

### BIOTECHNOLOGY

## Monsanto Pulls the Plug on Genetically Modified Wheat

Last week herbicide-resistant wheat became the latest casualty in the GM wars. It is one of a string of new genetically modified products, such as insect-resistant potatoes, that have been shelved because of fear of consumer objections. Monsanto's decision to halt plans to commercialize Roundup Ready wheat is not a huge setback for the company, biotech proponents are quick to point out. Indeed, ag-biotech is booming: In 2003, 68 million hectares in 18 countries were planted with GM crops, a 15% increase from 2002. But Monsanto's decision does reflect an industrywide trend, observers say: With market demand uncertain, companies like Monsanto are retreating from risky projects and sticking mainly to tried-and-true moneymakers—varieties of corn, soybeans, canola, and cotton.

"The companies have chosen their battlefield. Monsanto has said GM wheat isn't worth the fight," says Harry Klee of the Uni-

versity of Florida in Gainesville. "They're only going to work on the blockbusters." For now, that means more of the same traits that benefit the farmer's bottom line and not new types of fruits or vegetables aimed for a consumer market. For the longer term, however, companies are investing in products that they hope will appeal to grocery shoppers, such as healthier oils and longer-lasting produce.

Under development since 1997, Roundup Ready wheat is designed to tolerate the her-



**Wheat retreat.** Farmers feared that growing herbicide-tolerant wheat would jeopardize their exports to GM-averse countries.

bicide glyphosate. As with Monsanto's hugely successful Roundup Ready soybeans and corn, this product would allow farmers to control weeds by spraying the plants with a cheap, potent herbicide that is also relatively benign to the environment. Glyphosate resistance is such a popular approach that other companies are trying to get into the action (see story on p. 1089).

But wheat hasn't turned out to be a smart business choice. For starters, the market for this particular type of wheat, known as hard red spring wheat, accounts for just 20% of the 30 million tons of wheat U.S. farmers ship abroad each year. In announcing its decision, Monsanto cited a 25% decrease in acreage planted in hard red spring wheat since 1997 (due mainly to the higher prices farmers can get for corn and soybeans). And weed control isn't as big an issue for wheat as for soybeans. "For the majority of wheat-growing regions, this would have been just another choice," says wheat breeder James Anderson of the University of Minnesota, Twin Cities.

A less tangible challenge is that unlike the bulk of GM corn or soybeans, wheat is consumed directly by humans, not animals. The product, although useful to some farmers, offered no direct benefit to consumers in terms of taste, price, or nutrition, and many consumers in Asia and Europe aren't keen on the idea of further tampering with the "staff of life."

The real kicker was the fact that the European Union and Japan, the largest ▶

### STEM CELL RESEARCH

## Zerhouni's Answer Buoy Supporters

President George W. Bush hasn't modified his position on stem cells. But some advocates see a 15 May letter from Elias Zerhouni, director of the National Institutes of Health (NIH), as a signal that a review may be in the offing.

Zerhouni was responding to a plea by 206 House members asking the White House to "modify" its policy prohibiting federal support of research on any human embryonic stem cell (hESC) lines created after 9 August 2001. Most of the four-page letter describes what NIH is doing for stem cell research. But what got advocates excited was this statement: "Although it is also fair to say that, from a purely scientific perspective, more cell lines may well speed some areas of hESC research, the President's position is

still predicated" on his opposition to the destruction of human embryos.

"I think it's a big deal," says Lawrence Soler of the Juvenile Diabetes Research Foundation. "This is the first time the Administration has indicated that access to more stem cell lines will speed research."

Representative Michael Castle (R-DE), one of the organizers of the House initiative, acknowledged that Zerhouni's statement is "certainly not a change in policy." But "I look upon it as an invitation to have further discussions." Castle and Representative Diana DeGette (D-CO) were hoping to meet this week with White House officials.

The pressure to broaden Bush's restrictions isn't confined to the House. Senators Arlen Specter (R-PA) and Tom Harkin

(D-IA) are circulating a similar letter that has so far gained 51 signatures. Earlier this month, former first lady Nancy Reagan—who has already written politicians in support of hESC research—spoke out publicly for the first time, saying, "I just don't see how we can turn our backs on this [research]."

States have also gotten involved. Last week New Jersey Governor James McGreevey inaugurated a stem cell research institute for which he has requested \$6.5 million, calling his state "the first ... in the nation to devote public funds to stem cell research." And in California (*Science*, 16 January, p. 293), activists have amassed nearly twice the 600,000 signatures needed to put a \$3 billion bond issue for stem cell research on the November ballot. —CONSTANCE HOLDEN

CREDIT: NATIONAL ASSOCIATION OF WHEAT GROWERS

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Moldova's proliferation threat



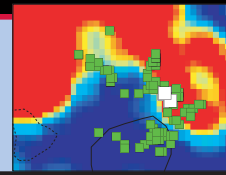
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Bringing Gran Sasso back to life



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Hot spots for ocean life



buyers of hard red spring wheat, have intimated that they would boycott all U.S. wheat if a GM variety were grown here. "Our customers are not concerned about the science or safety of Roundup Ready wheat. They're just simply trying to ensure that they don't have trouble marketing their product: flour," says Alan Tracy, president of U.S. Wheat Associates, the marketing arm of the American wheat-exporting industry. U.S. wheat farmers told Monsanto, no thanks; the \$5-billion-a-year market is just too big to gamble on for such limited benefits.

