Coming Soon to a Store Near You:

TRANSGENIC PLANTS

BY *SIMSON GARFINKEL*

MOST FRESH TOMATOES bought in the U.S. today are picked green, packed in crates, and ripen on their way to market. That's because all tomatoes contain polygalacturonase (PG), a natural protein that's the biological equivalent of a self-destruct device. Before tomatoes are ripe enough to make into a hearty sauce, PG is hard at work, literally digesting the tomato from the inside. In the wild, this helps the tomato get its seeds into the ground quickly. But for farmers and grocers, PG is a headache, responsible for countless tomatoes that aren't fit to sell.

The patented "Flavr Savr" tomato is different: it looks like a regular tomato, but it doesn't rot. It's been genetically modified. The DNA for the gene that tells the plant how to make PG has been snipped out, reversed and reinserted with biotechnology's finest scalpel.

Since this new tomato rots very slowly, farmers can leave it to ripen fully on the vine, resulting in a tomato that looks, smells, and tastes better than the majority of today's storebought ones. That spells more profits for grocers, farmers, and Calgene.

Based in Davis, California, Calgene — developer of this brave new tomato — is an eleven-year-old biotech startup company with 300 employees and $35 million in annual sales. The company filed for FDA approval in August 1991; if things go as planned, Calgene's tomato could be on supermarket shelves by 1993.

It is becoming increasingly apparent that the way most Americans will first experience the advancing biotechnology revolution won't be by undergoing a genetic test or by being cured of a disease; it will be by eating food, wearing cotton, or sniffing flowers that have been genetically engineered. Calgene is not the only company pursuing the green gene: according to a recent survey, at least twenty-five U.S. companies are applying recombinant DNA techniques to plant technology. And the products under development sound like an organic farmer's wish list: carrots that taste sweeter; cotton that insects don't eat; vegetables and grains that are immune to viruses — and much more. In the future, engineered plants might be more resistant to drought, impervious to soil salinity, able to fix their own nitrogen from the air, or even have improved photosynthesis capabilities.

Agribusiness has been breeding tomatoes tough enough to be kicked along the highway to market. Customers complain they don't taste like they used to. Now a biotech company is splicing tomato genes in the hope of improving flavor. Is it food (the Food and Drug Administration is currently pondering this question), and will you buy it?

Simson Garfinkel writes on science and technology issues. He took issue with Eric Drexler's theories about nanotechnology in WER #67 (p. 104).

—Richard Nilsen

Both the scientific community and environmentalists are less scared about the potential dangers of recombinant DNA than they were in the early 1980s. Few believe that, like some 1950s B-grade horror movie, a lone company's genetics experiment will go crazy and become a "superpest," wreaking havoc on an unsuspecting ecosystem. "Some of the forecasts of disasters for biotech organisms were wholly unrealistic," says Dr. Rebecca Goldburg, a scientist with the Environmental Defense Fund. But there are still a few dark corners in the genetically engineered field of the not-too-distant future — dangers

Calgene's Matt Krame in a 1990 field trial of the "Flavr Savr" tomat

not of som thing goi wrong, but things goin

One of the netically e while mos their time their resea that are res

Monsanto, oping a va that is resi cide. Roun interfering green. Far be able to c killing eve

Round-Up Altemus, a people and it doesn't Round-Up have to use plants tha chemicals with weed and not re

Goldburg For starte

'TS

ƷARFINKEL

ı, packed in
oes contain
ent of a self-
y sauce, PG
ıe wild, this
ınd grocers,
o sell.

ɔursuing the
rey, at least
ıg re—nbi-
gy. A the
an organic
ts that taste
cts don't eat;
hat are im-
much more.
ered plants
to drought,
y, able to fix
ı the air, or
ıtosynthesis

nunity and
less scared
ıgers of re-
ıey were in
ve that, like
or movie, a
experiment
become a
ıavoc on an
. "Some of
for biotech
ınrealistic,"
ırg, a scien-
d. Bu re
ically engi-
— dangers

Calgene's Matt Kramer in a 1990 field trial of the "Flavr Savr" tomato.

not of something going wrong, but of things going exactly as planned.

