AGBIOTECH: GM Technology Develops in the Developing World

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someone I want to court or someone I want to fight?" Kravitz's lab now hopes to identify the neural circuitry and chemical signals underlying such decisions by expressing female *fru* in specific subsets of neurons in male flies.

Bred for battle

Other labs have taken a different approach to studying aggression in *Drosophila*. Last September, two research teams reported breeding flies to be hyperaggressive. In one study, geneticists Ralph Greenspan and Herman Dierick of the Neurosciences Institute in San Diego, California, selected aggressive flies by introducing 120 males and 60 virgin females into an enclosure with 11 small cups filled with fly food. Males' first priority was mating, but after that they settled down on the food cups and started defending their territories.

In most encounters between males, one fly was clearly dominant from the beginning and would chase any intruders on his cup, Dierick says. But a few would stand their ground and fight back. These males are the most interesting, in Dierick's view. "The real question to me is what happens when a male decides to reciprocate?"

To get at that question, he extracted these dauntless flies from the fight cage and mated them with random females from the same generation. Then he started the process all over. After 21 generations, he'd created a superaggressive line of flies that were quicker to fight and fought longer and more intensely than a line of flies created by selecting random males from the fight cages. Next, Dierick used DNA microarrays to look for changes in gene expression in the aggressive flies. In this strain, 42 genes had increased or decreased their activity by 25% or more, Dierick and Greenspan reported in the September 2006 issue of *Nature Genetics*. These genes, they noted, have diverse roles, including muscle contraction, energy metabolism, and cuticle formation.

One gene in particular, *Cyp6a20*, has stood out so far as having a potentially significant influence on aggressive behavior. *Cyp6a20* was less active than normal in the aggressive line of flies, and deactivating it in a normal strain made the flies more aggressive. The gene encodes an enzyme that plays a role in many physiological processes, including pheromone signaling, and Dierick suspects that an underactive *Cyp6a20* gene makes flies more aggressive by making them hypersensitive to pheromones.

In the September 2006 issue of *PLoS Genetics*, a team led by Trudy Mackay of North Carolina State University in Raleigh reported the results of an attempt to pinpoint genes related to aggression in their own line of hyperaggressive flies. Mackay's group identified a much larger set of candidate genes—nearly 1500—and has so far found 15 that alter aggressive behavior when mutated. As in Greenspan and Dierick's study, the candidate genes covered a wide range of physiological functions.

One puzzle is that neither set of experiments turned up genes related to serotonin, the neurotransmitter with the longest legacy in the literature on aggression. One explanation, Dierick suggests, is that the breeding experiments didn't enhance (or repress) serotonin-related genes because there was little variation in these genes in the starting populations. Going forward, he says, establishing whether serotonin plays a role in fly aggression will be important for evaluating how applicable fly studies are for understanding aggression in other animals.

The broader implications of this work on fighting flies remains an open question. "It's far too early to speculate on what these studies might tell us about vertebrate aggression," cautions Hoffmann. Kravitz is more optimistic. Genes shape complex behaviors such as aggression in all animals, he notes. "If we understand how that happens in flies, it will give us some real information about how it might happen in other animals."

–GREG MILLER

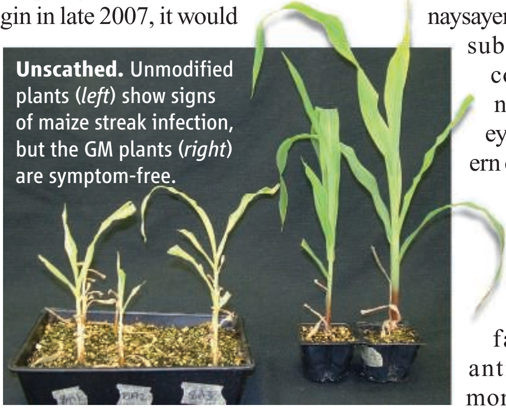
AGBIOTECH

GM Technology Develops in the Developing World

The first genetically modified crop developed entirely in Africa is gearing up for field trials. Its success would be a milestone

