BY DANIEL CRESSEY

# A NEW BREED

**The next wave of genetically modified crops is making its way to market — and might just ease concerns over 'Frankenfoods'.**

When the first genetically modified (GM) organisms were being developed for the farm, says Anastasia Bodnar, "we were promised rocket jet packs" — futuristic, ultra-nutritious crops that would bring exotic produce to the supermarket and help to feed a hungry world.

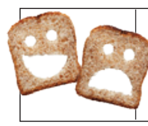
Yet so far, she says, the technology has bestowed most of its benefits on agribusiness — almost always through crops modified to withstand weed-killing chemicals or resist insect pests. This has allowed farmers to increase yields and spray less pesticide than they might have otherwise.

At best, such advances have been almost invisible to ordinary consumers, says Bodnar, a biotechnologist with Biology Fortified, a non-profit GM-organism advocacy organization in Middleton, Wisconsin. And at worst, they have helped to fuel the rage of opponents of genetic modification, who say that transgenic crops have concentrated power and profits in the hands of a few large corporations, and are a prime example of scientists meddling in nature, heedless of the dangers (see page 24).

But that could soon change, thanks to a whole new generation of GM crops now making their way from laboratory to market. Some of these crops will tackle new problems, from apples that stave off discolouration to 'Golden Rice' and bright-orange bananas fortified with nutrients to improve the diets of people in the poorest countries.

Other next-generation crops will be created

IMAGE: SERGE BLOCH



**GM CROPS: PROMISE & REALITY**
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using advanced genetic-manipulation techniques that allow high-precision editing of the plant's own genome. Such approaches could reduce the need to modify commercial crops with genes imported from other species — one of the practices that most disturbs critics of genetic modification. And that, in turn, could conceivably reduce the public disquiet over GM foods.

Or maybe not. Whatever promise these crops may show in the laboratory, they will still have to demonstrate their benefits in painstaking, expensive and detailed field trials; jump through multiple regulatory hoops; and reassure an often sceptical public.

SERGE BLOCH

That last part will not be easy, says Philip Bereano, who studies the political and social aspects of new technologies at the University of Washington, Seattle. He points out that the arguments over GM organisms run the gamut from concerns about safety and labelling to ethical issues with the patenting of life. "People are concerned about what they're feeding their kids," he says, "and that is not going to change."

Nevertheless, most GM-organism researchers seem convinced that the worst of the technology's problems are over, and that its future is bright. If you are looking for the jet-pack era of GM organisms, says Bodnar, "it is happening now."

The first wave of GM crops was marketed mainly to farmers, with the goal of making their jobs easier, more productive and more profitable. In 1996, for example, biotechnology firm Monsanto of St Louis, Missouri, introduced the first of its popular 'Roundup Ready' products: a soya bean equipped with a bacterial gene that allows it to tolerate a Monsanto-made glyphosphate herbicide known as Roundup. This meant that farmers could kill off the majority of weeds with one herbicide rather than several, without damaging the crop. Other GM crops soon followed, including Monsanto's *Bt* cotton: a plant modified to produce a bacterial toxin that discourages destructive bollworms and cuts down on the need for pesticides.

Farmers will continue to be a core market for the coming generation of GM organisms. At Rothamsted Research in Harpenden, UK, for example, scientists are working on GM plants that will need even less pesticide than Bt cotton, and maybe none at all. The key is an 'alarm pheromone' that some species of wild plant have evolved to mimic the chemical warning signals put out by aphids — a major crop pest in the temperate zones — when they are under attack. Putting the genes for this defence into wheat has created a crop that could trick the insects into thinking that they are in peril and drive them away. Unlike Bt cotton and other existing GM organisms, such a crop would need no insect-killing chemical for protection from pests.

