Why Brexit could jump start UK GMO, CRISPR research—once stifled by ‘dead hand’ of EU regulation

Britain is really good at biology. In physics and chemistry, or painting and music, we have often failed to match the Germans, the French or the Italians. But in the bio-sciences, nobody can equal us. Here’s an astonishing list of firsts that happened on this damp island: William Harvey and the circulation of the blood. Robert Hooke and the cell. Edward Jenner and vaccines. Charles Darwin and natural selection. Alexander Fleming and antibiotics. Francis Crick and James Watson (and Rosalind Franklin and Maurice Wilkins) and the structure of DNA. Fred Sanger and DNA sequencing. Patrick Steptoe and Robert Edwards and the first test-tube baby. Alec Jeffreys and DNA fingerprinting. Ian Wilmut and Dolly the Sheep. The biggest single contribution to the sequencing of the human genome (the Wellcome Trust).

Annoyingly, the exciting new tool of genome editing is the one that got away. The best of the new tools, known as CRISPR, emerged from the work of a Spaniard, Francisco Mojica, who first spotted some odd sequences in a microbe’s genome that seemed to be part of a toolkit for defeating viruses. Then a few years ago French, American, Finnish, Dutch and Chinese scientists turned this insight into a device for neatly snipping out specific sequences of DNA from a genome in any species, opening up the prospect of neatly rewriting DNA to prevent disease or alter crops. Two American universities are squabbling over the patents (and Nobel prize hopes). Further improvements are coming thick and fast.

But we are well placed to catch up with superb labs straining at the leash to apply these new tools. The biggest immediate opportunity is in agriculture, and here leaving the European Union is absolutely key. There is no clearer case of a technology in which we will be held back if we do not break free from the EU approach. It would not be a race to the bottom in terms of safety and environmental standards, but the very opposite: a race to the top.

For example, if we allowed the genetically modified blight-resistant potatoes that have been developed at the Sainsbury Laboratory in Norfolk to be grown in fields here in the UK, we would be able to greatly reduce the spraying of fungicides on potato fields, which at present happens up to 15 times a year, harming biodiversity and causing lots of emissions from tractors. That would be a big improvement, not a regression, in environmental terms. But at the moment commercializing the Sainsbury Lab potato is in practice impossible because of onerous EU rules.

Other countries are already dashing ahead with the new technology. Last year a review of the patenting of CRISPR products in agriculture found that, whereas America had taken out 872 patent families and China 858, the European Union had taken out only 194. The gap is growing.

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Europe’s Court of Justice ruled that CRISPR crops are GMOs in 2018.
Image: The Institute of International and European Affairs

The reason is nothing to do with the quality of research in Europe. It is all about regulation. When genome editing first came along, the European Commission decided to delay for several years making up its mind about how to regulate the release of genome-edited organisms while it waited for the European Court of Justice to decide whether to treat this new technology as if it were like genetic modification (the process invented a generation ago for transferring genes between species) or a form of mutation breeding (the process invented two generations ago for randomly scrambling the genes of plants under gamma rays in the hopes of generating better varieties).

If it was like genetic modification, then it would be subject to draconian rules that amount to a de-facto ban. Nobody even tries to commercialize a GMO crop in Europe any more because you enter a maze of delay, obfuscation, uncertainty, expense and red tape from which you never emerge.

The result is that European agriculture is more dependent on chemical sprays than it would have otherwise been, as shown by research at Gottingen University: on average, GMOs have reduced the application of pesticides to crops wherever they have been grown by 37 per cent. So we have missed out on biological solutions and had to stick with chemical ones instead.

If on the other hand genome editing is like mutation breeding, then you can go ahead and plant a crop straight away here with no restrictions. This is, of course, mad, since mutation breeding is more likely (though still very unlikely) to produce an accidentally harmful result even than GMOs, but it's an older technique and has been used for much of the food you eat, including organic food, and for some reason nobody at Greenpeace objects.

