Gene technologies

January 2016

Science writer Lisa Martin shares her thoughts on where new gene technologies might lead.

Can you imagine a world without trees? What if all the oranges disappeared? Or if we could no longer grow rice, a staple crop for two-thirds of the world's population?

Whether for food, feed, fuel, fibre, or just to look pretty in the garden, many of the plants we take for granted are under threat because of climate change, or pests and diseases that can wipe out whole fields of crops.

New genetic engineering technologies offer exciting opportunities to speed up the traditional plant breeding process and generate high-yielding, disease-resistant, climate change-proof varieties that will not only stop our favourite plants from disappearing, but could also help to alleviate challenges in the developing world like hunger and malnutrition.

But how does plant genetic engineering work - and is it safe?

Transgenics and beyond

In the 1990s, transgenics, or 'genetic modification' (GM), was a revolutionary advance on slow, traditional plant breeding methods based on artificial selection. The technique uses *Agrobacterium* to insert genes from the DNA of one organism into another. It has given us several commercially available GM crops, including herbicide-tolerant soybean and insect-resistant corn. It is also being used to develop plants that can produce lifesaving vaccines, and 'biofortified' crops with higher vitamin content, like Golden Rice.

But with *Agrobacterium*, we cannot precisely control where the new gene goes, or if it will 'stick'. New gene editing (GE) techniques are emerging to make genetic modification more precise – but how do they work?

Genome editing to feed the world

Professor Bing Yang from Iowa State University in the US wants to thwart 'rice blight', a disease caused by a bacterial pathogen called *Xanthomonas oryzae* (Xoo), which causes rice plants to shrivel and die. As rice is a staple food crop for millions of people around the world, it can be devastating for farmers if rice blight takes hold in their fields.

Professor Yang and his colleagues used 'type 1 genome editing' technology to alter DNA in the rice genome without introducing DNA from another organism.

How does Type 1 genome editing work?

Nucleases are enzymes that bind to DNA at a specific sequence and make a cut in the DNA at a particular place. Other enzymes then move in to repair the DNA damage. However, this repair is often imperfect – which makes it a great system for gene editing!

Scientists have worked out how to make synthetic nucleases designed to cut DNA, like a pair of molecular scissors, at a precise sequence on the DNA molecule, creating a 'double-stranded break'. As the repair mechanism is not perfect this can 'edit' the function of that gene. So, for example, if the cut was made in the middle of a gene, the error-prone repair mechanism might cause that gene to be switched off.

In Professor Yang's case, engineered nucleases called TALENs (Tal Effector Nucleases) were used to deactivate rice plants' disease-susceptibility genes, or 'S' genes for short. These are genes that are normally present in rice but are not normally active. Xoo can switch the S genes on to help it infect and kill the plant, so by deactivating the S genes completely, Professor Yang and his team were able to develop Xoo-resistant rice.

This variety will need to be thoroughly tested before it can be grown and sold commercially: to make sure it grows well in the field, has no unwanted environmental impacts, that the genetic modification has not caused other, undesired mutations, and that it contains no toxins or allergens, for example. This could take several years, but if successful, Xoo-resistant rice could help rice growers all around the world to grow more food for their families, and to lift them out of poverty by generating a higher income.

Type 3 genome editing

In the last few years, genome-editing technology has been refined further, opening up many fascinating possibilities. Utilising an engineered system called 'CRISPR-Cas', originally discovered in bacteria and archaea, scientists can now snip and stitch DNA much more precisely. As well as deactivating whole genes, with this approach we can also remove genes, change genes or correct faulty genes.

Plant synthetic biology

The technique has opened up a whole new area of biology called 'synthetic biology', and plant scientists are leading the field. Professors Jim Hasseloff from the University of Cambridge and Anne Osbourn from the John Innes Centre research institute in Norwich are leading a project called OpenPlant, which seeks to build a catalogue of artificially created DNA 'parts'. Just as you can put different Lego bricks together to build a house, or a car, or a spaceship, these DNA parts can be put together in different combinations to engineer whole transcriptional networks and systems within plants.

An amazing example of plant synthetic biology is Professor Giles Oldroyd's work on wheat. Wheat does not normally have a symbiotic relationship with nitrogen-fixing bacteria, so farmers must add nitrogen fertilisers to their soils to improve wheat yields. Professor Oldroyd and his colleagues at the John Innes Centre, however, are working towards engineering wheat plants that have nitrogen-fixing genes incorporated into their own genome. This would save farmers thousands of pounds, as well as being much better for the environment.

Another example comes from the lab of Professor June Medford at Colorado State University in the US. This team has engineered a plant to include a synthetic 'de-greening circuit' that turns leaves from green to white when certain chemicals are detected in the air. Imagine if plants could be used as carbon monoxide detectors, or to sense chemical warfare agents!

The future of gene editing

The opportunities for genetic modification and genome editing are seemingly limitless, and could help to remedy some serious problems in agriculture and forestry. It's possible, for example, that we might be able to modify oranges to resist the bacterial 'citrus greening disease' sweeping through orange-groves in the US and threatening our morning glass of orange juice.

Here in the UK, with Ash Dieback disease predicted to kill around 80 million Ash trees over 20 years, scientists like Dr Richard Buggs from Queen Mary University of London are trying to find resistance genes in the Ash tree's genome. Perhaps we could develop Ash Dieback-resistant trees using transgenics? Maybe we could use CRISPR-Cas to edit the fungal pathogen's genome and remove its virulence?

Genome editing: GM or not GM?

However exciting the opportunities for genome edited plants are, none of them will ever make it out of the laboratory without government approval. This is based on legal frameworks, scientific evidence and public opinion.

For 'traditional' GM crops, the European Union takes a 'precautionary principle' approach. While in theory, most countries in the EU may grow GM crops, very few are cultivated in practice because they are subjected to a lengthy, strict, expensive approval process. If there is any doubt that a crop is not safe, it will not be approved.

Genome editing technologies, on the other hand, pose a problem for regulators: like GM, DNA is artificially modified, but unlike GM, it contains no foreign DNA. Gene-edited DNA is virtually indistinguishable from 'natural' DNA, and arguably, many of the 'edits' might occur in nature, or as a result of commonly used mutagenesis methods. Does it matter that we are giving nature a helping hand? Should we consider gene-edited plants in the same way as transgenic ones?

The general consensus among scientists is that genome editing is different from GM and should be regulated differently, but the European Union is currently undecided as to what this regulation should be. Taking the precautionary approach means that while doubts exist, however small, we are unlikely to be sitting down to a dinner of gene-edited vegetables any time soon.

Further information

This YouTube video nicely shows how TALENs work – it's explained in a medical context, but works in the same way for plants too: https://www.youtube.com/watch?v=zDkUFzZoQAs.