods has long been bundled with other concerns, such as a resentment of American agribusiness. Whatever it is based on, however, the European attitude reverberates across the world, influencing policy in countries where GM crops could have tremendous benefits. "In Africa, they don't care what us savages in America are doing," Zilberman says. "They look to Europe and see countries there rejecting GM, so they don't use it." Forces fighting genetic modification in Europe have rallied support for "the precautionary principle," which holds that given the kind of catastrophe that would emerge from loosing a toxic, invasive GM crop on the world, GM efforts should be shut down until the technology is proved absolutely safe.

But as medical researchers know, nothing can really be "proved safe." One can only fail to turn up significant risk after trying hard to find it—as is the case with GM crops.

THE BOTTOM LINE

The vast majority of the research on genetically modified (GM) crops suggests that they are safe to eat and that they have the potential to feed mil-

lions of people worldwide who currently go hungry. **Yet not all criticisms** of GM are so easily rejected, and pro-GM scientists are often dismissive and even

unscientific in their rejection of the counterevidence. **A careful analysis** of the risks and benefits argues for expanded deployment and safety testing of GM crops.

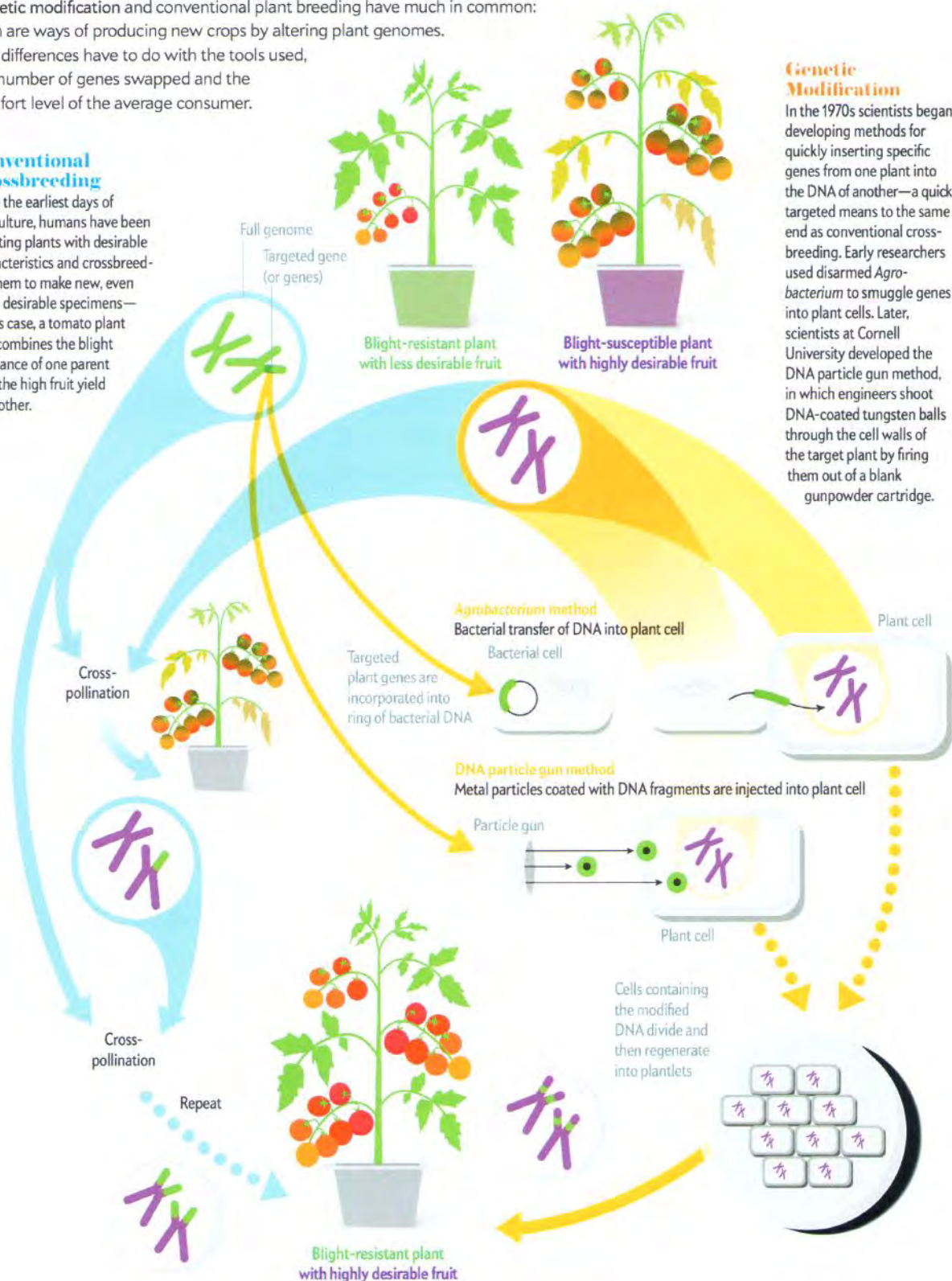
How to Build a Better Plant

Genetic modification and conventional plant breeding have much in common: both are ways of producing new crops by altering plant genomes.

The differences have to do with the tools used, the number of genes swapped and the comfort level of the average consumer.

Conventional Crossbreeding

Since the earliest days of agriculture, humans have been selecting plants with desirable characteristics and crossbreeding them to make new, even more desirable specimens—in this case, a tomato plant that combines the blight resistance of one parent with the high fruit yield of another.



Genetic Modification

In the 1970s scientists began developing methods for quickly inserting specific genes from one plant into the DNA of another—a quick, targeted means to the same end as conventional crossbreeding. Early researchers used disarmed *Agrobacterium* to smuggle genes into plant cells. Later, scientists at Cornell University developed the DNA particle gun method, in which engineers shoot DNA-coated tungsten balls through the cell walls of the target plant by firing them out of a blank gunpowder cartridge.

A CLEAN RECORD

THE HUMAN RACE has been selectively breeding crops, thus altering plants' genomes, for millennia. Ordinary wheat has long been strictly a human-engineered plant; it could not exist outside of farms, because its seeds do not scatter. For some 60 years scientists have been using "mutagenic" techniques to scramble the DNA of plants with radiation and chemicals, creating strains of wheat, rice, peanuts and pears that have become agricultural mainstays. The practice has inspired little objection from scientists or the public and has caused no known health problems.

The difference is that selective breeding or mutagenic techniques tend to result in large swaths of genes being swapped or altered. GM technology, in contrast, enables scientists to insert into a plant's genome a single gene (or a few of them) from another species of plant or even from a bacterium, virus or animal. Supporters argue that this precision makes the technology much less likely to produce surprises. Most plant molecular biologists also say that in the highly unlikely case that an unexpected health threat emerged from a new GM plant, scientists would quickly identify and eliminate it. "We know where the gene goes and can measure the activity of every single gene around it," Goldberg says. "We can show exactly which changes occur and which don't." [For more on how GM plants are analyzed for health safety, see "The Risks on the Table," by Karen Hopkin; *SCIENTIFIC AMERICAN*, April 2001.]

And although it might seem creepy to add virus DNA to a plant, doing so is, in fact, no big deal, proponents say. Viruses have been inserting their DNA into the genomes of crops, as well as humans and all other organisms, for millions of years. They often deliver the genes of other species while they are at it, which is why our own genome is loaded with genetic sequences that originated in viruses and nonhuman species. "When GM critics say that genes don't cross the species barrier in nature, that's just simple ignorance," says Alan McHughen, a plant molecular geneticist at U.C. Riverside. Pea aphids contain fungi genes. Triticale is a century-plus-old hybrid of wheat and rye found in some flours and breakfast cereals. Wheat itself, for that matter, is a cross-species hybrid. "Mother Nature does it all the time, and so do conventional plant breeders," McHughen says.

Could eating plants with altered genes allow new DNA to work its way into our own? It is theoretically possible but hugely improbable. Scientists have never found genetic material that could survive a trip through the human gut and make it into cells. Besides, we are routinely exposed to—we even consume—the viruses and bacteria whose genes end up in GM foods. The bacterium *B. thuringiensis*, for example, which produces proteins fatal to insects, is sometimes enlisted as a natural pesticide in organic farming. "We've been eating this stuff for thousands of years," Goldberg says.

In any case, proponents say, people have consumed as many as trillions of meals containing genetically modified ingredients over the past few decades. Not a single verified case of illness has ever been attributed to the genetic alterations. Mark Lynas, a prominent anti-GM activist who last year publicly switched to strongly supporting the technology, has pointed out that every single news-making food disaster on record has been attributed to non-GM crops, such as the *Escherichia coli*-infected organic bean sprouts that killed 53 people in Europe in 2011.

