Large Plots Are Next Test For Transgenic Crop Safety

MONTEREY, CALIFORNIA—For 20 years, agricultural biotechnologists have been promising a new era of transgenic crops that will not only be cheaper to grow but will also taste better and resist spoilage. Earlier this year, the first fruit of the gene-splicing art—Calgene's long-lived Flavr-Savr tomato—hit the market, and plenty more are getting ripe for commercial introduction: This year alone, 486 field tests of transgenic crops ranging from corn to walnuts were launched in the United States, compared with a mere five in 1987. But the arrival of these new agricultural products may yet be delayed by nagging fears that weeds might pick up resistance to herbicides, viruses, and pests from engineered crop plants and wreak havoc on agricultural production.

PHOTOS BY D. GONSALVES

No contest. The papaya ring spot virus devastated papaya plants not treated with a virus-resistant gene.

Researchers are divided on just how seriously to take such fears, but they agree on one thing: Small, carefully managed experimental plots have yielded insufficient data on transgenic hazards. What's needed to gain a complete picture of genetic exchange between transgenic crops and other plants and to measure the true environmental impacts are tests covering thousands of acres—or commercialization of several transgenic crops. "Our assessments are at a stage where we can only address long-term problems by addressing them in large-scale field trials," says plant geneticist Philip Dale of the John Innes Centre in Norwich, United Kingdom. And that presents a Catch-22: If the dangers are real, activity of that magnitude could lead to precisely what critics fear—new strains of weeds and other plants that cannot be tamed by conventional methods.

Last month, researchers and regulators from 35 countries gathered here to sift through the latest safety data on small-scale transgenic field tests that have been conducted around the world.* What they heard seems likely to fuel rather than end the debate, however.

For activists, the message is that all transgenic crops must be tested for their ability to transfer genes to close relatives growing nearby before large-scale trials are conducted, says ecologist Jane Rissler of the Union of Concerned Scientists. Those who preach caution were especially disturbed by unpublished data from a team of Welsh researchers suggesting that transgenic sugar beets could transfer genes to weed relatives.

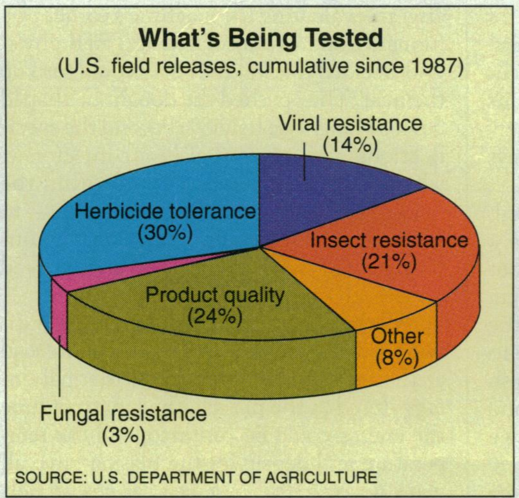
A DNA analysis of three subspecies of sugar beet in southwestern France—cultivated, wild, and weed beets—found that the genetic makeup of weed beets falls between that of the cultivated and the wild beets. To University of Wales population geneticist Pierre Boudry and his colleagues, that suggests the cultivated beets have bred with wild beets to form weeds, populations of which have exploded in the past 25 years. Indeed, he predicts that "commercial release of a transgenic sugar beet with a herbicide-resistant gene will lead to the escape of transgenes into the wild populations and the development of herbicide-resistant weeds."

Those concerns are heightened by results from another study (*Science*, 11 March, p. 1423) suggesting that viral RNA or DNA, inserted in a plant to make it virus-resistant, may recombine with genetic material from an invading virus to form new, more virulent strains. The researchers who conducted this study, Michigan State University plant biologists Ann Greene and Richard Allison, first created transgenic cowpea plants that expressed two thirds of the cowpea chlorotic mottle bromovirus (CCMV) capsid RNA gene. Then they inoculated the plants with a strain of virus missing that particular segment of the CCMV capsid gene.

Without the gene fragment, the virus can replicate but cannot infect the entire plant. However, the researchers found that four of 125 transgenic plants were systematically infected with CCMV, suggesting the RNA of the mutant CCMV strain and the plant RNA had recombined. The researchers concluded that RNA recombination "should be considered when analyzing the risks posed by virus-resistant transgenic plants."

In response, biotech proponents say that most crops being developed pose little risk to the environment, citing as proof recent findings from transgenic squash. In 1990, Asgrow Seed Company of Kalamazoo, Michigan, began small-scale field trials of a squash endowed with genes that code for coat proteins of two common viruses—the zucchini yellow mosaic virus and the watermelon mosaic virus-2. By a mechanism known as coat-protein mediated resistance, squash engineered to produce the coat proteins are better able to resist viral infection. As a result, such transgenic squash would need less insecticide to battle the insects that transmit the viruses.

In tests of wild squash growing near experimental plots, Asgrow scientists have found no evidence that the wild squash have bred with transgenic plants to form virus-resistant wild squash. At the same time, a survey sponsored by Asgrow found that 14 wild squash plants collected at nine sites in the United States and Mexico resisted infection when researchers exposed them to viruses in the lab; that finding supports the discovery that wild squash having no contact with transgenic varieties of squash still possess genes allowing them to resist the zucchini yellow mosaic virus. Taken together, says molecular biologist Hector Quemada, Asgrow's associate director for vegetable biotechnology, these data suggest that "it's unlikely viral-resistance genes from the transgenic squash will be



* Third International Symposium on the Biosafety Results of Field Tests of Genetically Modified Plants and Micro-organisms, 13–16 November, Monterey, California.

a problem [in the environment]."

