Office of the Prime Minister's Chief Science Advisor
Kaitohutohu Mātanga Pūtaiao Matua ki te Pirimia

Title:

INTERN REPORT: Biotechnology and gene editing resources

Author:

OPMCSA - Intern - Revel Drummond

Output type:
PDF

Pages:
pp 8

Date:
Jun-2024

Language:
English

Review:
-

Versions

Record number:	Version:	Date V1 created:	Date:	Printed version
PMCSA-24-6-2-V1	V1	5-Jun-2024	5-Jun-2024	N
DOI:	-			
ISBN:	-			

Archive page link:
https://dpmc.govt.nz/our-programmes/special-programmes/prime-ministers-chief-science-advisor-archives/archive/gerrard-2021-2024

Notes:
Internal report to PMCSA

Biotechnology and gene editing resources

Revel Drummond, OPMCSA Fellow

Gene editing is a recently developed tool used as part of many biotechnology processes. It is of particular importance to Aotearoa New Zealand as it may be used to develop new innovative crop and pasture plants that will benefit our agricultural systems, as well as being of value in other areas. However, there are also potential risks that will need to be managed.

Gene editing is simpler to use and less expensive than earlier methods of genetic modification and has the potential to make changes to an organism's DNA in a more controlled fashion. But there is still the possibility of unintended changes, and for the change, even if precise, to have unintended impacts on the organism – so there remains a need for regulatory oversight.

However, the technology is developing very rapidly and the New Zealand regulations, developed more than 20 years ago, are not suitable for managing it.

Juliet briefed the PM on Gene editing in August 2019, and her briefing is available here. In 2023, Juliet provided an updated briefing letter to the Prime Minister.

Introduction

The pattern for all life forms on Earth is written in the shared code of DNA but it is not immutable. DNA sequences change: from generation to generation, from mother to son to daughter, and during the course of an organism's life. Indeed, changes to the DNA sequence are a necessary part of life and the continuing tug-of-war between the species as they adapt to changing environments and ecosystems. Without the changes in DNA seen from parent to offspring, life would not have developed the splendid diversity we see on our planet.

Similar to other technologies, biotechnology can be seen as the focused control of natural processes. People have leveraged changes in DNA since long before they understood how it worked, or even that it existed. Over millennia, humans have employed controlled crossbreeding and artificial selection to create new plant and animal varieties. Through selective breeding, numerous alterations in DNA sequences were combined indirectly, with farmers choosing desirable outcomes. Now, with the utilisation of tools to directly modify DNA, it has become feasible to significantly speed up the rate of change and even direct these changes to potentially advantageous sections of the genome.

Humanity has also directly harnessed the power of microbes using biotechnology. Traditionally, microbes have been used to make everything from bread to beer to yogurt, but using biotechnology, microbes can be used to make proteins such as the enzymes in washing powder and the insulin used to treat diabetes. Originally using only careful selection to change their properties, we now also directly modify microbes' DNA to make them more efficient and to have them make a wider range of products, including many medicines.

More recently humans have considered the possibility of altering our own DNA. After the discovery that some diseases run in families it was suggested that these disorders might be encoded in their DNA. In fact, an increasing number of illnesses and disorders can be traced to unfortunate mutations in DNA. There is the potential that tools that can directly modify DNA can be used to alter the DNA people with these mutations from the disease-causing to the healthy form.

Gene editing is a recent addition to the suite of tools used to manipulate DNA. The inventors were awarded the Nobel Prize in Chemistry 2020. The core principle is that an enzyme that cuts DNA is guided to a carefully selected target DNA sequence. The DNA at the target site is cut, modified, or replaced and its function is altered as a result. These changes can lead to small changes to the overall organism like a morning glory flower that was once purple is now white, or large changes like chickens that can no longer catch Bird Flu.

However, the use of DNA technologies does not come without risk. As with any technology it may lead to benefit but can also produce harm. Only by careful consideration can regulatory systems maximise benefit while at the same time reducing harm to acceptable levels.