In the large scheme, Monsanto's decision probably wasn't a nail-biter: Last year the company invested less than \$5 million, or roughly 1% of its R&D, on GM wheat. Most of Monsanto's R&D dollars are focused on improving its big four GM crops, for instance, by creating varieties that better resist pests or provide higher yields or produce higher quality food or fiber. Monsanto says its next product will likely be Roundup Ready Flex for cotton, which will allow farmers to spray glyphosate for more of the growing season. Further up the pipeline is drought-tolerant corn, which would protect yields during dry years and open up new areas for corn planting.

Monsanto and other agbiotech companies are also working on products that will have added value for consumers. Many of these employ conventional breeding but use existing GM varieties as breeding stock. For example, Monsanto scientists are working on Roundup Ready soybeans that have reduced or no trans fats. That product is targeted for market next year. After that, they hope to introduce soybeans with more monounsaturated, or heart-healthy, fats. Also on the list are better tasting soy protein and soybeans enhanced with omega-3 fatty acids, which provide a cardiovascular benefit. DuPont is pursuing many of the same goals.

Yet it's rare to find examples outside of corn, soy, and canola. One exception is Syngenta's StayRipe banana, which is designed to ripen more slowly and last longer in the fruit bowl. The company hopes to market it by 2006. Still, even though Syngenta is the second largest fruit- and vegetable-seed company in the world, its direct investment in GM technology in those products is "inconsequential," says spokesperson Christopher Novak; Syngenta invests the majority of its roughly \$160 million R&D effort in corn and soy.

Syngenta also has a wheat product in the pipeline that it thinks might fare better than

Monsanto's: a GM variety that has firmer grains and resists head blight, a disease caused by a fungus called *Fusarium*. In addition to reducing yields, *Fusarium* creates mycotoxins that can contaminate flour. The modified version could improve quality and safety of flour, says Tracy, but he doubts that will be a strong selling point for consumers.

BIOTECHNOLOGY

## A New Tack on Herbicide Resistance

Crops that can withstand herbicides have been a huge economic success for genetic engineering. About 80% of the U.S. market in soybeans and cotton is now in plants that tolerate glyphosate, a safe, cheap, potent, and environmentally friendly herbicide trademarked as Roundup. "Roundup Ready" agriculture has also been a gravy train for Monsanto, which invented the herbicide and is still the only company that's commercialized glyphosate-tolerant plants. But the herbicide patent has expired, and rivals are now trying to crack the monopoly on protected plants.

On page 1151, a team of researchers describes a new detoxifying enzyme that allows plants to resist glyphosate. If the plants make it to market, they could heat up competition, lower the price of genetically modified crops, and stimulate further innovation. Stephen Duke of the U.S. Department of Agriculture in University, Mississippi, says the approach to finding the new enzyme was fast and effective—"brilliant work."

Glyphosate inhibits a key enzyme that plants use to make amino acids. Monsanto engineered resistance by adding the gene for a similar microbial enzyme that isn't affected. The technology has been phenomenally successful in several crops, but it didn't win acceptance by wheat farmers (see previous story). Hoping to find another way to protect plants, researchers with Verdia Inc. and Maxygen Inc., both in Redwood City, California, and Pioneer Hi-Bred International Inc. in Johnston, Iowa, took a cue from an-

other technology—one in which a microbial enzyme is used to modify an herbicide called glufosinate. Although the new variety is already in field trials, it probably won't be ready for market approval before the latter half of the decade. Like Monsanto, Syngenta has said it won't commercialize the wheat unless growers support the decision. If they do, Monsanto says it may dust off its Roundup Ready wheat and try again. —ERIK STOKSTAD

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First, the researchers searched for an enzyme that would detoxify glyphosate. After growing several hundred strains of common microbes, they determined that the most effective was a soil microbe called *Bacillus licheniformis*. The team identified three related genes encoding the enzyme, called glyphosate *N*-acetyltransferase (GAT).

To speed the search for the best enzyme, the researchers fragmented the genes, shuf-

fled the pieces, and added them back to bacteria. Then they selected those more effective at acetylating glyphosate. After 11 rounds of selection, the enzyme was nearly 10,000 times more efficient. In a test of its potential, corn plants were outfitted with the gene. They tolerated six times the concentration of glyphosate that farmers normally apply, with no apparent effect on health or reproduction—more



**Battlefield?** Herbicide-tolerant crops may have some new competition.

than enough commercial potential, says Verdia's Linda Castle. Preliminary studies suggest that the enzyme's byproduct is as nontoxic to mammals as is glyphosate, Castle says. She adds that GAT should work in other crops as well.

It will take at least 5 years before these plants can be stacked up against Roundup Ready crops, predicts Jonathan Jones of the John Innes Centre in Norwich, U.K. But if the new technology does pan out, he says, it will spur agbiotech companies to come up with even more genetic traits that improve crop production. —ERIK STOKSTAD

CREDIT: WAYNE MEHRE/PIONEER HI-BRED