Critics often disparage U.S. research on the safety of genetically modified foods, which is often funded or even conducted by GM

companies, such as Monsanto. But much research on the subject comes from the European Commission, the administrative body of the E.U., which cannot be so easily dismissed as an industry tool. The European Commission has funded 130 research projects, carried out by more than 500 independent teams, on the safety of GM crops. None of those studies found any special risks from GM crops.

Plenty of other credible groups have arrived at the same conclusion. Gregory Jaffe, director of biotechnology at the Center for Science in the Public Interest, a science-based consumer-watchdog group in Washington, D.C., takes pains to note that the center has no official stance, pro or con, with regard to genetically modifying food plants. Yet Jaffe insists the scientific record is clear. "Current GM crops are safe to eat and can be grown safely in the environment," he says. The American Association for the Advancement of Science, the American Medical Association and the National Academy of Sciences have all unreservedly backed GM crops. The U.S. Food and Drug Administration, along with its counterparts in several other countries, has repeatedly reviewed large bodies of research and concluded that GM crops pose no unique health threats. Dozens of review studies carried out by academic researchers have backed that view.

Opponents of genetically modified foods point to a handful of studies indicating possible safety problems. But reviewers have dismantled almost all of those reports. For example, a 1998 study by plant biochemist Árpád Pusztai, then at the Rowett Institute in Scotland, found that rats fed a GM potato suffered from stunted growth and immune system-related changes. But the potato was not intended for human consumption—it was, in fact, designed to be toxic for research purposes. The Rowett Institute later deemed the experiment so sloppy that it refuted the findings and charged Pusztai with misconduct.

Similar stories abound. Most recently, a team led by Gilles-Éric Séralini, a researcher at the University of Caen Lower Normandy in France, found that rats eating a common type of GM corn contracted cancer at an alarmingly high rate. But Séralini has long been an anti-GM campaigner, and critics charged that in his study, he relied on a strain of rat that too easily develops tumors, did not use enough rats, did not include proper control groups and failed to report many details of the experiment, including how the analysis was performed. After a review, the European Food Safety Authority dismissed the study's findings. Several other European agencies came to the same conclusion. "If GM corn were that toxic, someone would have noticed by now," McHughen says. "Séralini has been refuted by everyone who has cared to comment."

Some scientists say the objections to GM food stem from politics rather than science—that they are motivated by an objection to large multinational corporations having enormous influence over the food supply; invoking risks from genetic modification just provides a convenient way of whipping up the masses against industrial agriculture. "This has nothing to do with science," Goldberg says. "It's about ideology." Former anti-GM activist Lynas agrees. He recently went as far as labeling the anti-GM crowd "explicitly an antiscience movement."

PERSISTENT DOUBTS

NOT ALL OBJECTIONS to genetically modified foods are so easily dismissed, however. Long-term health effects can be subtle and nearly impossible to link to specific changes in the environment. Scien-

tists have long believed that Alzheimer's disease and many cancers have environmental components, but few would argue we have identified all of them.

And opponents say that it is not true that the GM process is less likely to cause problems simply because fewer, more clearly identified genes are switched. David Schubert, an Alzheimer's researcher who heads the Cellular Neurobiology Laboratory at the Salk Institute for Biological Studies in La Jolla, Calif., asserts that a single, well-characterized gene can still settle in the target plant's genome in many different ways. "It can go in forward, backward, at different locations, in multiple copies, and they all do different things," he says. And as U.C.L.A.'s Williams notes, a genome often continues to change in the successive generations after the insertion, leaving it with a different arrangement than the one intended and initially tested. There is also the phenomenon of "insertional mutagenesis," Williams adds, in which the insertion of a gene ends up quieting the activity of nearby genes.

True, the number of genes affected in a GM plant most likely will be far, far smaller than in conventional breeding techniques. Yet opponents maintain that because the wholesale swapping or alteration of entire packages of genes is a natural process that has been happening in plants for half a billion years, it tends to produce few scary surprises today. Changing a single gene, on the other hand, might turn out to be a more subversive action, with unexpected ripple effects, including the production of new proteins that might be toxins or allergens.

Opponents also point out that the kinds of alterations caused by the insertion of genes from other species might be more impactful, more complex or more subtle than those caused by the intraspecies gene swapping of conventional breeding. And just because there is no evidence to date that genetic material from an altered crop can make it into the genome of people who eat it does not mean such a transfer will never happen—or that it has not already happened and we have yet to spot it. These changes might be difficult to catch; their impact on the production of proteins might not even turn up in testing. "You'd certainly find out if the result is that the plant doesn't grow very well," Williams says. "But will you find the change if it results in the production of proteins with long-term effects on the health of the people eating it?"

It is also true that many pro-GM scientists in the field are unduly harsh—even unscientific—in their treatment of critics. GM proponents sometimes lump every scientist who raises safety questions together with activists and discredited researchers. And even Séralini, the scientist behind the study that found high cancer rates for GM-fed rats, has his defenders. Most of them are nonscientists, or retired researchers from obscure institutions, or nonbiologist scientists, but the Salk Institute's Schubert also insists the study was unfairly dismissed. He says that as someone who runs drug-safety studies, he is well versed on what constitutes a good-quality animal toxicology study and that Séralini's makes the grade. He insists that the breed of rat in the study is commonly used in respected drug studies, typically in numbers no greater than in Séralini's study; that the methodology was standard; and that the details of the data analysis are irrelevant because the results were so striking.

Schubert joins Williams as one of a handful of biologists from respected institutions who are willing to sharply challenge the GM-foods-are-safe majority. Both charge that more scientists

would speak up against genetic modification if doing so did not invariably lead to being excoriated in journals and the media. These attacks, they argue, are motivated by the fear that airing doubts could lead to less funding for the field. Says Williams: "Whether it's conscious or not, it's in their interest to promote this field, and they're not objective."

Both scientists say that after publishing comments in respected journals questioning the safety of GM foods, they became the victims of coordinated attacks on their reputations. Schubert even charges that researchers who turn up results that might raise safety questions avoid publishing their findings out of fear of repercussions. "If it doesn't come out the right way," he says, "you're going to get trashed."

There is evidence to support that charge. In 2009 *Nature* detailed the backlash to a reasonably solid study published in the *Proceedings of the National Academy of Sciences USA* by researchers from Loyola University Chicago and the University of Notre Dame. The paper showed that GM corn seemed to be finding its way from farms into nearby streams and that it might pose a risk to some insects there because, according to the researchers' lab studies, caddis flies appeared to suffer on diets of pollen from GM corn. Many scientists immediately attacked the study, some of them suggesting the researchers were sloppy to the point of misconduct.

A WAY FORWARD

THERE IS A MIDDLE GROUND in this debate. Many moderate voices call for continuing the distribution of GM foods while maintaining or even stepping up safety testing on new GM crops. They advocate keeping a close eye on the health and environmental impact of existing ones. But they do not single out GM crops for special scrutiny, the Center for Science in the Public Interest's Jaffe notes: *all* crops could use more testing. "We should be doing a better job with food oversight altogether," he says.

Even Schubert agrees. In spite of his concerns, he believes future GM crops can be introduced safely if testing is improved. "Ninety percent of the scientists I talk to assume that new GM plants are safety-tested the same way new drugs are by the FDA," he says. "They absolutely aren't, and they absolutely should be."

Stepped-up testing would pose a burden for GM researchers, and it could slow down the introduction of new crops. "Even under the current testing standards for GM crops, most conventionally bred crops wouldn't have made it to market," McHughen says. "What's going to happen if we become even more strict?"

That is a fair question. But with governments and consumers increasingly coming down against GM crops altogether, additional testing may be the compromise that enables the human race to benefit from those crops' significant advantages. ■

MORE TO EXPLORE

Food, Inc.: Mendel to Monsanto—The Promises and Perils of the Biotech Harvest. Peter Pringle. Simon & Schuster, 2003.

Tough Lessons from Golden Rice. Martin Enserink in *Science*, Vol. 320, pages 468–471; April 25, 2008.

Case Studies: A Hard Look at GM Crops. Natasha Gilbert in *Nature*, Vol. 497, pages 24–26; May 2, 2013. www.nature.com/news/case-studies-a-hard-look-at-gm-crops-1.12907

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Watch a video on how genetically modified crops are made at ScientificAmerican.com/sep2013/gmo

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Lecture to Oxford Farming Conference, 3 January 2013

3 January 2013

323 comments

Lecture to Oxford Farming Conference, 3 January 2013

[Please check against delivery - see video below for speech as given.]

07 Mark Lynas from [Oxford Farming Conference](#) on [Vimeo](#).

I want to start with some apologies. For the record, here and upfront, I apologise for having spent several years ripping up GM crops. I am also sorry that I helped to start the anti-GM movement back in the mid 1990s, and that I thereby assisted in demonising an important technological option which can be used to benefit the environment.

