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A review of gene editing for the benefit of plant health

Policy Report

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Royal Botanic Garden Edinburgh

The James Hutton Institute

This work was commissioned by Scotland's Centre of Expertise for Plant Health Funded by Scottish Government through the Rural & Environment Science and Analytical Services (RESAS) Division under grant agreement No PHC2021/03

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Please cite this report as follows: M. Elliot & I. Toth (2021). A review of gene editing for the benefit of plant health: Policy Report. PHC2021/03. Scotland's Centre of Expertise for Plant Health (PHC). DOI: 10.5281/zenodo.5929583

Available online at: planthealthcentre.scot/publications

Dissemination status: Unrestricted

Acknowledgements: We would like to thank all those who participated in the workshops run by the Plant Health Centre on this topic, and who contributed comments and edits to the report, including: Janis Antonovics (University of Virginia), Damian Bienkowski (JHI), Richard Buggs (RBGK), Fiona Burnett (SRUC), Stephen Cavers (UKCEH), Sarah Green (FR), Karen Halliday (University of Edinburgh), Nigel Halford (Rothamstead Research), Wendy Harwood (John Innes Centre), Pete Hollingsworth (RBGE), Sonia Humphris (JHI), David Michie (NFUS), Ruth Mitchell (JHI), Attila Molnar (University of Edinburgh), Chris Quine (FR), Mark Tailor (JHI), Lesley Torrance (JHI), and Robbie Waugh (JHI).

