Genome Editing and the Future of Food

Area of research interest: <u>Novel and non-traditional foods, additives and processes</u> Project status: Completed

In December 2020, the Food Standards Agency (FSA) and the N8 AgriFood Food Systems Policy Hub held an online workshop entitled 'Genome Editing and the Future of Food' with sixty stakeholders from academia, government and industry. Genome editing (GE) technologies are becoming more widespread and have distinct advantages over more traditional genetic modification (GM) technologies. The workshop aimed to horizon scan for emerging GE techniques in our food supply systems to inform future risk assessment and risk management decisions. This report provides a snapshot of the current and potential future use of GE in food and feed based on discussions at that workshop.

What is genome editing?

Genome editing involves the deletion, modification, insertion or replacement of DNA in the genome of a living organism. Unlike earlier genetic modification (GM) techniques, GE targets DNA changes to highly specific locations in the genome, enabling avoidance (or removal) of foreign DNA sequences required for the editing process and reducing off-target effects. GE enables editing of specific sequences, for instance sequences known to be responsible for susceptibility to disease.

Emmanuelle Charpentier and Jennifer Doudna won the Nobel Prize in Chemistry 2020 for discovery and development of the CRISPR-Cas system, which is widely used as a research tool across diverse species in the plant, animal and microbial kingdoms. Other GE technologies include Transcription activator-like effector nucleases (TALENs) and Zinc Finger Nucleases (ZFNs).

The DNA sequence changes introduced through GE are often indistinguishable from those arising through natural or induced mutation processes used in traditional breeding, raising a challenge for authorities in detection and regulation. Achievement of other traits will require introduction of foreign DNA.

Methods to introduce the GE tools into organisms and the technologies required to select and regenerate GE organisms vary depending on the organism. These can introduce mutations unrelated to, and often indistinguishable from, those made by the GE itself. Off-target effects can also happen during the GE process.

What are the key problems that genome editing technologies are being used to solve?

In the food and feed supply chain, GE has the potential to address a range of pressing issues such as net zero carbon farming, animal welfare, disease resistance, fecundity and yield. Key targets include:

• Enhanced disease and pest resistance in plants and animals, for instance helping prevent blue ear in pigs, lice infestation in fish farming and bacterial blight in rice.

- Climate resilience and reduced environmental impacts for instance: reducing reliance on antibiotics in animal rearing; crops that are drought-tolerant or have reduced need for fertilisers; microbes that can recycle industrial waste gases into food and feed.
- Animal welfare, which has been difficult to address through traditional breeding, is being tackled by GE, for instance optimising nutrition and preventing disease.
- Nutritional value is an important target for GE, for instance leaner meat, iron and vitamin content in cereals, new sources of protein for feed, and plant based and cultured meat alternatives.

Snapshot of genome edited food and feed products in development

- Disease resistant banana, coffee varieties with reduced caffeine (Tropic Biosciences)
- Herbicide and disease tolerant oilseed rape, rice and potato; herbicide tolerant flax; oilseed rape with healthier oil (Cibus)
- Raspberries and blackberries (black and red) with improved taste, shelf life and off-season availability (Pairwise)
- High oleic low linolenic soybean (HOLL), winter oats, high fibre wheat, high saturated fat soybean (palm oil substitute), alfalfa with improved digestibility (Calyxt)

Horizon scanning impact of GE up to 2050

GE could allow us to change to a healthier and more environmentally sustainable diet. It could enable creation of plant-based or cultured 'meat' and dairy products that replicate the taste, mouthfeel and nutritional role of animal products in human diet. Allergens could be eliminated or foodstuffs engineered for the needs of different stages in peoples' lives.

GE based disease resistance could deliver agriculture with reduced chemical input, animal husbandry without antibiotics and aquaculture without pesticides. It might allow rapid domestication of plant species, diversifying the crops on which we rely for food and increasing resilience to emerging pests and disease.

GE could increase carbon fixation in crops reducing the land, and other inputs, needed to produce a given amount of food. We could develop feed for ruminants that reduces methane release and adapt fruit and vegetables to reduce post-harvest spoilage and waste. Food packaging could be biosynthesised from wastes and by-products by GE microorganisms.

GE could enable carbon capture, for instance developing soil micro-organisms better able to fix carbon, nitrogen or other nutrients, reducing fertiliser inputs and increasing soil carbon stores. Food mileage could be reduced as a result of being able to grow crops in a wider range of geographies, climates and production systems.

Societal aspects of genome editing

Regulation of GE varies across the world. The EU regulates GE in the same way as GM, using a 'process-driven' approach similar to that currently used in New Zealand and India. The USA and Canada use a 'product trigger' where regulation is driven by the novelty of the trait rather than the technology used to create it. Australia has recently removed regulation of gene editing in plants and animals where no templates are used to introduce new genetic material. Argentina has developed new regulation with products derived from GE assessed on a case-by-case basis to establish if they are GM organisms or not.

The regulatory framework affects where GE products are commercialised, for instance there are no upcoming GE products in the UK, and outputs of UK research are being commercialised in areas of the world where the regulatory regime allows their use. It also affects what products are commercialised: only 'blockbuster' traits will justify the investment needed to achieve regulatory compliance in Europe and cost prevents smaller companies from entering the market. Commercialisation of GE products is also made more challenging by dispute over the core patents covering GE and thousands of patents based on these. These 'patent jungles' are difficult and risky for companies to navigate.

Trust in GE technology by the general public will be key to its acceptance in the food supply chain. Gaining that trust will depend on evidence that it delivers products which are useful to the general public (including gains for the environment) and transparency around its application in food and feed products. Better understanding of modern GE is needed to inform public debate about the technology.

Case studies

Disease resistance in banana

Banana production is important for local economies and food security around the world. The fungus, Fusarium wilt tropical race 4 (TR4), could wipe out the banana variety, Cavendish, which accounts for nearly 50% of global banana production.

Commercial bananas are sterile and propagated by clonal expansion so options for breeding are limited, however, whole genome sequences are available and CRISPR-Cas9 works well in this species.

In the UK, start-up biotech company, <u>Tropic Biosciences</u>, is using GE to produce bananas which disrupt TR4 virulence. In an alternative approach, researchers in Australia are <u>using GE to turn on</u> a dormant gene in the Cavendish banana that confers resistance to TR4.

The GE bananas would have to go through a rigorous regulatory approval process before they could enter the UK market.

Genome editing for disease resistance in pigs

Classical breeding for disease resistance is impractical for farmed animals because it would involve infecting huge numbers of animals. However, genome sequence is available for all major farm animal species together with the techniques for GE.

Porcine respiratory and reproductive syndrome (PRRS) causes reproductive failure in sows and diarrhoea, pneumonia and increased mortality in piglets.

Researchers at the Roslin Institute in Scotland used GE to remove a section of the pig gene that encodes a protein to which the PRRS virus binds. They went on to show that the <u>GE pigs were</u> resistant to infection by the virus.

Completion of full regulatory approval would be needed before any products from GE pigs could enter the UK market.

Genome editing of microbes in the food system

GM microbes have played a key role in our food system for decades, with one of the earliest examples being the production of rennet in GM fungi for cheese making. More recently <u>Perfect</u> <u>Day</u> have developed GM microbes that produce whey and casein, enabling animal-free production of milk protein. The <u>CRISPR/Cas9 GE system was first identified in yogurt culture</u>

<u>microbes</u> as a mechanism for these bacteria to protect themselves against viruses. The potential uses of GE in microbes within food and feed are diverse and likely to impact the way in which food and feed is produced, flavours and food content, efficiency and waste as well as optimal nutrition for animals and people.