As an environmentalist, and someone who believes that everyone in this world has a right to a healthy and nutritious diet of their choosing, I could not have chosen a more counter-productive path. I now regret it completely.

So I guess you'll be wondering – what happened between 1995 and now that made me not only change my mind but come here and admit it? Well, the answer is fairly simple: I discovered science, and in the process I hope I became a better environmentalist.

When I first heard about Monsanto's GM soya I knew exactly what I thought. Here was a big American corporation with a nasty track record, putting something new and experimental into our food without telling us. Mixing genes between species seemed to be about as unnatural as

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you can get – here was humankind acquiring too much technological power; something was bound to go horribly wrong. These genes would spread like some kind of living pollution. It was the stuff of nightmares.

These fears spread like wildfire, and within a few years GM was essentially banned in Europe, and our worries were exported by NGOs like Greenpeace and Friends of the Earth to Africa, India and the rest of Asia, where GM is still banned today. This was the most successful campaign I have ever been involved with.

This was also explicitly an anti-science movement. We employed a lot of imagery about scientists in their labs cackling demonically as they tinkered with the very building blocks of life. Hence the Frankenstein food tag – this absolutely was about deep-seated fears of scientific powers being used secretly for unnatural ends. What we didn't realise at the time was that the real Frankenstein's monster was not GM technology, but our reaction against it.

For me this anti-science environmentalism became increasingly inconsistent with my pro-science environmentalism with regard to climate change. I published my first book on global warming in 2004, and I was determined to make it scientifically credible rather than just a collection of anecdotes.

So I had to back up the story of my trip to Alaska with satellite data on sea ice, and I had to justify my pictures of disappearing glaciers in the Andes with long-term records of mass balance of mountain glaciers. That meant I had to learn how to read scientific papers, understand basic statistics and become literate in very different fields from oceanography to paleoclimate, none of which my degree in politics and modern history helped me with a great deal.

I found myself arguing constantly with people who I considered to be incorrigibly anti-science, because they wouldn't listen to the climatologists and denied the scientific reality of climate change. So I lectured them about the value of peer-review, about the importance of scientific consensus and how the only facts that mattered were the ones published in the most distinguished scholarly journals.

My second climate book, *Six Degrees*, was so sciency that it even won the Royal Society science books prize, and climate scientists I had become friendly with would joke that I knew more about the subject than them. And yet, incredibly, at this time in 2008 I was still penning screeds in the *Guardian* attacking the science of GM – even though I had done no academic research on the topic, and had a pretty limited personal understanding. I don't think I'd ever read a peer-reviewed paper on biotechnology or plant science even at this late stage.

Obviously this contradiction was untenable. What really threw me were some of the comments underneath my final anti-GM *Guardian* article. In particular one critic said to me: so you're opposed to GM on the basis that it is marketed by big corporations. Are you also opposed to the wheel because because it is marketed by the big auto companies?

So I did some reading. And I discovered that one by one my cherished beliefs about GM turned out to be little more than green urban myths.

I'd assumed that it would increase the use of chemicals. It turned out that pest-resistant cotton and maize needed less insecticide.

I'd assumed that GM benefited only the big companies. It turned out that billions of dollars of benefits were accruing to farmers needing fewer inputs.

I'd assumed that Terminator Technology was robbing farmers of the right to save seed. It turned out that hybrids did that long ago, and that Terminator never happened.

I'd assumed that no-one wanted GM. Actually what happened was that Bt cotton was pirated into India and roundup ready soya into Brazil because farmers were so eager to use them.

I'd assumed that GM was dangerous. It turned out that it was safer and more precise than conventional breeding using mutagenesis for example; GM just moves a couple of genes, whereas conventional breeding mucks about with the entire genome in a trial and error way.

But what about mixing genes between unrelated species? The fish and the tomato? Turns out viruses do that all the time, as do plants and insects and even us – it's called gene flow.

But this was still only the beginning. So in my third book *The God Species* I junked all the environmentalist orthodoxy at the outset and tried to look at the bigger picture on a planetary scale.

And this is the challenge that faces us today: we are going to have to feed 9.5 billion hopefully much less poor people by 2050 on about the same land area as we use today, using limited fertiliser, water and pesticides and in the context of a rapidly-changing climate.

Let's unpack this a bit. I know in a previous year's lecture in this conference there was the topic of population growth. This area too is beset by myths. People think that high rates of fertility in the developing world are the big issue – in other words, poor people are having too many children, and we therefore need either family planning or even something drastic like mass one-child policies.

The reality is that global average fertility is down to about 2.5 – and if you consider that natural replacement is 2.2, this figure is not much above that. So where is the massive population growth coming from? It is coming because of declining infant mortality – more of today's youngsters are growing up to have their own children rather than dying of preventable diseases in early childhood.

The rapid decline in infant mortality rates is one of the best news stories of our decade and the heartland of this great success story is sub-Saharan Africa. It's not that there are legions more children being born – in fact, in the words of Hans Rosling, we are already at 'peak child'. That is, about 2 billion children are alive today, and there will never be more than that because of declining fertility.

But so many more of these 2 billion children will survive into adulthood today to have their own children. They are the parents of the young adults of 2050. That's the source of the 9.5 billion population projection for 2050. You don't have to have lost a child, God forbid, or even be a parent, to know that declining infant mortality is a good thing.

So how much food will all these people need? According to the latest projections, published last year in the Proceedings of the National Academy of Sciences, we are looking at a global demand increase of well over 100% by mid-century. This is almost entirely down to GDP growth, especially in developing countries.

In other words, we need to produce more food not just to keep up with population but because poverty is gradually being eradicated, along with the widespread malnutrition that still today means close to 800 million people go to bed hungry each night. And I would challenge anyone in a rich country to say that this GDP growth in poor countries is a bad thing.

But as a result of this growth we have very serious environmental challenges to tackle. Land conversion is a large source of greenhouse gases, and perhaps the greatest source of biodiversity loss. This is another reason why intensification is essential – we have to grow more on limited land in order to save the rainforests and remaining natural habitats from the plough.

We also have to deal with limited water – not just depleting aquifers but also droughts that are expected to strike with increasing intensity in the agricultural heartlands of continents thanks to climate change. If we take more water from rivers we accelerate biodiversity loss in these fragile habitats.

We also need to better manage nitrogen use: artificial fertiliser is essential to feed humanity, but its inefficient use means dead zones in the Gulf of Mexico and many coastal areas around the world, as well as eutrophication in fresh water ecosystems.

It is not enough to sit back and hope that technological innovation will solve our problems. We have to be much more activist and strategic than that. We have to ensure that technological innovation moves much more rapidly, and in the right direction for those who most need it.

In a sense we've been here before. When Paul Ehrlich published the Population Bomb in 1968, he wrote: "The battle to feed all of humanity is over. In the 1970s hundreds of millions of people will starve to death in spite of any crash programs embarked upon now." The advice was explicit – in basket-case countries like India, people might as well starve sooner rather than later, and therefore food aid to them should be eliminated to reduce population growth.

It was not pre-ordained that Ehrlich would be wrong. In fact, if everyone had heeded his advice hundreds of millions of people might well have died needlessly. But in the event, malnutrition was cut dramatically, and India became food self-sufficient, thanks to Norman Borlaug and his Green Revolution.

It is important to recall that Borlaug was equally as worried about population growth as Ehrlich. He just thought it was worth trying to do something about it. He was a pragmatist because he believed in doing what was possible, but he was also an idealist because he believed that people everywhere deserved to have enough to eat.

So what did Norman Borlaug do? He turned to science and technology. Humans are a tool-making species – from clothes to ploughs, technology is primarily what distinguishes us from other apes. And much of this work was focused on the genome of major domesticated crops – if wheat, for example, could be shorter and put more effort into seed-making rather than stalks, then yields would improve and grain loss due to lodging would be minimised.

Before Borlaug died in 2009 he spent many years campaigning against those who for political and ideological reasons oppose modern innovation in agriculture. To quote: "If the naysayers do manage to stop agricultural biotechnology, they might actually precipitate the famines and the crisis of global biodiversity they have been predicting for nearly 40 years."

And, thanks to supposedly environmental campaigns spread from affluent countries, we are perilously close to this position now. Biotechnology has not been stopped, but it has been made prohibitively expensive to all but the very biggest corporations.

It now costs tens of millions to get a crop through the regulatory systems in different countries. In fact the latest figures I've just seen from CropLife suggest it costs \$139 million to move from discovering a new crop trait to full commercialisation, so open-source or public sector biotech really does not stand a chance.

There is a depressing irony here that the anti-biotech campaigners complain about GM crops only being marketed by big corporations when this is a situation they have done more than anyone to help bring about.