About 100 km north of Durban, South Africa, in a greenhouse chamber no larger than a walk-in closet, Frederik Kloppers clips a slender vial to a baby maize plant's new leaf. Inside the tube sits an insect with a potentially deadly bite, at least deadly to corn. This African leafhopper (*Cicadulina mbila*) carries maize streak virus, a scourge endemic to sub-Saharan Africa that devastates fields. Kloppers, a plant pathologist and technical manager at Pannar Seeds in Greytown, South Africa, gathers a dozen more tubes from the insect house and clips them to additional plants. Tomorrow, after the bugs have eaten their fill, he'll remove the tubes and then wait.

The fruit of more than a dozen years of effort, these maize plants have been genetically altered to resist infection by the virus. In greenhouse studies so far, the plant is highly resistant. If it proves equally hardy in field trials scheduled to begin in late 2007, it would be a milestone: the first-ever genetically modified (GM) crop developed by Africans for Africa.



Unscathed. Unmodified plants (*left*) show signs of maize streak infection, but the GM plants (*right*) are symptom-free.

CREDIT: DIONNE SHEPHERD/UNIVERSITY OF CAPE TOWN

But Kloppers and the plant's inventors, microbiologist Jennifer Thomson, virologist Edward Rybicki, and collaborators at the University of Cape Town (UCT), have much larger goals in mind. In a region where chronic hunger is the norm, GM maize could help alleviate grain shortages and potentially even boost economic development, says Thomson. And because plans call for selling the seed to small-scale and subsistence farmers for minimal profit, the inventors also hope it will help burnish the dim reputation of GM technology.

None of that is assured, Thomson and Rybicki concede. The plant could still fail in the field, as other African GM crop varieties such as sweet potato and cassava have done. The failures not only have disappointed the technology's advocates, but they've also fanned the flames of anti-GM sentiment. Although South Africa is one of the few African countries to permit farmers to plant GM crops within its borders, naysayers there, who still have substantial clout, have condemned the technology as a mere moneymaking tool for Western companies. Moreover, they remain unconvinced that homegrown efforts such as UCT's maize will succeed. Another failure would give anti-GM groups even more ammunition. The

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stakes are high, and the UCT scientists are treading carefully.

The problem

Maize is not native to Africa. It likely sailed across the Atlantic from the New World as cargo during the early 1500s, according to historian James McCann of Boston University. Maize flourished and displaced other native crops during the 20th century because it grows in only a few months and requires relatively little labor—one pass of the plow instead of the three or four necessary for crops such as sorghum and millet. In sub-Saharan Africa, maize has become the staple food; it makes up more than 50% of calories in local diets. In Malawi alone, maize occupies 90% of cultivated land and accounts for 54% of Malawians' caloric intake.

Maize streak virus is likely homegrown, say scientists. It lives in native grasses. At some point, the virus adapted itself to maize and is now able to jump between grasses and corn through the bite of an infected leafhopper, which itself isn't sickened by the virus.

Like any other infection, the wrath of maize streak waxes and wanes with different environmental conditions. Some years, crop losses are minimal. But in bad years, such as 2006, it can wipe out from 5% to 100% of a farmer's maize crop.

For the past 25 years, African crop scientists have been trying to breed resistant maize by crossing plants that carry some degree of natural resistance. But the task has not been wholly successful. The trait is conferred by several genes on different chromosomes and isn't consistently transmitted to the next generation. "It's not quite clear how resistance genes are inherited," says Kloppers of Pannar Seeds. Moreover, traditionally bred varieties do not completely resist the virus, Kloppers explains. Many tolerate an infection but still produce stunted or deformed cobs.

A solution

In 1988, when Thomson took over as head of microbiology at UCT, GM technology seemed a perfect solution. Rybicki's plant virology group there was already intensively studying the virus. Perhaps they could engineer a way to stop it in its tracks?