Examples

The real-world applications of gene editing are no longer theoretical. For example:

- In human health, these tools are being used in an increasing number of clinical trials, including a trial that began in Aotearoa in July 2022, where it is hoped that a one-off CRISPR treatment will provide a new way to support individuals with hypercholesterolaemia to control their LDL cholesterol levels. Early results, released in November of 2023, suggest that the treatment is effective. In December 2023, the US FDA approved a CRISPR-based treatment for Sickle Cell Anaemia.
- Agricultural applications are widespread, including the development of disease-resistant plants and animals and produce with modified properties – like GABA-enriched tomatoes which can be purchased in Japan and soybean oil that's free from trans-fat in the US. Gene editing can be part of the response to climate change. For example, it offers a way to develop crops that are more heat tolerant or able to withstand droughts and other extreme weather events, which are becoming increasingly common.
- Gene drives, a specific application of CRISPR which leads to selected genes spreading through a population more rapidly than by chance alone, have potential applications in pest management and the control of vector-borne disease. Again, this technology has moved beyond the lab, with a biotech company using gene drives to control mosquito population sizes in multiple countries and University of Adeliade researchers having had laboratory success in controlling mice populations.

Previous analysis of the gene editing landscape in NZ

In 2016, the Royal Society Te Apārangi published an evidence update outlining the science and history of gene editing, new techniques, and possible applications. In 2019, the Royal Society Te Apārangi developed a series of gene editing scenarios in healthcare, pest control, and the primary industries, which it used to explore scientific, ethical, social, and legal questions associated with gene editing and its applications. The subsequent report on gene editing also included a section on New Zealand's regulatory framework, arguing that Aotearoa needed to develop its own perspective on gene editing, informed by public engagement, and should ensure our regulatory frameworks are fit for purpose.

In a briefing to the Prime Minister in 2019 in response to the Royal Society Te Apārangi report, the Prime Minister's Chief Science Advisor, Juliet Gerrard, agreed that Aotearoa New Zealand lacks a clear regulatory and legal framework on gene editing, and that current frameworks need modernising. She also endorsed the panel's observation that the gene editing debate requires widespread public engagement. In particular, she noted the importance of substantive engagement with Māori. In 2023, Professor Gerrard provided an updated briefing letter to the Prime Minster. It reiterated her agreement with the widely held view that our current legal and regulatory frameworks are not appropriate for the genetic tools available in 2023.

The Climate Change Commission's 2021 report[1] advising the government on emissions budgets included these two comments:

> *44 Several submissions proposed genetic engineering (GE) as an approach to reducing emissions, while others were very wary about the market and environmental consequences of using GE in Aotearoa. Some submissions discussed the need for more evidence of effectiveness in farming systems in Aotearoa.*
> *45 The regulatory environment must not hinder the roll-out of effective new emissions-reducing technologies and practices.*

The Productivity Commission's report[2] on 'frontier firms' in New Zealand included these two comments:

- *Modern genetic modification (GM) technologies such as gene-editing offer potential new opportunities for boosting productivity, improving health outcomes, reducing biosecurity risks, and responding to climate-change risks and other environmental problems effectively and efficiently.*
- *The regulatory framework for GM tools was last reviewed in 2001 and does not reflect technological advances since that time. The Government should review the GM regulatory framework, to ensure it is fit for purpose. This review should include wide engagement with industry, iwi and Māori interests, and the general public.*

[1] see Section 17.1.4 page 308

[2] see Section 10.4 page 162

The WELL NZ report on GM is a reference document from Te Puna Whakaaronui, the joint Government and industry food and fibre sector think tank, on modern genetic technologies and their regulation in NZ. The stated goal of the document was "to provide an unbiased, fact-based resource for those seeking to better understand the current state of genetic technology and associated regulations around the world".

In 2019 Maui Hudson and colleagues published a research article, Indigenous perspectives on gene editing in Aotearoa New Zealand, that examined how Māori viewed the potential impact of gene editing in the context of their world view. They note that "The outcomes of this pilot study identified that while Māori informants were not categorically opposed to new and emerging gene editing technologies *a priori*, they suggest a dynamic approach to regulation is required where specific uses or types of uses are approved on a case by case basis."

The Aotearoa Circle reported in 2024 on modern genetic technology in NZ agricultural production systems. "The primary objective of this report is to enhance comprehension regarding the potential environmental impacts of genetic technology and the trade-offs associated with various regulatory approaches".