In the EU the system is at a standstill, and many GM crops have been waiting a decade or more for approval but are permanently held up by the twisted domestic politics of anti-biotech countries like France and Austria. Around the whole world the regulatory delay has increased to more than 5 and a half years now, from 3.7 years back in 2002. The bureaucratic burden is getting worse.

France, remember, long refused to accept the potato because it was an American import. As one commentator put it recently, Europe is on the verge of becoming a food museum. We well-fed consumers are blinded by romantic nostalgia for the traditional farming of the past. Because we have enough to eat, we can afford to indulge our aesthetic illusions.

But at the same time the growth of yields worldwide has stagnated for many major food crops, as research published only last month by Jonathan Foley and others in the journal *Nature Communications* showed. If we don't get yield growth back on track we are indeed going to have trouble keeping up with population growth and resulting demand, and prices will rise as well as more land being converted from nature to agriculture.

To quote Norman Borlaug again: "I now say that the world has the technology — either available or well advanced in the research pipeline — to feed on a sustainable basis a population of 10 billion people. The more pertinent question today is whether farmers and ranchers will be permitted to use this new technology? While the affluent nations can certainly afford to adopt ultra low-risk positions, and pay more for food produced by the so-called 'organic' methods, the one billion chronically undernourished people of the low income, food-deficit nations cannot."

As Borlaug was saying, perhaps the most pernicious myth of all is that organic production is better, either for people or the environment. The idea that it is healthier has been repeatedly disproved in the scientific literature. We also know from many studies that organic is much less productive, with up to 40-50% lower yields in terms of land area. The Soil Association went to great lengths in a recent report on feeding the world with organic not to mention this productivity gap.

Nor did it mention that overall, if you take into account land displacement effects, organic is also likely worse for biodiversity. Instead they talk about an ideal world where people in the west eat less meat and fewer calories overall so that people in developing countries can have more. This is simplistic nonsense.

If you think about it, the organic movement is at its heart a rejectionist one. It doesn't accept many modern technologies on principle. Like the Amish in Pennsylvania, who froze their technology with the horse and cart in 1850, the organic movement essentially freezes its technology in somewhere around 1950, and for no better reason.

It doesn't even apply this idea consistently however. I was reading in a recent Soil Association magazine that it is OK to blast weeds with flamethrowers or fry them with electric currents, but benign herbicides like glyphosate are still a no-no because they are 'artificial chemicals'.

In reality there is no reason at all why avoiding chemicals should be better for the environment – quite the opposite in fact. Recent research by Jesse Ausubel and colleagues at Rockefeller University looked at how much extra farmland Indian farmers would have had to cultivate today using the technologies of 1961 to get today's overall yield. The answer is 65 million hectares, an area the size of France.

In China, maize farmers spared 120 million hectares, an area twice the size of France, thanks to modern technologies getting higher yields. On a global scale, between 1961 and 2010 the area farmed grew by only 12%, whilst kilocalories per person rose from 2200 to 2800. So even with three billion more people, everyone still had more to eat thanks to a production increase of 300% in the same period.

So how much land worldwide was spared in the process thanks to these dramatic yield improvements, for which chemical inputs played a crucial role? The answer is 3 billion hectares, or the equivalent of two South Americas. There would have been no Amazon rainforest left today without this improvement in yields. Nor would there be any tigers in India or orang utans in Indonesia. That is why I don't know why so many of those opposing the use of technology in agriculture call themselves environmentalists.

So where does this opposition come from? There seems to be a widespread assumption that modern technology equals more risk. Actually there are many very natural and organic ways to face illness and early death, as the debacle with Germany's organic beansprouts proved in 2011. This was a public health catastrophe, with the same number of deaths and injuries as were caused by Chernobyl, because E.-coli probably from animal manure infected organic beansprout seeds imported from Egypt.

In total 53 people died and 3,500 suffered serious kidney failure. And why were these consumers choosing organic? Because they thought it was safer and healthier, and they were more scared of entirely trivial risks from highly-regulated chemical pesticides and fertilisers.

If you look at the situation without prejudice, much of the debate, both in terms of anti-biotech and organic, is simply based on the naturalistic fallacy – the belief that natural is good, and artificial is bad. This is a fallacy because there are plenty of entirely natural poisons and ways to die, as the relatives of those who died from E.-coli poisoning would tell you.

For organic, the naturalistic fallacy is elevated into the central guiding principle for an entire

movement. This is irrational and we owe it to the Earth and to our children to do better.

This is not to say that organic farming has nothing to offer – there are many good techniques which have been developed, such as intercropping and companion planting, which can be environmentally very effective, even if they do tend to be highly labour-intensive. Principles of agro-ecology such as recycling nutrients and promoting on-farm diversity should also be taken more seriously everywhere.

But organic is in the way of progress when it refuses to allow innovation. Again using GM as the most obvious example, many third-generation GM crops allow us not to use environmentally-damaging chemicals because the genome of the crop in question has been altered so the plant can protect itself from pests. Why is that not organic?

Organic is also in the way when it is used to take away choice from others. One of the commonest arguments against GM is that organic farmers will be 'contaminated' with GM pollen, and therefore no-one should be allowed to use it. So the rights of a well-heeled minority, which come down ultimately to a consumer preference based on aesthetics, trump the rights of everyone else to use improved crops which would benefit the environment.

I am all for a world of diversity, but that means one farming system cannot claim to have a monopoly of virtue and aim at excluding all other options. Why can't we have peaceful co-existence? This is particularly the case when it shackles us to old technologies which have higher inherent risks than the new.

It seems like almost everyone has to pay homage to 'organic' and to question this orthodoxy is unthinkable. Well I am here to question it today.

The biggest risk of all is that we do not take advantage of all sorts of opportunities for innovation because of what is in reality little more than blind prejudice. Let me give you two examples, both regrettably involving Greenpeace.

Last year Greenpeace destroyed a GM wheat crop in Australia, for all the traditional reasons, which I am very familiar with having done it myself. This was publicly funded research carried out by the Commonwealth Scientific Research Institute, but no matter. They were against it because it was GM and unnatural.

What few people have since heard is that one of the other trials being undertaken, which Greenpeace activists with their strimmers luckily did not manage to destroy, accidentally found a wheat yield increase of an extraordinary 30%. Just think. This knowledge might never have been produced at all, if Greenpeace had succeeded in destroying this innovation. As the president of the NFU Peter Kendall recently suggested, this is analogous to burning books in a library before anyone has been able to read them.

The second example comes from China, where Greenpeace managed to trigger a national media panic by claiming that two dozen children had been used as human guinea pigs in a trial of GM golden rice. They gave no consideration to the fact that this rice is healthier, and could save thousands of children from vitamin A deficiency-related blindness and death each year.

What happened was that the three Chinese scientists named in the Greenpeace press release

were publicly hounded and have since lost their jobs, and in an autocratic country like China they are at serious personal risk. Internationally because of over-regulation golden rice has already been on the shelf for over a decade, and thanks to the activities of groups like Greenpeace it may never become available to vitamin-deficient poor people.

This to my mind is immoral and inhumane, depriving the needy of something that would help them and their children because of the aesthetic preferences of rich people far away who are in no danger from Vitamin A shortage. Greenpeace is a \$100-million a year multinational, and as such it has moral responsibilities just like any other large company.

The fact that golden rice was developed in the public sector and for public benefit cuts no ice with the antis. Take Rothamsted Research, whose director Maurice Moloney is speaking tomorrow. Last year Rothamsted began a trial of an aphid-resistant GM wheat which would need no pesticides to combat this serious pest.

Because it is GM the antis were determined to destroy it. They failed because of the courage of Professor John Pickett and his team, who took to YouTube and the media to tell the important story of why their research mattered and why it should not be trashed. They gathered thousands of signatures on a petition when the antis could only manage a couple of hundred, and the attempted destruction was a damp squib.

One intruder did manage to scale the fence, however, who turned out to be the perfect stereotypical anti-GM protestor – an old Etonian aristocrat whose colourful past makes our Oxford local Marquess of Blandford look like the model of responsible citizenry.

This high-born activist scattered organic wheat seeds around the trial site in what was presumably a symbolic statement of naturalness. Professor Pickett's team tell me they had a very low-tech solution to getting rid of it – they went round with a cordless portable Hoover to clear it up.

This year, as well as repeating the wheat trial, Rothamsted is working on an omega 3 oilseed that could replace wild fish in food for farmed salmon. So this could help reduce overfishing by allowing land-based feedstocks to be used in aquaculture. Yes it's GM, so expect the antis to oppose this one too, despite the obvious potential environmental benefits in terms of marine biodiversity.

