The Big Read Agritech

Gene editing: how agritech is fighting to shape the food we eat

From battling disease in banana crops to overcoming avian flu scientists are seeking wider acceptance for the technology

Emiko Terazono in Norwich and Clive Cookson in London FEBRUARY 10, 2019

A brightly lit lab two hours north-east of London might be an odd place to find people trying to save the world's most popular banana. But examining a Petri dish — the contents of which might contribute to that fight — are plant biologists devoted to just such a cause.

The humble fruit is under attack from a pernicious strain of Panama fungus disease which is destroying plantations around the world, threatening to devastate crops and cripple a $36bn a year industry on which some developing economies depend. Impervious to chemical treatments the fungus has, over the past three decades spread to China, south-east Asia, Australia and the Middle East. Tropical plant specialists say it is only a matter of time before it reaches Latin America, devastating the farms which provide three-quarters of the world's banana exports.

Now scientists believe they might be able to stop the fungus in its tracks using gene editing, which shuts down specific genes or tweaks them to work differently. Advocates of gene editing view it as not just a way to combat fungal diseases but a vital contribution to producing safer crops with higher yields to feed a growing global population. According to UN estimates, the number of people on earth will grow by almost 2bn to a projected 9.8bn by 2050.

"This is a revolutionary technology," says Ofir Meir, chief technology officer of the Norwich-based Tropic Biosciences, owner of the Petri dishes. Since the banana is a monoculture based on a single genetic clone, "you cannot breed out [disease] like you can do with other crops," he notes, adding: "This technology was generated to fit this need."

Banana crops across the world have been hit by a strain of Panama fungus disease that has wreaked havoc but scientists hope gene editing can help create a variety resistant to the disease © Reuters

Launched two-years ago, Tropic is one of several agritech start-ups using gene editing. This manipulation of an organism's existing genes is distinct from conventional genetic modification which transfers whole genes between species and has met extensive opposition from environmental and consumer groups concerned about the possible long-term impact on ecology and human health

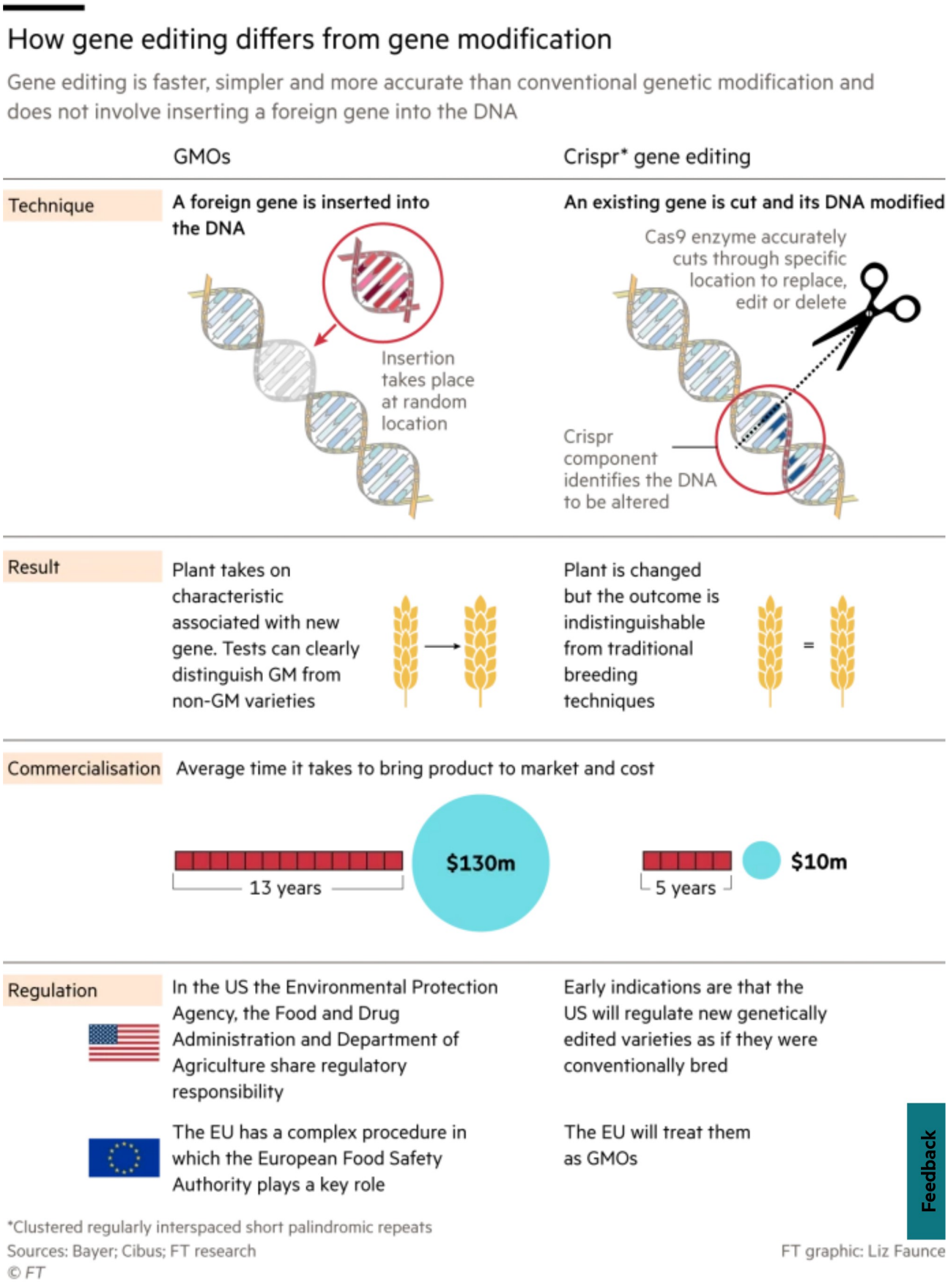
Gene editing proponents hope it can avoid such criticism and the regulatory scrutiny that has thwarted the rollout of GM in the EU in particular, because it works with existing genes rather than adding foreign DNA to the plant. In the US and Canada, the initial response of authorities has been that gene edited crops will not fall under the regulatory regime of GMOs.