One of the most disturbing developments with genetically engineered plants, says Goldburg, is that while most of the companies in the industry spend their time talking about insect and virus resistance, their research dollars go toward developing plants that are resistant to herbicides.

Monsanto, for instance, is in its fourth year of developing a variety of canola (a source of vegetable oil) that is resistant to the company's Round-Up herbicide. Round-Up is an amazingly potent herbicide: by interfering with photosynthesis, it kills everything green. Farmers planting Monsanto's new canola will be able to control weeds by spraying with Round-Up, killing everything but their cash crop.

Round-Up is an ideal herbicide, according to Jim Altemus, a Monsanto spokesman: it isn't very toxic to people and, since it breaks down in contact with soil, it doesn't collect in groundwater. And because Round-Up is so powerful, says Altemus, farmers will have to use it less: "Our whole premise in developing plants that are tolerant to herbicides is that fewer chemicals are going to be in the environment to deal with weeds. Many times the problems will be minor and not require any chemical remediation."

Goldburg and other environmentalists aren't biting. For starters, they say, companies are developing

The way most Americans will first experience the advancing biotechnology revolution won't be by undergoing a genetic test or by being cured of a disease; it will be by eating food, wearing cotton, or sniffing flowers.

crops that are resistant to pesticides that are much more dangerous than Round-Up. Calgene, says Goldburg, is developing cotton that tolerates bromoxynil, while the Agriculture Research Service in Albany, New York, is now testing potatoes tolerant to 2,4-D. (Round-Up itself isn't that safe: runoff in streams and rivers has been shown to kill aquatic life.) The actual result of herbicide-tolerant plants, say environmentalists, will be strong pressures on farmers to use more herbicides, and use them more often.

Five of the seven largest pesticide manufacturers (Bayer, Ciba-Geigy, ICI, Rhone-Poulenc, and Monsanto) are also ranked among the world's twenty-five largest seed companies; all are using biotechnology to develop herbicide-resistant plants, according to a 1987 article in *Rural Advancement Fund International Communique*. The industry's goal is to profit by selling patented seeds that only work with specific, patented pesticides.

"Are chemical companies going to develop herbicide-tolerant plants so they can sell fewer chemicals?" asks Goldburg.

To make things worse, Goldburg says, your taxes are paying for some of the research though USDA research grants. In 1990, Senator Patrick Leahy, chair of the Senate Agriculture Committee, introduced a bill that would have prohibited the "USDA from funding mission-oriented research to develop herbicide-tolerant plants," says Goldburg. The bill was withdrawn after pressure from the USDA and industry.

Companies like Monsanto do hope to sell fewer chemicals with their insect-resistant vegetables, cotton and grains. Last summer, Monsanto conducted six outdoor tests of its insect-resistant cotton in Alabama, Mississippi, Louisiana, Arizona, and at two locations in Texas. The tests compared the insect-resistant cotton with cotton protected by a weekly application of conventional insecticide; a third field at each location was left untreated as a control.

In all the trials, the genetically engineered cotton fared as well as the chemically protected plants: less than 8 percent of the cotton bolls on each plant were destroyed, according to Dr. David Fischoff, director of Monsanto's Plant Molecular Biology division. By comparison, between 10 percent and 40 percent of the bolls on the unprotected plants were destroyed.

> "As soon as you put a *Bacillus thuringiensis* gene into a plant, you are selecting for an insect population that is resistant to *B.t.*"

The gene that protected the plants is based on a gene from *Bacillus thuringiensis* (B.t.), bacteria commonly used by organic farmers as an alternative to synthetic chemical pesticides. The B.t. bacteria produce a powerful toxin that dissolves an insect's gut on contact. Farmers using it today spray the bacteria directly on their crops. Over the past decade, Fischoff's group has isolated one of the B.t. genes, which is responsible for producing the toxin. The company's scientists have modified the gene so that the plant will produce the toxin in significant amounts. Finally, the gene has been successfully inserted into both cotton and tomatoes. The plants now produce the B.t. toxin in every root, leaf, stem and fruit.