I don't know about you, but I've had enough. So my conclusion here today is very clear: the GM debate is over. It is finished. We no longer need to discuss whether or not it is safe – over a decade and a half with three trillion GM meals eaten there has never been a single substantiated case of harm. You are more likely to get hit by an asteroid than to get hurt by GM food. More to the point, people have died from choosing organic, but no-one has died from eating GM.

Just as I did 10 years ago, Greenpeace and the Soil Association claim to be guided by consensus science, as on climate change. Yet on GM there is a rock-solid scientific consensus, backed by the American Association for the Advancement of Science, the Royal Society, health institutes and national science academies around the world. Yet this inconvenient truth is ignored because it conflicts with their ideology.

One final example is the sad story of the GM blight-resistant potato. This was being developed

by both the Sainsbury Lab and Teagasc, a publicly-funded institute in Ireland – but the Irish Green Party, whose leader often attends this very conference, was so opposed that they even took out a court case against it.

This is despite the fact that the blight-resistant potato would save farmers from doing 15 fungicide sprays per season, that pollen transfer is not an issue because potatoes are clonally propagated and that the offending gene came from a wild relative of the potato.

There would have been a nice historical resonance to having a blight-resistant potato developed in Ireland, given the million or more who died due to the potato famine in the mid 19th century. It would have been a wonderful thing for Ireland to be the country that defeated blight. But thanks to the Irish Green Party, this is not to be.

And unfortunately the antis now have the bureaucrats on their side. Wales and Scotland are officially GM free, taking medieval superstition as a strategic imperative for devolved governments supposedly guided by science.

It is unfortunately much the same in much of Africa and Asia. India has rejected Bt brinjal, even though it would reduce insecticide applications in the field, and residues on the fruit. The government in India is increasingly in thrall to backward-looking ideologues like Vandana Shiva, who idealise pre-industrial village agriculture despite the historical fact that it was an age of repeated famines and structural insecurity.

In Africa, 'no GM' is still the motto for many governments. Kenya for example has actually banned GM foods because of the supposed "health risks" despite the fact that they could help reduce the malnutrition that is still rampant in the country – and malnutrition is by the way a proven health risk, with no further evidence needed. In Kenya if you develop a GM crop which has better nutrition or a higher yield to help poorer farmers then you will go to jail for 10 years.

Thus desperately-needed agricultural innovation is being strangled by a suffocating avalanche of regulations which are not based on any rational scientific assessment of risk. The risk today is not that anyone will be harmed by GM food, but that millions will be harmed by not having enough food, because a vocal minority of people in rich countries want their meals to be what they consider natural.

I hope now things are changing. The wonderful Bill and Melinda Gates foundation recently gave \$10 million to the John Innes Centre to begin efforts to integrate nitrogen fixing capabilities into major food crops, starting with maize. Yes, Greenpeace, this will be GM. Get over it. If we are going to reduce the global-scale problem of nitrogen pollution then having major crop plants fixing their own nitrogen is a worthy goal.

I know it is politically incorrect to say all this, but we need a a major dose of both international myth-busting and de-regulation. The plant scientists I know hold their heads in their hands when I talk about this with them because governments and so many people have got their sense of risk so utterly wrong, and are foreclosing a vitally necessary technology.

Norman Borlaug is dead now, but I think we honour his memory and his vision when we refuse to give in to politically correct orthodoxies when we know they are incorrect. The stakes are high. If we continue to get this wrong, the life prospects of billions of people will be harmed.

So I challenge all of you today to question your beliefs in this area and to see whether they stand up to rational examination. Always ask for evidence, as the campaigning group Sense About Science advises, and make sure you go beyond the self-referential reports of campaigning NGOs.

But most important of all, farmers should be free to choose what kind of technologies they want to adopt. If you think the old ways are the best, that's fine. You have that right.

What you don't have the right to do is to stand in the way of others who hope and strive for ways of doing things differently, and hopefully better. Farmers who understand the pressures of a growing population and a warming world. Who understand that yields per hectare are the most important environmental metric. And who understand that technology never stops developing, and that even the fridge and the humble potato were new and scary once.

So my message to the anti-GM lobby, from the ranks of the British aristocrats and celebrity chefs to the US foodies to the peasant groups of India is this. You are entitled to your views. But you must know by now that they are not supported by science. We are coming to a crunch point, and for the sake of both people and the planet, now is the time for you to get out of the way and let the rest of us get on with feeding the world sustainably.

Thankyou.

Posted in: [agriculture](#), [developing countries](#), [food](#), [genetic engineering](#)

323 comments



Pekka Taipale says:

3 January 2013 at 2:38 pm

Excellent. Thank you.

Reply



Eimhin says:

4 January 2013 at 10:28 pm

Hi, its 15degrees celcius in Ireland today...this time last year the waterfall in town was frozen. Whats a myth? The reduction of tangible reality from matter to form in successive steps of transformation, none of which resemble the former a.k.a, science, or experienced reality?

Now this probably won't get past the moderator, but I want someone to read this, even if only the person who decides my say contradicts their intentional end in publishing this pice of manipulation-in-formation. Certain things are not mythos, look around you, are conditions getting better or worse, try to see beyond yourself, look at the community at large. For whom are things getting better, what is going on in the margins? Our 'progress' is one in which value is reduced, as per the scientific method, to a symbol of that which it represents...and this symbol becomes the object of material greed. Certain things reek of inevitability. Technology by itself is all well and good, but Einstein may have agreed with Leanardo da Vinci's destruction of some of his own inventions as a result of his foresight into the reult of their consequence. Human nature being such as it is, choose wisely. Given the greed of the mass-human, what guarantees can you assure yourself of?

Transgenic Crops

1

Biotechnology has already created plants that withstand pests and fruits that resist spoilage. Recent advances confirm its environmental soundness and commercial viability

by Charles S. Gasser and Robert T. Fraley

Modification of crop plants to improve their suitability for cultivation has persisted for at least 10,000 years. Early farmers produced better crops simply by saving the seeds of desirable plants. During the past century, plant breeding has become more rigorous in its approach. Significant improvements in crops have resulted from the successful crossbreeding of different individuals of the same species. More recently, researchers have made advances in crossing sexually incompatible species of the same family. Now there exists a promising method of developing superior plants: genetic engineering. By using recombinant DNA techniques, biologists can direct the movement of specific and useful segments of genetic material between unrelated organisms.

That approach can add a significant degree of diversity to the total repertoire of traits from which the plant breeder can choose. In the laboratory, plants can now be made to withstand insects, viruses and herbicides. Fruits can be made to resist spoilage, and grains may become more nutritious and economical.

Biologists created the first transgenic plants less than 10 years ago. Since then, researchers have applied genetic engineering to more than 50 plant spe-

cies. The technique has helped investigators gain critical insights into the fundamental processes that govern the development of plants, and the first commercial introductions of such genetically modified plants are now only a few years away.

Although genetic engineering is more complex than traditional plant-breeding practices, it is just as safe. In both methods, new DNA enters the plant's genome and is stably maintained and expressed. A recent National Academy of Sciences report concluded that "crops modified by molecular and cellular methods should pose risks no different from those modified by classical genetic methods for similar traits." This past February the White House stated that genetically engineered products should not be subject to additional federal regulations, because they do not pose any unreasonable risk.

In this article, we shall describe the methods used at present to engineer plants genetically. We shall also outline the rationale of and progress in the current applications.

The first practical—and still the most widely used—system for genetic engineering of plants relies on an innate ability of the plant pathogen *Agrobacterium tumefaciens*. This bacterium can transfer a portion of its DNA into plant cells. It does so by introducing a set of genes into one or more of its own DNA fragments. These fragments, called transferred DNA (T-DNA), then integrate into chromosomes of infected plant cells and induce the cells to produce elevated levels of plant hormones. These hormones cause the plant to form novel structures, such as tumors or prolific root masses, that provide a suitable environment and nutrient source for the *Agrobacterium* strain. This bacterial infection is called crown gall disease.

For the bacterium to be an effective vehicle for DNA transfer, its disease-causing genes had to be removed. This

alteration is known as disarming. Researchers at the Monsanto Company and Washington University and groups directed by Jozef Schell of the Max Planck Institute for Plant Breeding in Cologne and by Marc van Montagu of the State University of Ghent in Belgium first accomplished the task in 1983. They relied on traditional DNA recombination to delete the genes that cause tumors. Disarming thus eliminates the bacterium's ability to cause disease but leaves the mechanism of DNA transfer intact [see "A Vector for Introducing New Genes into Plants," by Mary-Dell Chilton; SCIENTIFIC AMERICAN, June 1983].

The first engineered gene, constructed with *Agrobacterium* in the early 1980s by groups at the Max Planck Institute in Cologne and at Monsanto, made plant cells resistant to the antibiotic kanamycin, a compound that inhibits plant growth. The engineering of kanamycin resistance represented a breakthrough for two reasons. First, it showed that foreign genes and proteins could be expressed in plants. Second, it demonstrated that kanamycin resistance is useful as a "marker." Because only a small number of cells take up, integrate and express introduced DNA, marker genes help investigators to identify those cells into which genes have successfully been introduced.