> Brexit is a fantastic opportunity to do something no European continental competitor is allowed to

Genome editing is an even more precise and predictable technique than GMOs. It involves no transfer of foreign DNA and the incision is made at a specific location in a genome, not at random. It is clearly the safest of all these three techniques, and so said the European Court's advocate general in his advice to the court. But in July 2018 the ECJ, being a political entity, decided otherwise and told the commission what it wanted to hear, that it should treat genome-edited plants and animals as if they were GMOs.

There was fury and dismay throughout the laboratories of Europe. There would have been more in Britain if academics had not feared playing into the hands of Brexiteers while remaining was still a possibility. A Canadian biotech professor tweeted that this was a good day for Canada since it removed a competitor continent from the scene. The absurdity is illustrated by the fact that in some cases it is impossible to distinguish a genome-edited variety from a variety bred by hybridisation or lucky selection with the same trait. Stefan Jansson from Umeå University in Sweden put it like this: "Common sense and scientific logic says that it is impossible to have two identical plants where growth of one is, in reality, forbidden while the other can be grown with no restrictions; how would a court be able to decide if the cultivation was a crime or not?"

Brexit therefore offers a fantastic opportunity to do something no European continental competitor is effectively allowed to do, and that will benefit the environment. We have great laboratories here, in Norwich, Nottingham, Rothamsted and Edinburgh among other places. But the private sector of plant biotechnology is all but extinct in Britain and will take some jump-starting.

Twenty years ago there were 480 full-time equivalent, PhD-level, private sector jobs in agricultural biotechnology in this country. Today there are just ten. That is what has happened to that whole sector in this country as a result of the misinformed and misguided green campaign against GMOs. Until politicians signal a sea change, the private sector will shun the UK's wonderful labs and the breakthroughs will be applied overseas, if at all.

As a new online tool called the Global Gene Editing Regulation Tracker has shown, America, Canada, Argentina, Brazil, Japan and much of the rest of the world are moving towards a nimbler and more rational regulatory approach: namely judging a crop not by the method used to produce it, but by the traits it possesses. If you can make a potato resistant to blight, what matters is whether the potato is safe, not whether it was made by conventional breeding, gamma-ray mutagenesis or genome editing.

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[Visit GLP's global gene-editing regulation tracker and index to learn more.]

In the EU, if you made this potato by gamma-ray mutation breeding, scrambling its DNA at random in a nuclear reactor, the regulations would say: “No problem. Go ahead and plant it.” If you made it by the far more precise method of genome editing, in which you know exactly what you have done and have confined your activities to one tiny bit of DNA, you are plunged into a Kafkaesque labyrinth of regulatory indecision and expense. The House of Lords Science and Technology Committee, on which I sit, recommended we switch to regulation by trait, a few years back but it was not possible before Brexit.

Genome editing can bring not just environmental benefits but animal welfare benefits too.
In 2017, scientists at the Roslin Institute near Edinburgh announced that they had genome-edited pigs to protect them against a virus called porcine reproductive and respiratory syndrome, PRRS. They used CRISPR to cut out a short section from the pig gene that made the protein through which the virus gained access to cell. The change therefore denied the virus entry. They did this without altering the function of the protein made by the gene, so the animal grew up to be normal in every way except that it was immune to the disease.

This means less vaccination, less medication and less suffering. What is not to like? (Incredibly, when I mentioned this case in a speech in the House of Lords, a Green Party peer objected that eradicating a disease that causes suffering in pigs might be a bad thing in case it allows a change in pig husbandry techniques. Even Marie Antoinette was never quite that callous.) But commercialising that animal in the UK is currently all but impossible until we change the rules.

Gene Editing

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Genome-editing technology could revolutionize conservation as well as agriculture. Looking far ahead into much more speculative science, the same scientists at the Roslin who made the virus-resistant pigs are now looking into how to control grey squirrels not by killing them, as we do now, but by using genome editing to spread infertility infectiously through the population, so that the population slowly declines while squirrels live happily into old age.