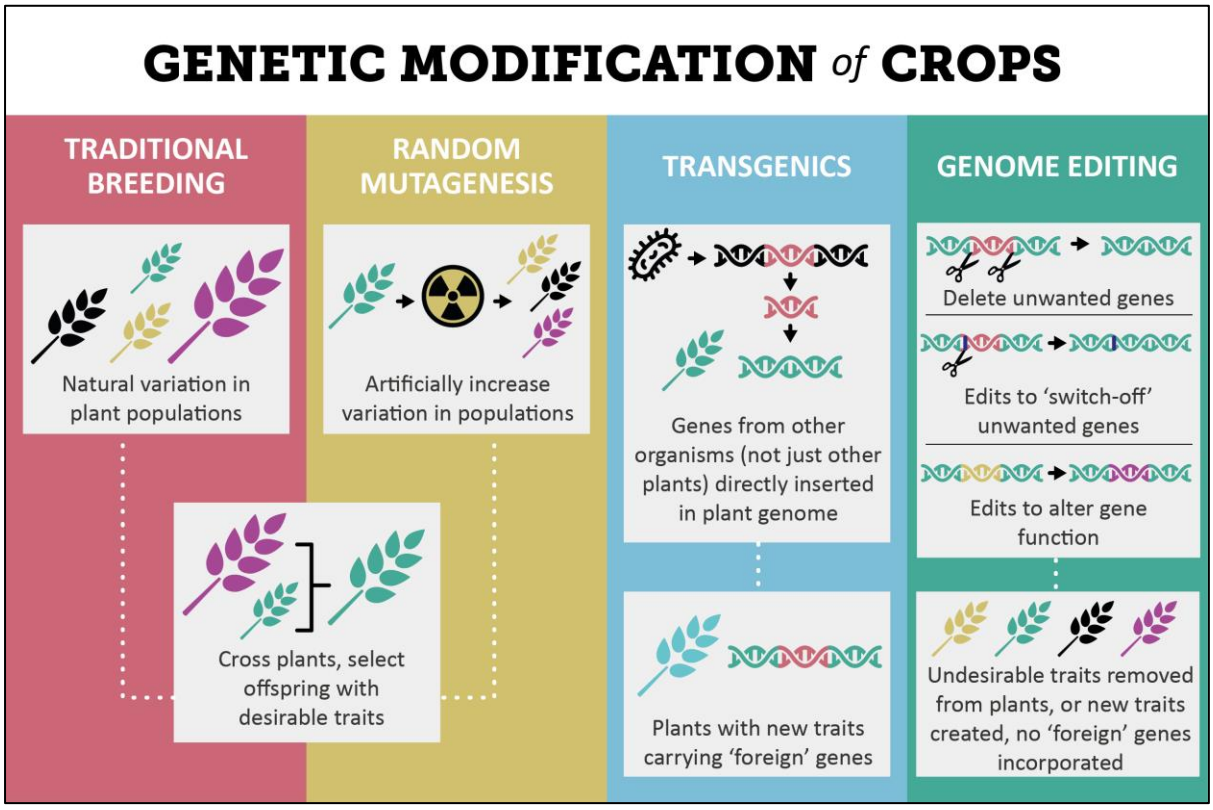
Executive Summary

- **Definitions:** Gene editing (GE), as defined in this document, is fundamentally different to previous methods such as genetic modification (GMO). GMO relies on the permanent introduction of "foreign" DNA which might not always be sourced from a plant (often referred to as transgenics) and could not occur naturally. GE, on the other hand, introduces small, targeted changes to a plant's existing DNA resulting in potentially beneficial permanent mutations. With some GE procedures, "foreign" DNA is transiently introduced into the plant, but is often then removed to create a finished product with no foreign DNA. Cisgenics, which could be generated by GE or other biotechnology methods, involves the perminant insertion of a gene(s) from a related species into the genome of an organism. Importantly, the outcomes of both GE and cisgenics could occur naturally.
- **Breeding opportunities:** GE and cisgenics are much closer to traditional forms of plant breeding that have been developed over many decades to produce crops with beneficial traits (including the use of radiation or chemical mutagenesis). GE and cisgenics therefore represent an opportunity to streamline traditional breeding techniques, speeding up the development of plants with resilient traits such as pest and disease resistance. These techniques offer many advantages over traditional breeding but also some disadvantages.
- **Agriculture:** Crop production in Scotland has a farm gate value of over £ 970 m. While crop losses due to pests and diseases occur even with full pesticides avaialbility, these losses would be substantially increased through the loss of pesticides. Exploring the potential of GE and cisgenics to protect crops would be a cost-effective approach to agricultural productivity, a plant sector where most of the biotechnological developments have so far been concentrated. Although it would be possible to deliver a limited number of GE crops to date, further investment in this area is required to guide methodological development and expand the range of crop targets available.
- **Forestry and horticulture:** Opportunities exist for the deployment of these technologies to forestry and horticulture, but further baseline research is required to guide methodological development and identify appropriate applications. Given the importance of forestry to the economy in Scotland, this fundamental knowledge gap needs to be addressed to enable the industry to take advantage of potential crop protection opportunities provided by GE, cisgenics and new gene technologies as they become available.
- **Natural environment:** Research on the potential of GE for plants in the wider natural environment is very much in its infancy, in part because current regulations prohibit deliberate release. If this type of research is to get underway, a revised regulatory framework would need to consider the appropriateness of such deliberate releases.
- **Regulations:** In the UK, GE plants can only be grown within the GMO regulations that were developed in the 1990s. This has led to a bottleneck in technological development. A new regulatory framework would improve clarity for researchers and allow for investment in the development of new gene technologies in Scotland. Defra has recently released similar findings from a recent public consultation.

What is GE?

Natural selection occurs in plant populations over time, allowing them to adapt to their environment. GE refers to a set of new techniques which can be used to intervene in this process in a number of ways, enabling plant breeders to select desirable traits, such as resilience to pests and diseases, more accurately and quickly.

The process of plant breeding is not new, the diagram below shows the current techniques in comparison to each other and GE.



Differences between GE and other breeding methods

- **Traditional breeding** – can take a long time, waiting for mutations to occur naturally. Non-beneficial traits can inadvertantly be selected if they are not visually obvious. GE can allow for a more targetted approach to selection by identifying and changing a particular part of a plants DNA.
- **Random mutagenesis** – using radiation and chemicals to produce mutations relies on an element of good fortune as to whether the resulting traits are beneficial or not. Many thousands of mutations can occur leading to off target effects and so narrowing down the plants with only beneficial traits can take time. As with traditional breeding, GE can make this process much more efficient, potentially speeding up the time needed to produce a new crop variety with pest or disease resistance.
- **Transgenics** (most often associated with genetically modified organsims [GMOs]) – the inserted DNA is from a different species or organism and stays in the engineered plant into

the future. While GE can be used to do the same thing, changes to the plant can also be made that leave no traces of foreign DNA in it.

- GE is relatively new and therefore there are currently limited plant species that can be worked on, and limited technologies for changing gene targets. If GE remains limited in this way then the numbers of new varieties produced will also be limited.
- Public perception and the confusion between the different breeding techniques has contributed to the slower development of new technologies. A new regulatory framework is therefore required in order to build public confidence in plants produced through new gene technologies such as GE.