Because plant cells are totipotent—that is, the undifferentiated cells can generate a whole organism—complete, reproductively competent plants can emerge from the transformed cells. Most methods today rely on the cells of explants, or small pieces of plant, for genetic engineering. Our colleague Robert B. Horsch of Monsanto popularized the use of a common paper hole punch to cut disks from leaves for *Agrobacterium*-mediated techniques. (He used to carry a punch in his coat pocket, always ready to give an impromptu demonstration of the leaf-disk transformation method.) *Agrobacterium*-mediated gene transfer is now routinely used in hundreds of industrial and aca-

CHARLES S. GASSER and ROBERT T. FRALEY collaborated on research in crop improvement at the Monsanto Company in St. Louis for five years. Gasser, now assistant professor at the University of California, Davis, received his Ph.D. in molecular biology from Stanford University. He is currently using genetic engineering methods to study plant development. Fraley, vice president of technology for Monsanto, received his doctorate from the University of Illinois. He has made pioneering contributions in gene transfer in plants and is deeply interested in the commercial development of engineered crops to address, in particular, food production in developing countries.

dem laboratories around the world. At Monsanto alone, more than 45,000 independent transgenic plant lines have been produced in this way.

Although the method is simple and precise, many plant species, including such critical grain crops as rice, corn and wheat, are not natural hosts for *Agrobacterium* and so are not readily transformed by the method. As a result, extensive efforts have been mounted to develop alternative systems.

One of the first was introducing free DNA into plant protoplasts. Protoplasts, plant cells that have had their cell walls removed by enzymes, must be used because the pores of cell walls are too small to allow the easy passage

of DNA. The only barrier in protoplasts is the plasma membrane. Polyethylene glycol, a thick organic polymer, can penetrate the plasma membrane to transport DNA. It is the most commonly used chemical delivery agent. Electroporation can also carry DNA across the plasma membrane. In this process, short, high-voltage pulses briefly produce pores in the protoplast membrane. The DNA molecules can enter through these spaces.

Because these procedures do not rely on any special biological interaction, they are, in principle, general methods of transforming cells. But the regeneration of plants from isolated protoplasts has proved problematic in many spe-

cies, especially the critical cereal grains. Corn and wheat respond very poorly, usually yielding infertile plants.

As a result, investigators have been searching for methods that introduce DNA into intact plant cells, those that still have their walls. A fairly obvious way is simply injecting the DNA. But microinjection has not been effective for several reasons. The fine needle tips break easily and clog frequently. Transforming cells one at a time is tedious, difficult work that would be inappropriate to a commercial operation. Furthermore, once DNA enters a cell, its incorporation into the genome of the recipient is by no means a certainty. A technician might have to inject DNA



GENETICALLY ENGINEERED RESISTANCE to the Colorado potato beetle (*Leptinotarsa decemlineata*) is shown in this false-color, infrared aerial image of test beds planted in a field recently irrigated by a center-pivot system at Hermiston, Ore.

The beetles defoliated fields of ordinary potato plants, leaving behind wet ground (green), but avoided plants that were able to produce their own insecticide (red). The white patches are wheat plants kept dry for an unrelated experiment.

into at least 10,000 cells just to ensure that one of them will take up the new gene.

To increase the efficiency of gene delivery, John C. Sanford of Cornell University envisioned a way to bombard many plant cells with genetic material. He surmised that small metal particles, about one or two microns in diameter, could first be coated with DNA. Sufficiently accelerated, the particles could penetrate the walls of intact cells and thus deliver the DNA. Because small holes in cell walls and membranes rap-

idly close by themselves, the punctures are temporary and do not irreversibly compromise the integrity of the cells. Although the particles remain in the cytoplasm, they are too small to interfere with any cellular functions.

In 1987 Sanford and his co-worker Theodore M. Klein constructed a practical device that used tungsten particles to bombard plant cells. Their DNA particle gun, as it is called, uses a .22-caliber blank cartridge as the motive force. Researchers at Agracetus in Middleton, Wis., have developed a similar

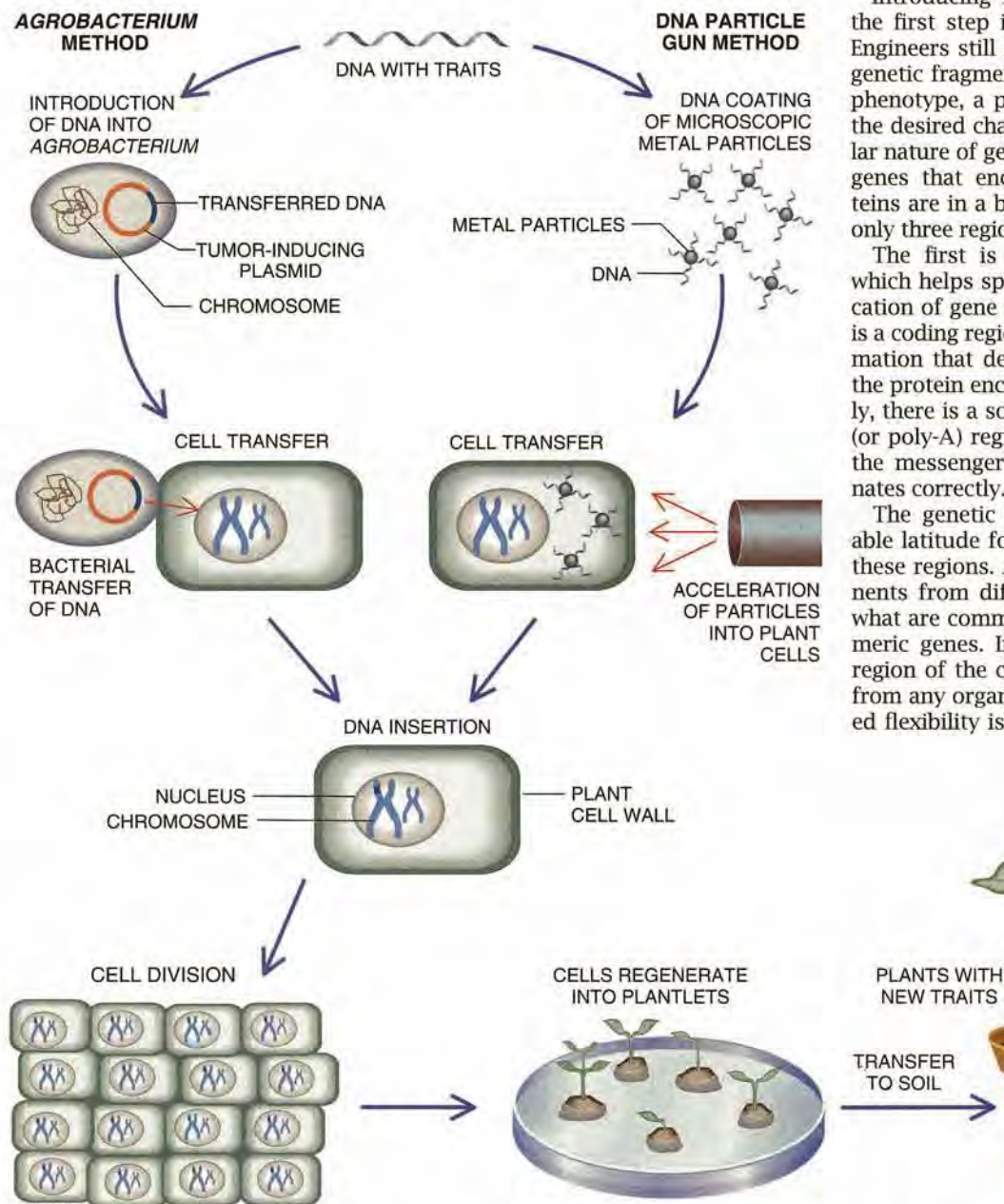
gun using gold particles propelled by the vaporization of a water droplet.

Both these particle guns have produced transgenic plants. Last year a group at DeKalb Plant Genetics in Groton, Conn., and a collaboration between Charles L. Armstrong of Monsanto and Michael E. Fromm, then at the U.S. Department of Agriculture in Albany, Calif., independently developed efficient, consistently functioning particle gun systems for the transformation of corn. Even more recently, we have collaborated with Indra Vasil's laboratory at the University of Florida in Gainesville to transform wheat plants.

Introducing DNA into cells is only the first step in transforming plants. Engineers still have to manipulate the genetic fragments to produce a useful phenotype, a plant variety possessing the desired characteristics. The modular nature of genes facilitates this task: genes that encode, or produce, proteins are in a broad sense made up of only three regions.