This technique, called gene drive, could transform the practice of conservation all around the world, especially the control of invasive alien species — the single greatest cause of extinction among birds and mammals today. We could eliminate the introduced mosquitos on Hawaii whose malaria is slowly exterminating the native honeycreeper birds. We could get rid of the non-native rats and goats on the Galapagos which are destroying the habitat of tortoises and birds.

We could get rid of the signal crayfish from America that have devastated many British rivers. For those who worry that gene drive might run riot, there is a simple answer: it can and will be designed in each case to last for a certain number of generations, not forever. And it will be wholly species-specific, so it cannot affect, say, the native red squirrel.

> Genome editing may one day allow the de-extinction of the great auk

Still more futuristically, genome editing may one day allow the de-extinction of the great auk and the passenger pigeon. To achieve this, we need to take four steps: to sequence the DNA of an extinct species, which we have done in the case of the great auk; to edit the genome of a closely related species in ?the lab, which is not yet possible but may not be far off as genome editing techniques improve by leaps and bounds; to turn a cell into an adult animal, which is difficult, but possible through primordial germ cell transfer, again pioneered at the Roslin Institute; and to train the adults for living in the wild, which is hard work but possible.

A pipette injects CRISPR-Cas9 gene-editing tools into a mouse embryo. Image: University of Utah Health Sciences

Genome editing is also going to have implications for human medicine. Here the European Union is less of a problem, and home-grown regulation is already in good shape: cautious and sensibly applied under the Human Fertilization and Embryology Authority. Britain has already licensed the first laboratory experiments, at the Crick Institute, on the use of genome editing in human embryos, but this is for research into infertility, not for making designer babies.

There is universal agreement that germ-line gene editing to produce human beings with new traits must remain off-limits and be considered in future only for the elimination of severe disease, not for the enhancement of normal talents. This view is shared around the world: the Chinese rogue scientist He Jiankui, who claims he used CRISPR to make two babies HIV-resistant from birth, was sentenced to three years in prison last December.

In practice, fears about designer babies are somewhat exaggerated. The same issue comes up about once a decade with every new breakthrough in biotechnology. It was raised about artificial insemination in the 1970s, about in-vitro fertilization in the 1980s, about cloning in the 1990s and about gene sequencing in the 2000s. Indeed, it has been possible to choose or selectively implant sperm, eggs and embryos with particular genes for a long time now and yet demand remains stubbornly low.

Most people do not want to use IVF or sperm donation to have the babies of clever or athletic people, as they easily could, but to have their own babies: the technology has been used almost exclusively as a cure for infertility. Indeed, the more we find out about genomes, the harder it becomes to imagine anybody wanting to, let alone being able to, enhance specific traits in future children by fiddling with genes: there are just too many genes, each with only very small effects, interacting with each other in the creation of any particular behaviour or ability.

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Imagine walking into a doctor's clinic and being presented with a catalogue of expensive genetic changes that could be made to your future baby's genes, each of which might have a tiny and uncertain effect. The truth is most people do not want to have especially clever or sporty offspring: they want children like themselves.

However, in contrast to germ-line gene editing, somatic genome editing will play a large part in medicine. It is already happening, for example in a process known as CAR-T cell therapy, in which an immune cell is genome-edited so that it will attack a specific tumour, then multiplied and injected back into the body as a form of live drug. If we encourage genome editing in Britain we will be in a position to cure some cancers, enhance agricultural yield, improve the nutrient quality of food, protect crops from pests without using chemicals, eradicate animal diseases, enhance animal welfare, encourage biodiversity and maybe bring back the red squirrel. If we do not, then China, America, Japan and Argentina will still push ahead with this technology and will follow their own priorities, leaving us as supplicants to get the technology second-hand.

Matt Ridley is a British journalist and businessman. He is the author of several books, including *The Red Queen* (1994), *Genome* (1999), *The Rational Optimist* (2010) and *The Evolution of Everything* (2015). Follow him on Twitter @mattwridley

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