Contents

1 Introduction

1.1 Gene editing definitions and safety

Gene Editing (GE) (aka genome editing), which includes targeted mutagenesis, is a relatively new technology that enables small, targeted DNA changes to be made within living cells. GE can be used to perform changes to a plant's genome (including the introduction of DNA), which could include cisgenics approaches (the insertion of a gene(s) from related species that could have occurred naturally – see below). However, in this review, the term GE refers only to instances where changes to DNA have occurred through gene or partial gene deletions or changes in the base composition (nucleotides) of a gene, again as could happen in nature (e.g., Bhat et al. 2020). Cisgenics, even when made using a GE approach, will be discussed separately. Also, any foreign DNA that may have been inserted as an early step in the GE process is removed from the final product, and the changes left are permanent and hereditable. In this context, GE can be seen as directly analogous to traditional plant breeding techniques with the benefit that changes, which would take conventional breeding many more years to achieve, can be made safely, rapidly and specifically. While there are several techniques defined under the term 'gene editing', most modern procedures use a method called CRISPR/Cas (Clustered Regulatory Interspaced Short Palindromic Repeats/CRISPR-associated protein), which has improved on previous methods ZFN (zinc finger) and TALEN (transcription activator-like effector nuclease) in terms of its accuracy, speed and cost. Cas is a natural protein found in bacteria that helps to defend against bacterial viruses (bacteriophages). The most widely used for CRISPR/Cas is Cas9, and will be referred to throughout this report, although others are also being exploited. The Cas9 protein can be reprogrammed to bind to and cut any piece of DNA if provided with a specific RNA guide sequence, which seeks out that target DNA (https://www.newscientist.com/definition/what-is-crispr/). While GE works particularly well in plants that have had research investment in both genome analysis and the understanding pest / pathogen infection and resistance pathways, such as wheat, new advances in GE are now making it possible for many less well studied plants to be amenable to such technology.

GE crops have been shown to pose marginal risk to the economy, human health and the environment (Lassoued et al. 2019). According to the European Commission (2020) and others (Nicolia et al 2014; Leopoldina and Akademieunion 2019) no genetic risk has been caused using biotechnology of any kind after more than 30 years of biosafety research.

1.2 Cisgenics

A genetically modified organism (GMO), as defined in EU legislation, is an organism in which the genetic material (DNA) has been altered in a way that does not occur naturally by mating or natural recombination (Plan and Van den Eede 2010) and is most closely associated with transgenics (the inserted DNA from a different species or organism that stays in the engineered plant into the future) (Rani and Usha 2013). Cisgenics, on the other hand, is where genes from related species are introduced into the genome of an organism as could occur in nature, which can be achieved using GE techniques or more traditional biotechnology approaches (van Hove and Gillund, 2017). However, there are very few examples of where this technique has been used to improve pest or disease resistance, one being late blight in potato

(see below). In addition, most publications describing this technology are 5-10 years older than those describing GE (as defined in the above section) and fewer in number, suggesting that GE may be overtaking cisgenics as the more promising approach.

1.3 Uses of Gene Editing

While this review focusses on the use of GE to generate crops resistant to pests and diseases, also referred to as biotic stress resistance / tolerance (e.g., Tyagi et al. 2020), it is important to remember that GE has also been used for the development of other traits for a wide variety of market-oriented applications (Fig. 1) in a growing number of countries (Fig. 2) (Menz et al. 2020; Nogue et al. 2016). To date these include 41 crop plants and ornamentals, with most applications being on rice and tomato followed by the main staple crops maize, wheat, potato and soy (Menz et al. 2020).