The first is a promoter sequence, which helps specify the timing and location of gene expression. The second is a coding region. It contains the information that determines the nature of the protein encoded by the gene. Finally, there is a so-called polyadenylation (or poly-A) region, which ensures that the messenger RNA transcript terminates correctly.

The genetic engineer has considerable latitude for mixing and matching these regions. Assembling the components from different genes results in what are commonly referred to as chimeric genes. In principle, the coding region of the chimeric gene can come from any organism. This unprecedented flexibility is the main advantage of



TRANSGENIC PLANTS are now commonly created by two methods. In the *Agrobacterium*-mediated technique, DNA with the desired trait is inserted into the tumor-inducing plasmid of the bacterium. The bacterium infects the plant cell

and transfers the DNA. In the particle gun method, metal particles coated with DNA are fired into the plant cell. In either case, the plant cell incorporates the DNA into its chromosome and then divides and regenerates into full plants.

genetic engineering over more traditional methods, which can transfer genes only between closely related species. Furthermore, by choosing various promoters, researchers can target gene expression to specific organs such as leaves, roots, seeds and tubers and, in many cases, to specific cell types within these complex tissues.

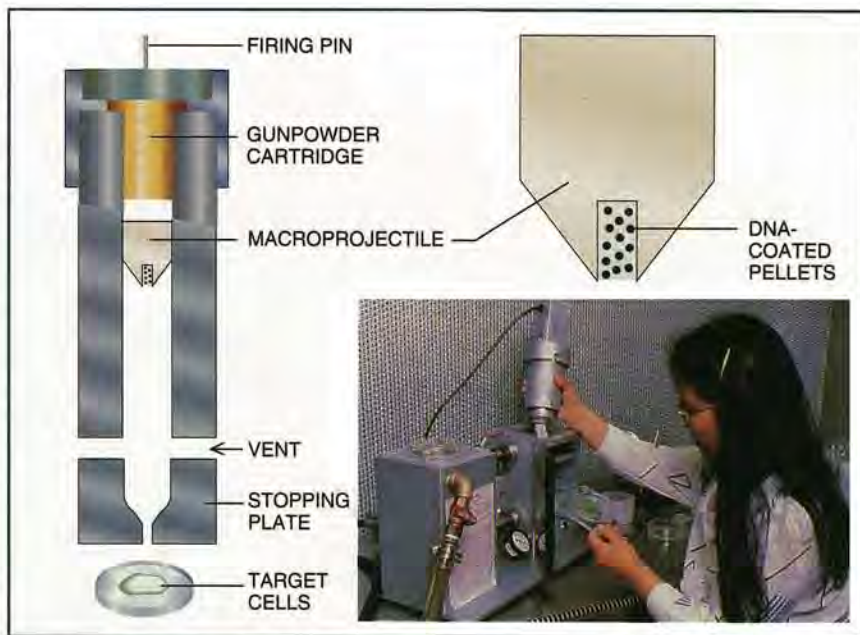
One of the most promising traits gene transfer offers is resistance to diseases. Exciting results have been achieved in creating plants resistant to viruses, an important matter because currently no direct way to treat virus-infected crops exists. Most infections reduce crop yield, but occasionally some prove catastrophic. Good farming practices, such as rotating crops and removing weeds and crop litter, can contain viruses, but only partially. Insecticides are sometimes used to control the pests responsible for transmitting the virus.

Genetic work on virus resistance builds on previous basic research in plant biology. It had long been observed that infection of a plant with a mild strain of a virus protected it from subsequent infection of a more virulent strain. Apparently, the replication of the mild virus strain interferes with a virulent strain's ability to infect. Investigators have applied "cross-protection" to shield greenhouse-grown tomatoes against contagion by intentionally infecting them.

Roger N. Beachy and his co-workers at Washington University reasoned that a single component of the virus might be responsible for the protection. Collaborating with Stephen Rogers of Monsanto and one of us (Fraleigh), the investigators constructed a vector to introduce and express in tobacco and tomato plants the coat protein of the tobacco mosaic virus (TMV). Plants so modified were then inoculated with a heavy concentration of the virus. The plants were found to be strongly resistant to infection, thus confirming Beachy's hypothesis of viral protection.

Subsequent experiments have shown that the expression of the TMV coat protein confers resistance only to strains of TMV and a few other closely related viruses. Still, the mechanism appears to be generally applicable; expression of the coat protein gene of almost any plant virus, at a sufficiently high level, protects against infection by that virus. Workers have now engineered effective tolerance to more than a dozen different plant viruses in a broad range of crop species.

Resistance to insect predation is another important goal for genetic engi-



DNA PARTICLE GUN developed by John C. Sanford of Cornell University fires tungsten pellets coated with DNA into plant cells. The pellets are held by a plastic macroprojectile, which is accelerated by a gunpowder charge. The plate stops the macroprojectile; momentum sends the pellets into the target. The vents allow air in front of the projectile to escape. In the photograph, a technician readying the device holds the "gun barrel" in her right hand; the cells to be transformed are in her left.

neering, especially in cotton, potato and corn plants. During the past three decades, gardeners and farmers have relied on the bacterium *Bacillus thuringiensis* (Bt), which produces an insecticidal protein. Most commonly used preparations of Bt are highly specific to the caterpillar larvae of lepidopteran insects—moths and butterflies—which are major pests. The Bt proteins bind to specific receptors located on the gut membranes of the target insects. The binding interferes with ion transport in the epithelial cells of the gut, thus disrupting the insect's ability to feed. These natural insecticides have no toxicity to mammals or even to any other species of insects.

The usefulness of the Bt-based insecticides is often limited by the ease with which they are washed from plants. Furthermore, their effectiveness in the field lasts only briefly. In the mid-1980s genetic engineers at several companies, such as Plant Genetic Systems in Ghent, Belgium, Agrigenetics in Middleton, Wis., Agracetus and Monsanto, succeeded in isolating from the bacterium genes for the insecticidal proteins. They used the particle gun and *A. tumefaciens* to insert the genes into tomato, potato and cotton plants. At first, the genes expressed poorly; the Bt proteins the plant produced killed only the most sensitive laboratory insects.

Monsanto scientists David A. Fis-

chhoff and Frederick J. Perlak made improvements. They redesigned the original bacterial gene to mimic more closely the plant DNA sequences. The changes dramatically enhanced insect control. Two years of field testing have confirmed that the presence of these Bt genes within cotton plants effectively controlled all major caterpillar pests, including the bollworm. These genetically engineered plants should reduce the use of insecticides on cotton by about 40 to 60 percent.

Scientists have screened extensively for naturally occurring *B. thuringiensis* strains that are effective on insects other than caterpillars. One such strain has led to the redesign of a gene that is effective against the Colorado potato beetle. In the summer of 1991, Russet Burbank potato plants expressing a beetle-control gene were tested at several sites from Maine to Oregon. Researchers found the potato plants to be essentially immune to beetle damage.

Bt may continue to offer additional genes for the control of plant pests. Scientists at Mycogen Corporation in San Diego have now discovered Bt genes active against plant parasitic nematodes, and Bt genes active against mosquitoes have been identified. Some researchers are trying to produce the mosquitoicidal protein in algae as a means to control malaria.

The target specificity of the Bt pro-

tein and its localization within the tissues of the plant ensure that the protein is active only against attacking insects. In contrast to topical insecticides, proteins in the plant obviously cannot be washed off. Extensive toxicological testing of *Bt* proteins and experience gained from more than 30 years of using *Bt*-based products confirm their safety. In fact, many researchers refer to *Bt* as the world's safest insecticide. Furthermore, the *Bt* protein, which makes up less than 0.1 percent of the total protein in the modified plants, breaks down in exactly the same fashion as any other protein—both in the soil and the digestive tract.

Besides the threat from viruses and insects, crops face a challenge from weeds. Weeds that compete for moisture, nutrients and sunlight can reduce a field's potential yield by 70 percent. Moreover, weed material in the harvest significantly reduces the value of the crop, and weeds serve as a habitat for pests.

In most cases, a combination of herbicide and careful cultivation effectively controls weeds. But because a herbi-

cide has a limited spectrum of activity, affecting only a small portion of the weeds, several kinds of chemicals are often used during the growing season.

Genetic engineering may offer a partial alternative to such weed control. The strategy is to create plants that can tolerate exposure to a single, broad-spectrum, environmentally safe herbicide. In contrast to views expressed by some critics of genetic engineering, the use of herbicide-tolerant plants will actually reduce the overall amount of herbicide applied.