Several gene editing techniques exist, but by far the most popular and versatile is the Crispr method — short for clustered regularly interspaced short palindromic repeats. And just six years after scientists published the first papers showing how Crispr could work in plants and animals, it is sweeping through the world's academic and corporate laboratories.

Some applications, such as more flavourful tomatoes and mushrooms that do not turn brown as they age or after they are cut — greatly extending shelf life and reducing waste — are close to being commercialised in the US.

How gene editing differs from gene modification

Gene editing is faster, simpler and more accurate than conventional genetic modification and does not involve inserting a foreign gene into the DNA



Feedback

For the scientists at Tropic the immediate aim is to use gene editing to produce bananas with an extended shelf-life and coffee beans minus caffeine. But within four to six years, says chief executive Gilad Gershon, it hopes to commercialise a Cavendish banana — the variety that accounts for about 95 per cent of the fruit sold worldwide — which is resistant to the fungus known

as TR4.

“We’re trying to do it a bit faster, but we’re happy with the progress we’re making,” he says, “it’s very exciting.”

Genome, or gene, editing is regarded by scientists as the biggest technical advance in bioscience since “recombinant DNA” technology — where genetic material from more than one source was combined — launched the era of genetic engineering in the 1970s. By the 1990s that technology had moved from the lab into agriculture. Two early entrants to the GM field are still the biggest sellers: herbicide tolerance, which enables farmers to spray their fields with weedkiller without destroying the crop, and insect resistance, which makes plants toxic to certain pests.

But gene editing gives researchers a fast and reliable way to make precise changes in specific genes. The Crispr-Cas9 procedure is more efficient than previous DNA technology, lowers costs and is expected to accelerate genetic engineering across the board.

Agricultural scientists are working on a multitude of gene editing projects, including low-gluten wheat, and peanuts which do not cause allergies.

Two of the founders of Tropic Science, Gilad Gershon, left, and Ofir Meir © Si Barber/FT

The technology holds promise for developing countries, which depend on certain crops that have become vulnerable to disease. Research backed by confectionery group Mars would enable cocoa, the key ingredient for chocolate mainly grown in west Africa, to withstand viruses.