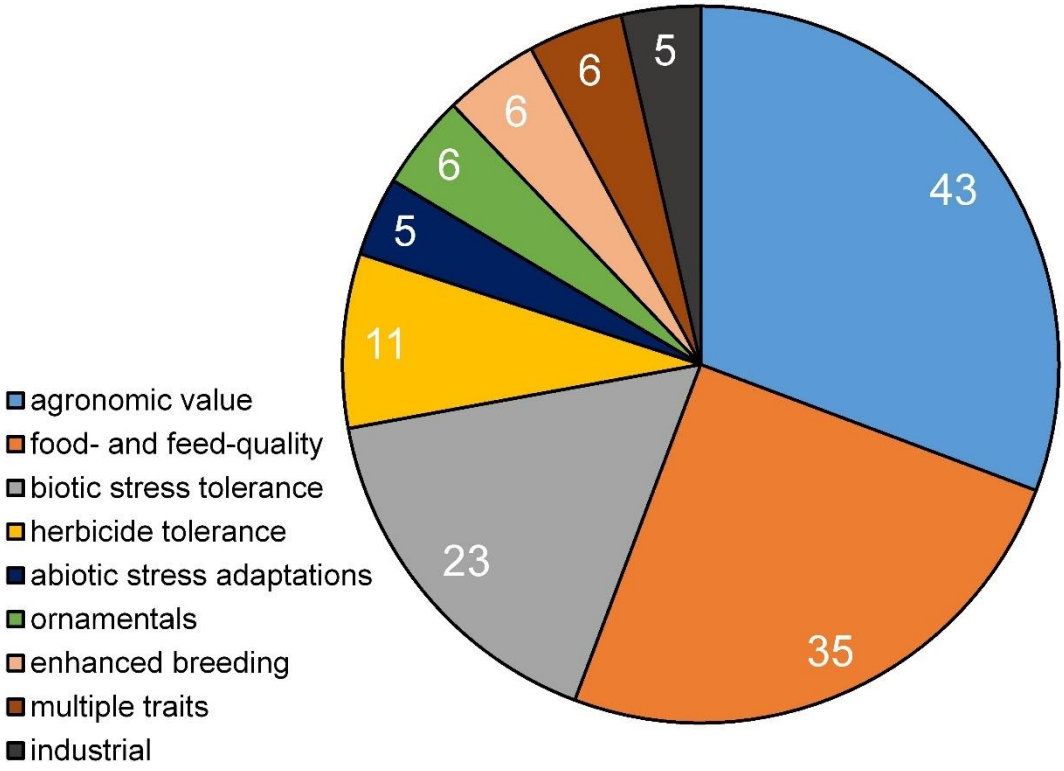


Figure 1 - Distribution of gene editing traits by application (from Menz et al 2020).

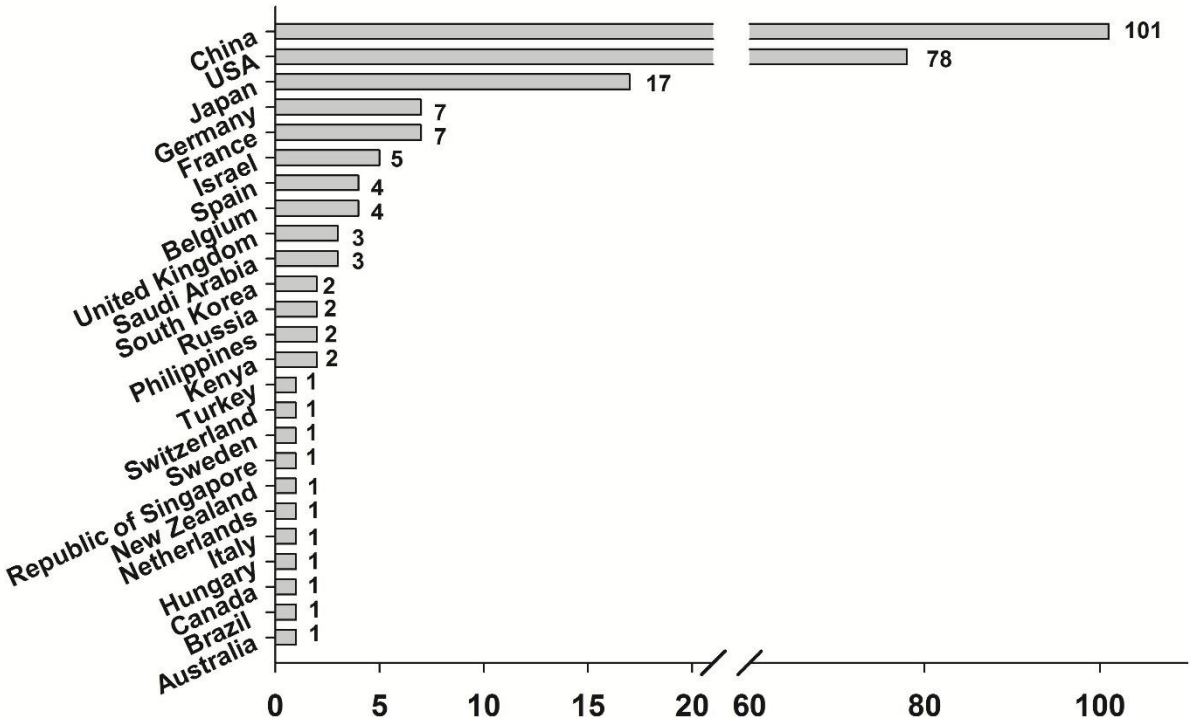


Figure 2 - Number of market orientated gene editing applications by countries in which the corresponding author is located (from Menz et al 2020).