Field trials are currently under way, says Maurice Moloney, director and chief executive of the Rothamsted centre. "In the greenhouse it's been very successful," he says. "If we can get it to work in the field, we'll be able to optimize it to make it a robust trait" suitable for large-scale deployment. From there, says Maloney, the team hopes to expand its efforts, searching for naturally evolved protections and deterrents in other crops, and working out how these might be enhanced or modified to fight particular pests. "For example, you could have a volatile chemical that also is a deterrent for caterpillars, stem borers and the like," says Maloney. "Potentially, if we can get this to work, the range of applications is phenomenal."

## LOCAL CONCERNS

Many GM-organism researchers are pushing work on crops sometimes neglected by the big agricultural companies. In the plant biotechnology group at the Swiss Federal Institute of Technology in Zurich, for example, Herve Vanderschuren leads a team working on cassava (*Manihot esculenta*), a tropical shrub with a tuber that is a staple food in the developing world. "There is not major investment in breeding or improvement of this crop," he says.

Vanderschuren and his team are genetically engineering cassava to be resistant to two particularly damaging viruses, by starting with a variety that is naturally resistant to cassava mosaic virus, and then inserting genes that confer resistance to cassava brown streak virus. The naturally resistant strain was already tailored to local needs and markets. That kind of local adaptation is a "very important part of the research we do here", says Vanderschuren — and something that is rarely embraced by huge agribusinesses that want to sell products worldwide. Vanderschuren and his team have successfully made the plants, and are now collaborating with colleagues in Africa to arrange tests to confirm that the cassava can be grown in the field.

Much of the work on crops in developing nations focuses on nutritional enhancement. The most famous example of this effort is Golden Rice, a modified version of the staple food of half the world. Its distinct yellow hue comes from the addition of β-carotene, a precursor to vitamin A that is deficient in many East Asian diets. After much painstaking development and many objections from opponents of GM organisms — the original version of Golden Rice was announced in 2000 — the crop is currently undergoing field trials in the Philippines (see I. Potrykus *Nature* **466,** 561; 2010). It could clear the final regulatory hurdles and reach farmers by 2014.

Others have followed in its wake. James Dale, director of the Centre for Tropical Crops and Biocommodities at Queensland University of Technology in Brisbane, Australia, for example, is trying to equip bananas with resistance to Panama disease, a fungal wilt that can devastate crops, as well as increased β-carotene and a suite of other nutrients including iron. "Levels of micronutrient deficiencies are really very high" in Uganda and all across Africa, he explains, and bananas are a staple of the diet.

Field trials have already been conducted in Australia.

Although most next-generation GM organisms are aimed at farmers, some target the next step in the chain: industrial food processors. For example, Chris Dardick, a molecular plant biologist at the US Agricultural Research Service's Appalachian Fruit Research Station in Kearneysville, West Virginia, explains that it is difficult to get plums into processed foods, because removing their hard, woody cores leaves shards behind. But starting with genes from a mostly stoneless, conventionally bred plum, Dardick and his team are in the early stages of engineering a fruit with no stone at all. "Our biggest concern was how such a thing would be embraced by industry and consumers. Most of the feedback we've gotten has been quite positive," he says.

And then there are GM organisms designed to appeal directly to the final consumers. One of the first will be the Arctic Apple, which does not brown rapidly after it is cut or bitten into. This is thanks to the insertion of genes from other apple varieties that produce lower than usual levels of polyphenol oxidase, a key enzyme in the chain of biochemical events that cause browning.

"My wife and I are apple growers ourselves. We were concerned because apple consumption has been declining," says Neal Carter, president of Okanagan Specialty Fruits in Summerland, British Columbia, the developer of the Arctic Apple. Carter says that apples are losing ground in the supermarket to carrots and other fresh produce that is sold in bags, cleaned, sliced and ready to eat. Making apples that could be processed in such a way without browning could be a real boon for the industry. And if the apples are received well, says Carter, Arctic avocados, pears and even lettuce could be next.