As the field tests indicate, the results are spectacular: "The insects stop feeding almost immediately: they don't have to feed much to get a dose that will deter them and kill them," said Fischoff. "After half a decade of lab work . . . we might have something that can move on to be a potential plant product," he added proudly.

Other scientists familiar with the insect-resistant plants are not quite as excited. "As soon as you put a B.t. gene into a plant, you are selecting for an insect population that is resistant to B.t.," says James Liebman, a plant pathologist at the University of California at Berkeley.

After all, the same thing has happened with virtually every synthetic pesticide, starting with DDT — if a farmer applies a pesticide repeatedly, the local insect species develop resistance to that insecticide. In the case of these Monsanto crops, the plants will be applying the pesticide for the farmer.

"B.t. has been one of the safest pesticides around, and for a long time," says Dr. Liebman. "It has low mammalian toxicity; people think it's great. If you put a B.t. gene in the plant, and that plant expresses the B.t. gene all the time, in all parts of the plant, then you have constant selection for resistance, and you can bet that you are going to get resistant insects probably in two or three years. That would be a real shame; it would ruin B.t."

Indeed, said Fischoff at the conference, B.t.-resistant insects have already been discovered. Monsanto plans eventually to deal with the resistance problem by using several different toxins, or by having the toxin produced only in certain parts of the plant, or only during certain times during the growing season. But all of those approaches require more work — and in some cases, new scientific discovery — before they can be commercialized. In the meantime, companies like Monsanto will probably bring the products they have to market.

Another promise of the new biotechnology is developing plants that are resistant to viruses. This is big news for farmers, who today have few defenses against most viral plant diseases.

Viruses are the simplest form of life — so simple that some biologists say they are not alive at all. A virus consists of two parts: an inner core made up of genetic material (either DNA or RNA), and an outer shell, called a "coat," made of protein. A virus infects a cell by attaching its coat to the cell's membrane, then injecting its genetic material into its victim. The virus then takes over the infected cell, forcing it to make more copies of the virus. Eventually the infected cell makes so many copies of the new virus that the cell bursts, and the newly created viruses go on to infect more cells.

To make a plant resistant to a particular virus, scientists isolate the DNA inside the virus that makes the virus's coat and splice it into the plant's genetic code. For reasons that aren't completely understood, if the plant is already producing the protein for a virus's coat, that virus can't infect the plant.

Work is proceeding quickly. Tomatoes have been engineered for resistance to tomato viruses X and Y; potatoes have been produced that won't succumb to the potato leaf-roll virus. Plants resistant to cucumber mosaic virus, tomato aspermy virus, and alfalfa mosaic virus have been developed.

Although at first there would seem nothing wrong with engineering plants for viral resistance, a recent article published by Dr. Gus de Zoeten at Michigan State University's Department of Botany and Plant Pathology has alarmed several ecologists. In the article, published in the journal *Phytopathology*, Zoeten hypothesizes that a plant rendered genetically immune to one kind of virus could be infected by another kind: inside the plant, the genes for the two viruses could mix, forming a new, hybrid virus.