GE has been used successfully to develop resistance against a range of plant pests and diseases (see below). This has been done in the UK and elsewhere, mainly in an experimental context in different plants, mostly from agriculture but some trees, and against different classes of pests and diseases including bacteria, viruses, oomycetes, fungi and insects.

1.4 Comparison between conventional breeding and gene editing

Conventional crop breeding is estimated to take ca 10-20 years, depending on the crop, the breeding material available, the varieties, availability of genetic markers, the trait being investigated and many other factors but can take longer for some crops and in some situations. Such methods include back-crossing and introgression breeding, inbreeding, hybrid breeding, mutation breeding and marker-assisted selection, with other methods in development (www.crops.org/about crops/breeding). By comparison, GE breeding can take as little as 5 years but again depends on factors such as the construct being made and the amenability of the plant to allow entry of DNA/RNA into its cells (a process known as transformation). In addition, such constructs may enter conventional breeding programmes and therefore potentially take just as long as these conventional procedures.

Traditional techniques of tree breeding for forestry can involve a period of at least 20 years between tree selection and production of commercial seed from an orchard (Forest Research, 1998). The process involves selecting trees with traits that are useful for forestry, often called "plus trees", and collecting seed from them. This is subsequently grown during 'progeny' tests at relevant test sites, allowing the breeder to identify the parent trees whose previously observed superiority is inherited by their offspring (progeny). This process involves long-term commitment and makes heavy demands on resources.

It is conceivable that GE could speed up the process described above for trees but there are several considerations (Pers. Comm. Richard Buggs, Kew):

Reason for long timescale	**Potential solutions**
Trees need to grow to maturity so that selection of resistance traits in mature individuals can be made.	Can be overcome without using GE (marker assisted breeding or genomic prediction) provided enough genomic knowledge exists.
Trees need to reach sexual maturity to produce a new generation.	Could be overcome by using GE or environmental manipulation to induce early flowering.
If resistance is absent you need to wait for mutations to cause them.	More potential for GE because novel techniques could be used to initiate mutations rather than having to wait for them to happen naturally.

1.5 Advantages and disadvantages of gene editing

GE has several advantages and disadvantages over other forms of plant breeding (see summary - Table 1).

1.5.1 Potential advantages

New resistant plants: Even after many decades of conventional breeding it has not always been possible to develop durable resistance in commercially acceptable plants, e.g., late blight in potato. GE offers a new approach to develop resistance where conventional breeding may have had limited success, since it allows new gene targets to be exploited, including multiple targets for multiple resistances.

More rapid development of resistant cultivars: Where conventional breeding has shown promise in the development of resistant varieties, GE plants could be developed more quickly (5 years versus 20 years plus for conventional), assuming there is sufficient knowledge of the gene targets for GE based on prior research. This will be especially important as pesticides are taken off the market. GE can reduce the need for extensive backcrossing, used in conventional breeding to move genes from one parent with an important agronomic trait to an elite variety, especially in the absence of genetic transformation. However, recent advances in transformation technologies are making it easier to carry out such procedures directly in the cultivar of interest.

Enabling existing cultivars to become resistant: Targeting a specific gene while leaving the remaining genome unaltered, is especially useful where resistance is required in an existing cultivar while avoiding changes to other properties, e.g., a blight resistant Maris Piper potato (the most widely grown variety in Scotland at ca 17% total production and a consumer favourite).

Increasing genetic diversity: Where breeding is hampered by a lack of diversity in the plant species, GE can help to increase that diversity through mutagenesis and sequence variation in selected genes.

Dealing with pathogens that overcome resistance: Due to the nature of GE, especially where it is deployed to alter the sequence of a given gene, further gene changes can be made rapidly if a pest / pathogen evolves to overcome the current resistance gene (akin to updates to flu vaccines), thereby returning a plant to a resistant phenotype.

Common gene targets used across plant and pest / pathogen groups: Genes for specific resistances are present in a wide range of different plant species, e.g., gene *eIF4E* used to develop resistance to viruses. GE technology therefore offers the potential to develop a wide range of new resistant plants against different pests / pathogens using knowledge of existing gene targets, and without the need to transfer genes from other species.

Reducing pesticide inputs: The use of GE and its rapid deployment in Scotland could lead to huge economic and environmental savings by avoiding the use of pesticide and fungicide applications.

Reducing economic losses: Many pests and pathogens continue to cause huge economic losses in Scotland. For example, late blight – ca £39.5 m pa. GE has the potential to significantly reduce such losses adding to the economic prosperity of Scotland.