There are two general approaches to engineering herbicide tolerance. Researchers at Monsanto and at Calgene in Davis, Calif., have been working to enable plants to tolerate glyphosate, the active ingredient of a herbicide called Roundup. Roundup is a broad-spectrum compound that can control broadleaf and grassy weeds. The compound kills plants by inhibiting the action of EPSP synthase. This enzyme is necessary for the production of the aromatic amino acids that a plant needs if it is to grow.

Genetic engineers are especially interested in Roundup because it is one of the most environmentally attractive her-

bicides. It does not affect animals, because animals do not have an aromatic amino acid pathway. Furthermore, it degrades rapidly in the environment into harmless, natural compounds.

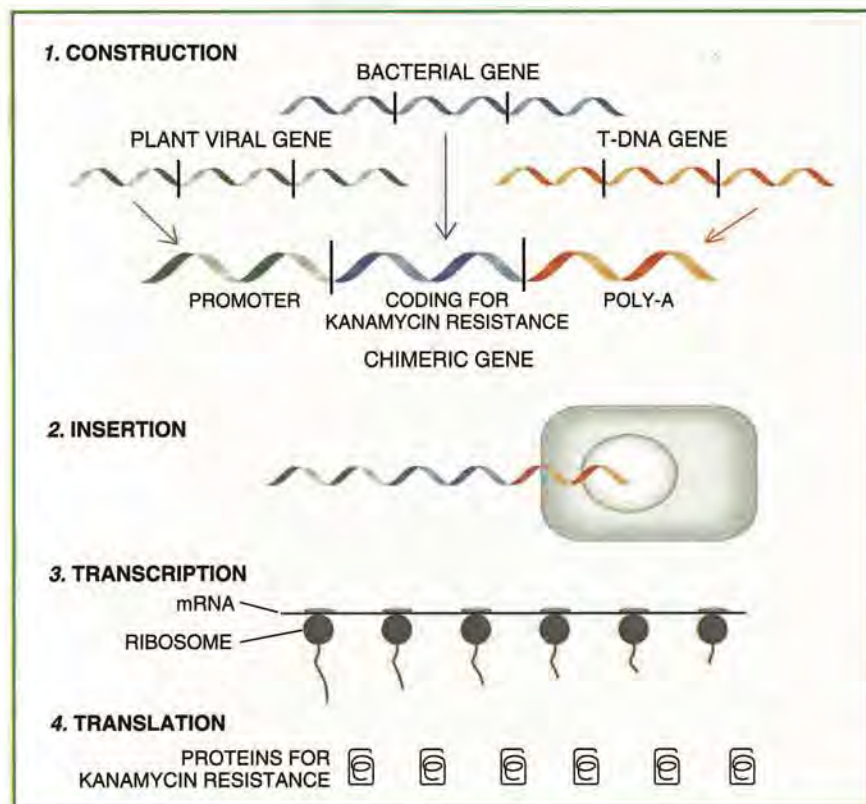
The first step in developing Roundup tolerance took place in 1983, when groups headed by Luca Comai and David M. Stalker of Calgene and Rogers and Ganesh Kishore of Monsanto isolated the genes for EPSP synthase from bacteria and plants. They also identified variants of the genes that produce proteins that have reduced sensitivity to Roundup. Later, investigators were able to construct genes that produced higher amounts of these proteins in plants. The genes were subsequently introduced into tomato, soybean, cotton, oilseed rape and other crops. As demonstrated by field tests performed during the past three years in the U.S., Canada and Europe, the crops were able to tolerate treatment with Roundup at levels that effectively controlled weeds. Researchers at Du Pont have used a technically similar approach to engineer plants that can tolerate certain kinds of sulfonylurea herbicides.

Scientists at Plant Genetic Systems and at the German company Hoechst took another approach to herbicide tolerance. From the microbe *Streptomyces hygroscopicus*, they isolated a gene for an enzyme that inactivates a herbicide called Basta, which affects the glutamine synthase pathway in weeds and thus interferes with their growth. But crop plants that have the gene inactivate Basta before damage can occur. Field tests performed on the Basta-tolerant plants demonstrate the effectiveness of the protection.

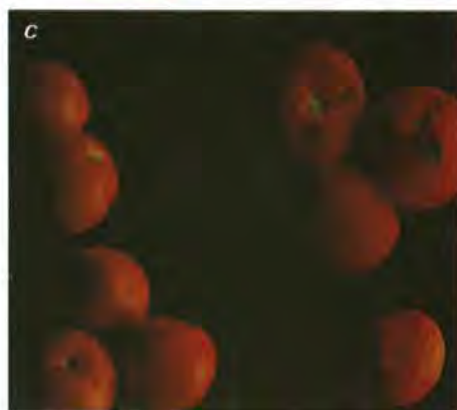
Engineered herbicide tolerance offers the farmer an alternative that is lower in cost and more effective than conventional weed-management measures. Careful selection of broad-spectrum herbicides should lead to an overall decrease in the use of weed-control chemicals and should enable farmers to replace existing herbicides with environmentally more attractive products.

Additional advances in the simplicity and breadth of genetic engineering techniques and increasing knowledge of plant biology promise to extend greatly the beneficial changes that gene transfer can confer. For example, researchers have already identified and isolated several genes that play a role in the biosynthesis of ethylene, the signal molecule that triggers the ripening of fruits. Delayed spoilage would allow harvesting at a later stage than is currently practical, which may improve the flavor and even the nutritional value.

To increase the shelf life of fruit, re-



CHIMERIC GENES can be constructed from the genes of different organisms. Here the chimeric gene for kanamycin resistance is assembled from diverse sources: the promoter region of a plant virus, the coding region of an *E. coli* bacterium and the poly-A site from the transferred DNA (T-DNA) of *Agrobacterium* (1). After the chimeric gene is inserted into a plant cell (2), it is transcribed into messenger RNA (mRNA) (3). The ribosomes translate the mRNA to produce the proteins (4).



GENETICALLY ENGINEERED SPECIES

ALFALFA	CRANBERRY	PAPAYA	SPRUCE
APPLE	CUCUMBER	PEA	STRAWBERRY
ASPARAGUS	EGGPLANT	PEPPER	SUGARBEET
BROCCOLI	FLAX	PLUM	SUGARCANE
CABBAGE	GRAPE	POPLAR	SUNFLOWER
CARROT	HORSERADISH	POTATO	SWEET POTATO
CAULIFLOWER	KIWI	RASPBERRY	TOBACCO
CELERY	LETTUCE	RICE	TOMATO
CORN	MUSKMELON	RYE	WALNUT
COTTON	OILSEED RAPE	SOYBEAN	WHEAT

GENETICALLY TRANSFORMED CROPS, shown to the left of their ordinary counterparts in each photograph, include herbicide-tolerant cotton plants (a), insect-resistant tobacco plants

(b) and tomato plants whose fruits resist spoilage (c). The list identifies familiar plant life in which genetic engineering has successfully been demonstrated.

searchers developed two genetic methods. The first is inserting so-called antisense versions of the ripening genes. Antisense molecules bind with specific messenger RNA to turn off the genes. Athanasios Theologis of the USDA in Albany, Calif., and Don Grierson of the University of Nottingham have shown that fruits of tomato plants with the antisense genes resist softening. In a different approach, Monsanto scientists Kishore and Harry Klee have introduced a gene into tomato plants that induces them to manufacture an enzyme. This enzyme degrades the precursor compounds that form ethylene, thus retarding spoilage.

Genetic engineers may also be able to fashion healthier foods: genes for proteins that have superior nutritional properties have been isolated. It should be possible to insert these genes into crops. Plants could also be tailored to produce specialty chemicals such as starches, industrial oils, enzymes and even pharmaceuticals. Preliminary trials are now under way.

More than 400 field tests of engineered plants have now been conducted

in the U.S. and Europe. The tests confirm the inherent safety and commercial validity of these approaches, and crops containing these traits should be available to farmers during the mid-1990s. Still, there are some limitations. In practical terms, genetic engineers can only modify traits expressed by no more than three to five genes. Furthermore, some crops do not respond to current gene-transfer methods, and isolating useful genes is sometimes difficult.

Yet to many in plant biotechnology, these challenges seem less likely to delay commercialization than are nontechnical issues. Genetically modified crops are being developed at a time when both public and political support for agricultural research is in general tepid. Concerns about food safety, the environmental impact of agriculture and a rapidly changing farm infrastructure have combined with a lack of understanding of new technologies to overshadow the long-term need for economical, high-quality food products. World food production will have to increase threefold during the next 40 years to

meet the needs of an estimated nine billion people. Biotechnology is one of the few new solutions to this problem.

Another important advantage of the genetic engineering of plants is that it provides the very latest technology to farmers in a very traditional package—the seed. Even the most impoverished nations will thus have access to the benefits without the need for high-technology supplies or costly materials. Although not a panacea, biotechnology promises to become an important component of agriculture around the world.

FURTHER READING

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