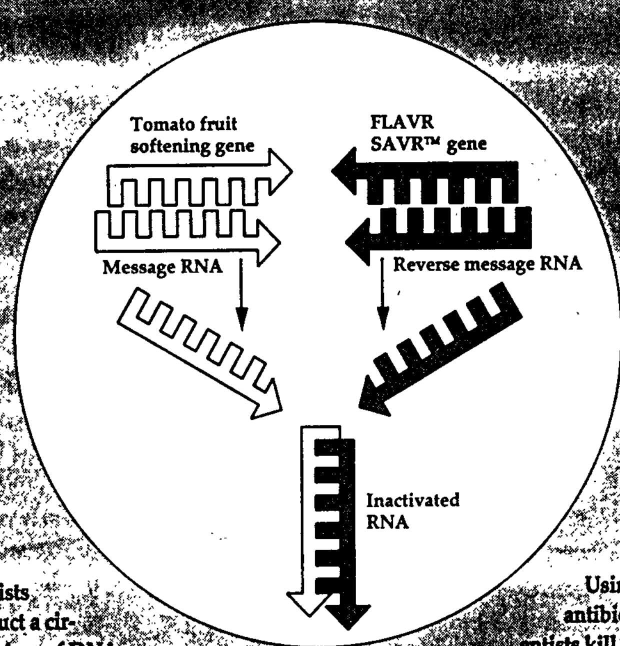
But the biggest danger of transgenic plants hasn't even been thought of yet, says Steven Witt, president of the San Francisco-based Center for Scientific Information and the author of three books on biotechnology (*WER* #51, p. 37). "If you look at any new technology, the risks that will probably come back to haunt us [are ones] nobody knows right now." Trying to understand the new world of biotechnology through eyes trained to look at chemical pesticides doesn't work. The world of genetically engineered plants has its own benefits, and dangers, that remain to be discovered.

Despite these concerns, a number of genetically engineered plants are out of the laboratory and involved in field trials. Expect them to start reaching consumers before 1995.

The new engineered varieties might create new markets. DNA Plant Technology Corp., in Cinnaminson, New Jersey, has produced genetically transformed chrysanthemums with pure white blossoms, according to a recent article in *Science* magazine. More than likely, the new chrysanthemums won't replace their colored cousins, but will be placed alongside them.

On the other hand, genetically engineered plants that are sweeter, juicier, and blemish-free might create a market climate that makes many of today's vegetables unsalable. That's a recipe for monopolies, because farmers will be only able to get each of these genetically enhanced crops from a single source. And they'll have to go back to that source every year to buy new seed: every biotech company spoken with for this article plans to sell only hybrid seed to its customers.

CALGENE'S TOMATO ALTERATION PROCESS



Scientists construct a circular piece of DNA (deoxyribonucleic acid), the basic component of all living matter and carrier of genetic information, which contains a special antibiotic-resistant gene (*kan*[1]) and Calgene's Flavr Savr gene (antisense polygalacturonase or antisense PG).

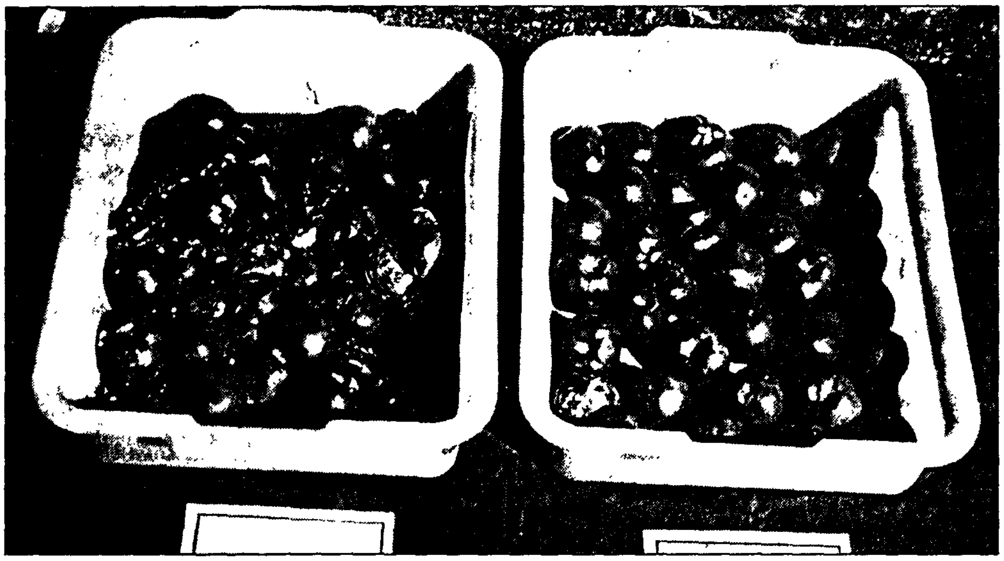
The newly constructed DNA, which now contains the two genes, is placed in special "disarmed" bacteria (Agrobacteria) capable of invading plant cells. The Agrobacteria adopt the new DNA.