Howard-Yana Shapiro, chief agricultural officer at Mars, says: “Because we have broken up the ecology of so many places, biodiversity has been disrupted. Things [pathogens] that sat benign for 500 or a thousand years are now looking for new hosts.”

The opportunity is not lost on large seed and chemical agribusinesses like Bayer, BASF and Corteva, the agricultural arm of DowDuPont, which are vying for pole position in the gene engineering race, although the low cost and potentially shorter times to market have also spawned start-ups like Tropic which are attracting tens of millions of dollars from venture capital investors.

For thousands of years, farmers and plant breeders have used selection and breeding techniques to develop crops. According to scientists, gene editing produces the same results as conventional

breeding methods, where plants are crossed or DNA mutations are generated with chemicals or radiation, but with more precision and speed.

Supporters had hoped the distinction between gene editing and the older genetic modification would be particularly important in Europe, which has lagged behind the Americas in the licensing of GM crops. Only two have made it through the approvals process for commercial cultivation over the past two decades in the EU: an insect resistant maize developed by Monsanto and approved in 1998; and a potato with altered starch qualities developed by BASF and approved in 2010 but later withdrawn due to a lack of demand.

The numbers behind the science

Sandra Lazauskaite with banana plants waiting to be genome-typed at Tropic Sciences in Norwich © Si Barber/FT

95%

Of bananas sold worldwide are of the Cavendish variety which scientists are trying to make resistant to the TR4 fungus which threatens the $36bn a year industry

2bn

People will be added to the world's population over the next 30 years bringing it close to 10bn and adding to the pressure on food production

49%

Of US adult respondents to a survey who still believe GM foods are worse for health than their non-GM equivalent

The European Court of Justice ruled in July that gene-edited crops should be subject to the same rules as GMOs, dashing hopes that the EU would take a more liberal attitude to the newer technology. However some legal and regulatory experts say the decision may not be as far-reaching as plant scientists fear.

"I believe that the ECJ ruling does not unequivocally state that all genome edited organisms are by definition GMOs and that in fact the ruling requires further clarification to understand what it means," says Piet van der Meer, a Dutch expert on European biosafety regulation.

In the US, the initial response from the Department of Agriculture has been that gene editing will be regulated in the same way as traditional breeding techniques so long as the outcomes produced are indistinguishable.

Yet despite 20 years of GM crops, and food, consumer suspicion in the US persists. According to a survey from the Pew Research Center last November, about half of US adults still believe GM foods are worse for human health than their non-GM equivalent.

Those who have campaigned against GM foods are generally opposed to the gene-edited variety, primarily for the same reasons: the potential impact on environmental ecosystems and human health. Opponents point to "off-target" events, or errors, that have led to unwanted mutations in the labs.

"Gene-editing crops isn't a natural process, it's not well understood," says Dana Perls, senior food and agriculture campaigner at Friends of the Earth. "It may result in a number of unforeseen consequences that are unsafe for people and the environment — and rushing them into the ecosystem could create a grave problem down the line."

Mars's Mr Shapiro counters that "more than a trillion meals" that include meat from livestock fed with GM crops have been consumed over the past 20 years without negative impacts.

He adds that many medicines generally accepted by the public, including insulin, are produced by genetically engineered organisms. "Every heart medicine I take, which is seven pills every morning to stay alive, is genetically engineered," says Mr Shapiro. "We have a schizophrenia about what is acceptable and what's not."

Activists in a 2008 demonstration in Germany against the US biotech company Monsanto © AFP

Venture capital backers stress the need for gene editing companies and scientists to get what they call "social licence" to operate from the public.

"They have to generate trust and explain what it is that they're doing," says Sanjeev Krishnan, chief

investment officer at S2G Ventures, a US venture fund focused on food and agricultural start-ups. "GMOs were very much a farmer-facing thing. [It was about] saving time and increasing productivity but didn't have a consumer benefit."

Winning over sceptical consumers may be hard though, say marketing specialists. Whether consumers will be able to distinguish between gene editing and GMOs is unclear, particularly as the boundaries between the two are likely to shift as the technology develops.

Sydney Scott, assistant professor of marketing in Olin Business School, at Washington University in St Louis, conducted several surveys on perceptions about GM foods. She says one negative factor about genetic engineering that gene editing may be able to counter is public mistrust towards the dominance of "Big Ag" or large agricultural seeds and chemical businesses.