## ADVANCED TECHNIQUES

Much of the genetic-modification work so far has been achieved with relatively crude but established techniques, such as a 'gene gun' that fires gold nanopellets coated with DNA from other organisms into the cells of the target plant, which incorporate the DNA at random sites in the genome. But new tools offer unparalleled precision in editing genes. For example, enzymes called transcription activator-like effector nucleases (TALENs) and zinc-finger nucleases (ZFNs) can cut DNA at specific points chosen by the experimenter. By controlling how this break is repaired, it is possible to introduce mutations, single-nucleotide changes or even whole genes at precise sites, says Dan Voytas, who works with such techniques at the University of Minnesota in St Paul. "We can do precise insertion so we know where in the chromosome the foreign gene resides." This allows researchers to put the new gene in a spot in the genome where its expression is optimal, and reduces the risk of disrupting the plant's genome in undesirable ways. Voytas's group has already shown that tobacco plants can be modified with ZFNs to introduce herbicide resistance[1]. Other groups have added herbicide resistance to maize (corn) with ZFNs[2] or have used TALENs to snip out the gene in rice that confers susceptibility to bacterial blight[3].

But Voytas says the "real power" of these techniques lies in the ability to confer new traits by modifying native plant genes. For example, rather than engineering plants to withstand dry conditions by incorporating genes from drought-tolerant bacteria (see *Nature* **466,** 548–551; 2010), researchers could adjust the multiple native genes that help plants to survive drought. "Really, the next stage of the development of the technology is to go in and to tweak multiple genes," says Voytas.

Derek Jantz, co-founder of Precision BioSciences, a biotechnology company based in Durham, North Carolina, is also excited about working with a plant's own genes. For example, all plants have an analogue of the bacterial *EPSPS* gene that is inserted into Monsanto's Roundup Ready crops. It should be possible to create similar herbicide resistance by editing a plant's own version, rather than bringing in an external gene[4].

Like other researchers in the genetic-modification industry, Jantz declines to talk about specific research projects because of commercial confidentiality. But in general terms, he says, "what we're trying to do is take advantage of the wealth of functional genomics data that is becoming available".

## A BREED APART

Some researchers are using genetic modification to accelerate conventional breeding techniques. Ralph Scorza, a plant scientist at the Appalachian Fruit Research Station, leads a team that has genetically modified plum trees. The modified trees can survive only in greenhouses. But thanks to the insertion of a gene from poplar trees, they begin to flower much earlier in their lifetimes than conventional varieties do, and then continuously thereafter. This means that researchers can breed the trees throughout the year, using selection, cross-breeding and other traditional techniques to develop traits such as disease resistance in just a few years, as opposed to the decade or more that conventional breeding might require. When the desired traits have been bred in, the transgenes that drive flowering can be bred out, leaving a modified but non-GM plant. Scorza and his colleagues are using this 'FasTrack' breeding strategy in an effort to generate resistance to the plum pox virus, and to increase the sugar content of the fruit. Researchers elsewhere are applying it to crops such as citrus.

> "The next stage of the development of the technology is to go in and to tweak multiple genes."

US regulators have already suggested that organisms modified with the newer techniques such that they contain no DNA from other species will be treated differently from conventional GM organisms. That might also alleviate public concerns. "We can overcome hopefully at least some of the opposition to the genetic modification," says Alan McHughen, a molecular geneticist at the University of California, Riverside.

Besides, notes Bodnar, there may be no stopping GM organisms. She points out that genetic engineering now has a relatively low bar to entry. 'Biohackers' working with bacteria are already conducting genetic modification experiments in their garages and spare bedrooms, and there is nothing to stop them from applying their skills to plants — or animals — in the future.

"It's becoming easier all the time. I think people are hungry for this kind of thing," says Bodnar. "The jet packs that everybody wanted — I think it's time for them to come out. If the marketplace isn't providing that from the top down, you may see it from the bottom up." ■ SEE NEWS FEATURE P.21

**Daniel Cressey** *is a reporter for* Nature *in London.*

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2. Shukla, V. K. *et al. Nature* **459,** 437–441 (2009).
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