The Agrobacteria containing the new genes are mixed with tomato-plant cells in a petri dish where the bacteria invade the cells, taking with them the two special genes.

Using an antibiotic, scientists kill off the plant cells that did not take up the new DNA containing the two genes. About 10 percent of the plant cells will have been successfully transformed (will have taken up the new DNA).

In separate containers, scientists prepare special growth media to enable the plant cells to produce shoots and roots, then transfer the plantlets to greenhouse pots. Selected plants proceed to tomato field trials for evaluation.

The tomatoes produced by the gene-spliced plants contain Calgene's Flavr Savr gene. Inside each tomato the gene blocks the production of the fruit-softening enzyme PG, causing the fruit to ripen normally but soften more slowly.



Twenty-five days after harvest, the tomatoes on the left are rotting. The genetically altered "Flavr Savr" tomatoes on the right are not.

"Without hybrid crops, can we make money on it?" Monsanto's Fischoff asks rhetorically. Fischoff says that it's unreasonable to think that biotech companies will want to gouge their customers: "Certainly, the goal in selling a product like this will be to price it so that there is a net positive return to the farmer."

From the public's point of view, possibly one of the most crucial problems still to be answered is the issue of labeling: should the government require that foods containing genetically manipulated ingredients be specially labeled?

"There is no reason to label it as 'transgenic,'" says Dr. Pamela Bridgen, executive director of the Association of Biotechnology Companies in Washington, DC. "Transgenic plants are around all over the place, from all the breeding that has been going on for the last 100 years."

Indeed, virtually all of the food for sale in the supermarket has been genetically altered: meat, vegetables — even the yogurt cultures. For as long as humans have farmed, agriculture has effected a steady pressure on the genetic makeup of plants and animals to mirror people's needs and desires.

"I can't imagine any reason why there should be a special labeling requirement for transgenic plants," says Dr. Kenneth Barton, vice president for research and development of Agrecetus, Inc., in Wisconsin. "I certainly think that there should be a labeling requirement for any plants that have particular hazards of some sort, [but] if it has gotten on the market, presumably they are generally recognized as safe. I just can't understand a rationale for singling out this type of breeding."

Privately, industry sources say the real reason that they are opposed to labeling is the potential for consumer fear: consumers might be scared enough by the idea of genetically engineered foods that they refuse to purchase them, no matter how well the stuff has been tested.

"I'm not taken in by the industry's argument that we shouldn't label because the public won't buy this," says the EDF's Dr. Goldburg. "They've been hyping this technology as the greatest thing for the public. If it's so great, the public should want to buy it. If not, then they're trying to pull the wool over the eyes of unsuspecting consumers."

For thousands of years, humanity has been tinkering with plant genetic material, trying to make crops that were better than those of the previous generation. Recombinant DNA technology is the most powerful technology that's come along for forcing plant genes to do our bidding: it's a tool that lets us direct the course of evolution, while making it happen on a much more rapid timescale.

Calgene's Chairman Roger Salquist has tasted the "Flavr Savr" tomato. "Am I afraid to eat them?" says Salquist. "The answer is no."

The danger is that our knowledge of plant microbiology tends to mask our ignorance of the ways that plants interact with their surrounding environment. A plant that is safe to eat might still be responsible for unanticipated ecological or economic damage elsewhere. The fruits of this new technology — intended and otherwise — may crop up in many places beyond the neighborhood supermarket. ❦