Opponents aren't convinced. In particular, they argue that results from the Asgrow-funded survey are inconclusive. "That's like identifying 14 humans without malaria and saying malaria isn't a problem," says ecological geneticist Norman Ellstrand of the University of California, Riverside. But federal regulators are siding with Asgrow. Last May, the U.S. Department of Agriculture's (USDA's) regulatory arm—the Animal and Plant Health Inspection Service (APHIS)—issued a preliminary ruling that growing the transgenic squash would have "no significant environmental impact." APHIS is expected to make the ruling final by the end of the year, which would allow Asgrow to market the squash.

Many scientists would be more comfortable with such rulings if questions about genetic exchange had first been resolved in closely monitored large-scale field tests. "It's crucially important that large field tests are done to pick up early signs of problems," says entomologist Gary Fitt, program leader at the CSIRO cotton research unit in Narrabri, Australia. But Cornell University plant pathologist Denis Gonsalves, who is developing a transgenic papaya for Hawaii's struggling papaya industry, notes that safety concerns "can be tested as transgenic plants are commercialized."

There is, however, one place where data from large-scale trials might already be available: China. Chinese scientists have recently launched massive field trials of transgenic tobacco, tomatoes, and rice on thousands of hectares (*Science*, 11 November, p. 966). "China will provide us with a large-scale opportunity to see what is going on," says University of Bristol biologist John Beringer. Indeed, geneticist Chen Zhangliang, head of the college of life sciences at Beijing University, told researchers attending the conference here that China would welcome U.S. and European scientists to monitor the fieldwork. However, Fang Rong-Xiang, deputy director of the Beijing Plant Biotechnology Laboratory of the Chinese Academy of Sciences, told *Science* after the presentation that Chen was speaking on his own behalf and that the Chinese authorities have not yet discussed the possibility of outside monitoring. In the meantime, says Fang, "we haven't seen any serious problems in our large-scale tests."

For many scientists in developing countries, that is reassurance enough, for environmental safety issues are secondary to the demands for increased production. "We are prepared to take more risks to tackle problems," says Ariel Alvarez-Morales, biotech director at the National Polytechnic Institute in Irapuato, Mexico.

Indeed, top government officials in the United States and elsewhere appear ready to usher in a new age of agriculture. Says conference co-organizer Alvin Young, director of the USDA's office of biotechnology: "The door to commercialization is about to really open wide." Just how wide, however, may depend on data from large-scale field trials in China and from environmental monitoring of the first batch of transgenic crops to hit the market.

–Richard Stone

JAPANESE UNIVERSITIES

Leo Esaki: An Outsider Brings A Culture Change to Tsukuba

TSUKUBA—Like most other doctoral students studying materials science at the University of Tsukuba, Toshiki Komatsu spends his days doing experimental work. But, in a rare breach of the inward-looking culture typical of Japanese universities, he conducts his experiments not on campus but across town at the National Institute of Materials and Chemical Research, funded by the Ministry of International Trade and Industry. There, under the direction of Fusae Nakanishi, who heads the institute's Molecular Systems Laboratory and serves as a visiting research adviser at the university, Komatsu studies polymers that harden or change when exposed to light.

"Revitalizing creative activity is the main reason I was invited to become president."

—Leo Esaki

TSUKUBA UNIVERSITY

Komatsu is in the vanguard of a wave of reforms set in motion by Nobel laureate Leo Esaki, who was tapped as Tsukuba's president in 1992. Esaki spent 30 years at IBM in the United States, but his research roots are in Japan: His 1973 Nobel Prize in physics for demonstrating the electron tunneling effect in semiconducting materials, for example, was done in the 1950s at a forerunner to Sony Corp.

Esaki's status as an outsider committed to changing the system—he is the first person without an academic background to lead a national university in Japan, and he had no previous ties to Tsukuba—was one of the reasons the Tsukuba faculty elected him. And he's moved quickly to establish a reputation as a reformer. One of Esaki's first moves was to encourage industry to play a bigger role in graduate education through a new program that enables doctoral candidates to work in 31 participating corporate and government labs located in the surrounding Tsukuba Science City.

For Komatsu, having the choice was crucial to his scientific progress. "There's no group at the university working on this specialty," he says. "So my professors introduced me to Nakanishi."

Such interactions were expected to be routine when Tsukuba was founded, in 1973, as a new type of national university in the midst of Japan's first high-tech city. But the flame of reform had long since died out when Esaki was brought in. Indeed, "revitalizing creative activity at University of Tsukuba is the main reason I was invited to become president," Esaki told a recent symposium he convened on the role of Japanese universities in a global society. His goal, he says, is to turn Tsukuba "into a first-rate research university" and to create a model university for the 21st century.

The cooperative graduate school program is just one of many ideas he has brought with him from the corporate world. Last spring, a university reform committee that he established recommended fundamental changes in the way Tsukuba does business, including a greater emphasis on graduate education, with a more interdisciplinary focus; increased use of outside peer review of existing programs; greater diversity of faculty and students; and increased spending on facilities both for graduate and undergraduate students (see table on p. 1474). It's a tall order, and to succeed Esaki must overcome institutional inertia, budgetary constraints, and national laws that limit what a university can do.

Graduate gains. Esaki believes that the key to raising the overall quality of research at the university is to shift Tsukuba's educational sights from undergraduate to graduate-level education—not just for science and engineering, but also for the humanities and