Timeline of events

- Thousands of years ago – Selective breeding used to increase the prevalence of plants and animals with desirable characteristics, especially in agriculture.
- 1930s – Chemical techniques and ionising radiation start to be used to accelerate the rate of genetic change.
- 1970s and 1980s – Genetic engineering techniques developed that enable genetic material to be inserted into genomes, but often with limited precision.
- 1996 – HSNO Act introduced in New Zealand, where a genetically modified organism is defined as any organism in which the genes or genetic material have been modified by *in vitro* techniques.
- 1998 – Regulations under the HSNO Act specify that organisms resulting from the use of chemical or radiation treatments in use before 1998 are not genetically modified.
- 2001 – Royal Commission on genetic modification finds that the basic institutional structures and regulatory framework for dealing with genetic modification technologies is appropriate, needing only 'fine tuning,' which takes place in 2003.
- 2005-2012 – Three new precision gene editing tools are developed (ZFNs in 2005, TALENs in 2010, and CRISPR in 2012).
- 2014 – Sustainability Council vs EPA case in the High Court which finds that plants created using gene editing tools like ZFN-s and TALEs are new organisms as defined by the HSNO Act, along with older technologies such as chemical and radiation mutagenesis previously thought exempt from regulation.
- 2015/2016 – Ministry for the Environment (MfE) produces a regulatory impact statement in the wake of the high court decision. The Organisms not Genetically Modified Regulations

(1998) are updated in 2016 to add a cutoff date of July 1998 for existing technologies to result in organisms not considered to be genetically modified.

- 2016 – Royal Society Te Apārangi publishes gene editing evidence update, detailing the emergence of gene editing tools and their increasing use in research and practice.
- 2019 – Royal Society Te Apārangi publishes report on gene editing scenarios and regulations; the report notes that the NZ regulatory system is not keeping pace with the advances in biotechnology.
- 2019 – PMCSA provides a briefing to the Prime Minister on the Royal Society Te Apārangi report, agreeing that Aotearoa lacks a clear regulatory and legal framework on gene editing, and that current frameworks need modernising.
- 2019 – Minister Parker asks officials to advise him of where "lower regulatory hurdles ought to be considered to enable medical uses that would result in no heritable traits, or laboratory tests where any risks are mitigated by containment".
- 2021 – Climate Change Commission provides advice to government on its first three emissions budgets; "several submissions proposed genetic engineering (GE) as an approach".
- 2021 – Productivity Commission calls for the regulatory settings governing genetic modification to be reviewed.
- 2021 – Food Safety Australia New Zealand begins a process to update the legal definition of gene technology used to determine whether new foods should be regulated as genetically modified.
- 2023 – PMCSA provides a letter to the Prime Minister updating her 2019 briefing and reiterating the need for a clear regulatory and legal framework on gene editing, and modernisation of the current frameworks for regulating genetically modified organisms.
- 2023 – MfE consults on proposed changes to New Zealand's legislation and regulations for genetically modified organisms used in laboratory settings and for biomedical therapies.
- 2023 – The National Party releases pre-election policy document "Harnessing Biotech" that suggests significant changes to the way genetic modification, and biotechnology in general, is regulated and used in New Zealand.
- 2024 – The NZ EPA releases a clarification that the progeny of GMOs that do not inherit the transgene are not regulated as genetically modified organisms under the HSNO Act.

Read more

- Legal considerations of gene editing in New Zealand, Victoria University of Wellington Law Review (01 October 2019).
- Te ao Māori views on genetic technologies, Frontiers in Bioengineering and Biotechnology (11 April 2019).
- Human genome editing recommendations from a WHO-convened expert committee (12 July 2021) which is summarised and contextualised in this *Nature* article (12 July 2021).
- A report on gene editing in agriculture (UN-FAO). A detailed report on the potential for using gene editing to address issues in agricultural systems.

- The regulators of biotechnology worldwide. The BCH lists the national competent regulators for biotechnology as part of managing the movement of genetically modified organism between countries.