"When you talk to people who are a bit worried [about genetic engineering], one of the things they will come up with is that, it's all in the hands of the big three or four multinational companies," says Professor Wendy Harwood, a plant scientist at John Innes Centre, a research lab in Norwich, a city that has become one of the centres of plant science in the UK.

The average time it takes for a GM product to reach the market is 13 years at a cost of about $130m, partly due to the stringent regulation. Only companies of a certain size can bear such large costs, leading to the predominance of multinationals in the sector.

However, that may be changing. Minnesota-based Calyxt, which uses a gene-editing technique called Talen, is an example of a smaller company looking to produce high nutrient crops. Its soyabeans are gene edited to produce high levels of oleic acid, a fatty acid found in olive oil and avocados linked to lower levels of bad cholesterol.

Tregg Cronin, a fourth-generation farmer based in South Dakota, annually grows 8,500 acres of grains, oilseeds and legumes. Last year he harvested 500 acres of soyabeans grown from seeds supplied by Calyxt, a subsidiary of French biotech group Cellectis.

Now Mr Cronin plans to almost double the acreage of soyabeans and is keen to find out more about the company's high-fibre wheat. Calyxt, which floated on Nasdaq in 2017 and is valued at just under $450m, buys back the harvested soyabeans for processing at a premium of up to 99 cents per bushel to the Chicago benchmark, which has attracted farmers battered by low prices and the US-China trade war.

"Consumers are demanding healthier food and it's the way the entire industry is heading," says Mr Cronin. "Calyxt is moving in that direction and that's why we want to work with them."

Although the US agriculture department has stated it would not regulate gene edited crops, Calyxt has voluntarily submitted reports to the department and the Food and Drug Administration, and is negotiating with food manufacturers to sell the oil. Mr Cronin adds that even in the US agricultural heartlands, gene editing is so new that only a handful of farmers are likely to know how different it is from GM products.

Nevertheless, he feels the technique is not at odds with his sustainable farming principles. “To our family farm it’s incredibly important to be proud of what we’re raising,” he says.

On the other side of the Atlantic, at Rothamsted Research which focuses on agricultural science north of London, plant biologist Professor Johnathan Napier says that advocates of genetic engineering must explain more clearly what they are doing, and why.

“It’s really important for the public to understand what the motivation is for people to do things,” says Prof Napier. “If you don’t fill that part of the narrative, there are plenty of people who are quite happy to do it for you.”

Poultry, fish and cattle become targets for gene editing

While the world's research labs house millions of mice genetically engineered for the sake of science, gene technology has been slow to enter the farm animal arena — partly due to industry fears that consumers will be even more resistant to eating GM animals than they are to GM plants.

The only genetically-engineered animal licensed for human food is AquAdvantage Atlantic salmon, which has two genes added from other fish to make it grow bigger and faster. Although approved by the US Food and Drug Administration in 2015 after a 20-year regulatory battle, opponents, including wild salmon fishers, have so far blocked its sale there. It has, however, been available in Canada since 2017.

AquaBounty, the company behind AquAdvantage salmon, has now developed a faster-growing variety of tilapia, a staple of fish farming, by tweaking existing genes rather than adding foreign DNA. It is not yet on sale, though Argentina has ruled that it is exempt from GM regulation.

Poultry is a prime target for gene editing, with scientists at Edinburgh university's Roslin Institute, the leading UK animal biotechnology laboratory, involved in several projects with chickens.

One is a collaboration with Wendy Barclay, virology professor at Imperial College London, to make influenza-resistant chickens as a buffer against the spread of avian flu to humans. "If we could prevent virus crossing from wild birds into chickens, we would stop the next pandemic at source," she says. Roslin is also working with Genus, the UK animal genetics company, to produce pigs resistant to the virus that causes porcine reproductive and respiratory syndrome (PRRS), one of the world's costliest animal diseases.

Elsewhere Recombinetics, a US gene editing company, is developing "polled" cattle that do not grow horns, which could end the unpleasant practice of removing budding horns from calves.

"Gene editing could be absolutely revolutionary for animal breeding," says Bruce Whitelaw, Roslin's genus chair of animal biotechnology.*Clive Cookson*

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