The design seemed simple enough: The team studied the proteins necessary for the virus to replicate. If they inserted a mutated viral gene into the plant, which in turn expressed a mutated protein necessary for the virus to replicate at very high levels, it could beat out the virus's normal protein and immobilize the virus, they reasoned.

CREDIT: DIONNE SHEPHERD/UNIVERSITY OF CAPE TOWN

Devastation. Transmitted by the bite of a leafhopper, maize streak virus devastates maize fields across Africa.

But getting the genes in proved tough, Thomson says. The UCT team first tried infecting maize with a widely used vector, *Agrobacterium tumefaciens*, carrying the genes, but to no avail. Ultimately, they successfully shot DNA into the plant using a gene gun. The GM maize plant carries a mutated form of a gene from the maize streak virus and two additional regulatory genes, one derived from maize itself and another from *Agrobacterium.*

Into the field

That was 6 years ago. Since then, the UCT scientists have been working closely with Kloppers at Pannar Seeds to test the plant's hardiness against infection. Kloppers has bred a previous version of the plant that carried an antibiotic-resistance gene through four generations. So far, it resists infection consistently. Moreover, the trait appears to be inherited in a dominant fashion.

Kloppers is repeating the experiment with a new group of plants that, because of environmental safety concerns, no longer carry an antibiotic-resistance gene. He expects to carry on crossing and checking inheritance and resistance through the next few months. Provided there are no major setbacks, he expects to apply for field trials during the latter part of this year.

Field trials are crucial to assess environmental and health risks, says Dionne Shepherd, a UCT postdoc who has been working on the project for the past 10 years. The scientists plan to examine whether the crop affects soil microorganisms and also whether it affects insects that feed on it. Other studies will also ensure that the added protein is indeed digestible and not an allergen.

If all goes well, the resistant maize will be the first GM crop to be field-tested in South Africa; to date, all GM crops planted in the country have been developed and tested elsewhere. The government is now developing its own expertise to evaluate environmental and human safety, says Shepherd, and because "UCT's maize is the most advanced locally produced GM product, they want to use our plant as a guinea pig," she adds.

To avoid the pitfalls that have beset other African GM crop varieties, the UCT scientists and Pannar have been working with regulators all along. At stake, they say, is not only their crop's fate, but also the technology's reputation.

A few years ago, Kenyan scientist Florence Wambugu, who was trained and supported by Monsanto, developed a sweet potato plant resistant to the feathery mottle virus. But when scientists field-tested the crop, traditionally bred resistant varieties outperformed it. Other efforts have also stumbled during field tests. Just a few months ago, scientists at the nonprofit Donald Danforth Plant Science Center in St. Louis, Missouri, announced that cassava plants genetically modified to resist cassava mosaic disease lost the trait after a few generations.

Both setbacks have fueled ongoing skepticism about GM technology. "All this talk about the technology's benefit for Africa is just a lot of PR hype to garner funding," says Mariam Mayet of the African Centre for Biosafety, an anti-GM lobby group in Richmond, South Africa. Most of the GM crops in the world are grown for animal feed or go toward food aid, Mayet says. "The benefit mainly goes to industrial agriculture, not to small-scale farmers."

Because UCT's maize is homegrown and was supported with very little corporate money—Pannar was the project's only corporate contributor—Thomson and Rybicki hope it can dodge some of these criticisms. Private foundations that typically give money with no strings attached and the South African government funded the project's bulk. To recoup its share of investment, Pannar expects the seed to cost no more than 15% higher than non-GM seed, says Kloppers. Small-scale or subsistence farmers would likely be charged much less, he adds.

If UCT's plant succeeds, it would be the first GM crop developed by a developing country. But Africans might not be the only beneficiaries. It might also become the poster child of what many argue is a useful and important technology—and for better or worse, one that desperately needs a public relations makeover.

–GUNJAN SINHA

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