Media content

- A TED talk on gene editing by Jennifer Doudna, who was jointly awarded the Nobel prize for Chemistry along with Emmanuelle Charpentier.
- Gene editing explained at 5 expertise levels by Neville Sanjana.
- From cancer-killing cells to fake burgers – is NZ ready for genetic modification? an NZHerald article (paywalled) which includes an interview with Juliet (17 October 2022).
- Report on GM and gene editing in the laboratory Newshub including David Parker (Environment Minister) .
- National Party biotech policy news release.
- An RNZ Nights interview with Revel; a wide ranging discussion on GM and gene editing.

Regulation in some example jurisdictions with relevance to NZ exports

	Base editing	Gene edits (InDel)	Prime editing	Gene replacement	Gene insertion	Cis-genics	Trans-genics
Argentina	NBT (case-by-case)				GMO (case-by-case)		
UK	QHP3.3	QHP3.1 (SDN-1)	QHP3.3	QHP3.2 (SDN-2/3)	GMO		
India		SDN-1		SDN-2	GMO		
EU*	NGT-1				NGT-2		
US (USDA)	340.1(b)(2)	340.1(b)(1)		340.1(b)(3)	GMO		
Australia		SDN-1		SDN-2	SDN-3	GMO	
NZ	GMO						

*proposed

Regulated as gene edited	Regulated as GMO

Glossary of terms related to gene editing

- Traditional/conventional breeding – a technique where two organisms are crossed to produce offspring for commercial (or other) reasons. Includes:
  - Selective breeding – a breeding technique where the parents and/or offspring are selected specifically for their known genetic characteristics.
- Mutagenesis – a technique where the DNA of an organism is permanently altered by the application of a chemical or physical agent (such as radioactivity or UV radiation).
- Genetic modification (GM) / genetic engineering (GE) – techniques where the DNA of an organism is altered by scientists through the permanent addition of DNA from another source. Includes:
  - Transgenic – modifying an organism with DNA from another species.
  - Cis-genic – modifying an organism with DNA from its own species.
- Null segregant – the offspring of a genetically modified organism that does not carry the modified and/or foreign DNA.
- New breeding techniques (NBTs) / precision breeding – techniques where the DNA of an organism is altered by scientists in a targeted and precise way. *Classified as genetic modification under New Zealand regulations*. Includes:
  - Gene editing / genome editing – a technique where a change to the DNA of an organism is triggered at a very specific point in the DNA by causing a cut in the DNA. The most common technology is known as CRISPR-Cas9.
  - In some regions (including Australia), products of gene editing are classified as:
    - SDN-1, where a small change DNA occurs at a targeted point in the genome, with no external DNA inserted.
    - SDN-2, where an existing gene is replaced with a new gene with a similar DNA sequence (for example, from the same or related species) and the new template DNA is physically inserted at the targeted point.
    - SDN-3, a new gene (from any species) is added at a targeted point in the genome and the new DNA is physically inserted.
  - Newer techniques fall outside these categories as they do not (completely) cut the DNA
    - Base editing – a technique that where a change to the DNA sequence of an organism is targeted at a single targeted point, without the permanent addition of DNA from another source.
    - Prime editing – a technique where a targeted point in the DNA sequence is rewritten using a temporary primer/template, without the permanent insertion of DNA from another source.

Negative events where GM plants or animals were involved

In an examination of media reports and other literature I was able to identify a number of instances where experimentation using genetically modified organisms was not carried out to the agreed standard, including here in NZ. See this report, and this report. Remedial actions were taken, and in all but one case the organism did not persist in the environment. In one case in the USA the organism (creeping bentgrass) has become established in agricultural environment (drainage ditches) but does not appear to have spread further. There have been a number a media reports about GM trials in NZ (here, here and here) but these do not indicate that failures in containment as required by law were permitted to occur, but rather the groups opposed to the use of GM were actively campaigning against the trials. Internationally, following release into production and sale there are a small number of cases where the organism has spread beyond its intended locations (See here, here and here). Finally, there is the rather unusual case of the orange petunia. Apparently made in Europe before being stolen and incorporated into worldwide breeding programs a transgenic petunia was sold around the world and in NZ before being detected and recalled.

Acknowledgments

I would like to thank the very many people who took the time to speak with me as I investigated the use and regulation of genetic modification as part of this fellowship. Also to the team at the OPMCSA who provided helpful advice and introductions. Finally, to PFR who allowed me the time to develop skills, relationships and knowledge that will help inform any transition to an agro-biotech future.