Rapid solution against new threats: GE offers the possibility of rapid development of resistant plants against new pest and pathogen threats that have not previously been active in Scotland.

New regulation and licencing (patent issues): New regulations / licencing that differentiate between GE from GMO would speed up the commercial use of GE breeding technologies.

1.5.2 Potential disadvantages / concerns

Limited plant targets: GE is currently limited to crops with well-established transformation and regeneration protocols, although research (current and future) is expanding this range and developing generic transformation protocols.

Limited technologies for changing gene targets: Generating loss of function mutations is relatively easy by CRISPR/Cas9, but precise within-gene changes by GE is still in its infancy.

Potential to limit number of varieties: If applied to a very limited number of species and varieties and it proves to be highly successful, e.g., development of a specific type of resistant crop, if not used sensibly GE has the potential to reduce the number of varieties grown in the field, therefore limiting heterogeneity and the resilience this encompasses.

Public perception: This will remain an issue, at least in the short term, whatever technology is used and how it is described. Consequently, it will also remain an issue for government, industry and other public bodies.

Failure to change regulation and licencing (patent issues): Failure to differentiate GE and GMO regulation would stifle innovation in breeding, with Scotland and the rest of the UK falling further behind other nations in the development of GE technologies and commercial (market-oriented) applications.

ADVANTAGES OF GENE EDITING	Public good	Public/Private good	Private good
Reduced disease pressure through: • New resistant plants • More rapid development of resistant cultivars • Enabling existing cultivars to become resistant • Increasing genetic diversity • Dealing with pathogens that overcome resistance • Common gene targets used across plant and pest/pathogen groups • Reducing pesticide inputs • Reducing economic losses • Rapid solution against new threats • New regulation and licencing (patent issues)	Increased output/efficiency from lower C footprint (/unit product) = lower GHG emissions	Climate adaptation = New and more resilient varieties of crops will stand up better to the vagaries of Scotland's changing climate	Increased quantity of crop for sale, reducing economic losses
	Less pesticides = more wildlife	Opportunities for Scottish research institutes?	Increased quality of crop for sale, increasing market returns
	Less pesticides = less pollution	Increased business resilience with GE providing rapid solutions against new threats	More rapid production of crop for sale, increasing economic returns and more rapid response to new and existing threats
	Protection against new threats to plants in the environment, parks, woodlands (social amenities)		Improved environmental efficiency of Scottish produce, improving competitiveness, marketability, and adding value to Scottish produce using crops as inputs (e.g., feed for Scotch beef, farmed salmon)
	Sustainable production of varieties of choice for consumer.		
	Reduced food prices		
DISADVANTAGES OF GENE EDITING	**Public good**	**Public/Private good**	**Private good**
• Limited plant targets • Limited technologies for changing gene targets • Potential to limit number of varieties • Failure to change regulation and licencing (patent issues) • Public perception	Public perception remains an important issue	Concerns by industry, government, other public bodies and industry over public perception	Limited gene targets and number of varieties could reduce the variety of plants grow in the field and threatening resilience due to lack of heterogeneity
		Failure to change regulation and licencing could delay implementation, add to cost for breeders and stifle research innovation.	Limited technologies available currently to manipulate genes may affect breeders in the short term but these are likely to improve in future.

Table 1 – Advantages and disadvantages of gene editing for plant health, for public and private good

2 Gene Editing and Potential for Agriculture in Scotland

Considerable progress has been made in the use of GE to develop pest and pathogen resistant crop varieties (see reviews by Tyagi et al 2020 and Tiwari et al. 2021). The following paragraphs describe some of these findings with particular emphasis on crops relevant to Scotland, together with an indication of the impact that such a technology could have on production, social and economic factors.

2.1 Potato

Potato production in Scotland has an output of 1.16 m tn worth approximately £250 m, with seed exports worth over £50 m and, together with barley, is the economically most valuable crop grown in Scotland (Scottish Government, 2020b). The main pests and diseases of potato in Scotland include late blight (*Phytophthora infestans*), PCN (potato cyst nematode), PVY, spraing (tobacco rattle virus), blackleg (*Pectobacterium atrosepticum*) and powdery scab (*Spongospora subterranea*) (Wale et al. 2008). Two examples of these diseases where GE has been undertaken are given below:

2.1.1 Late blight disease

Late blight disease (caused by *Phytophthora infestans*) is the most damaging potato pest worldwide and Scotland's most costly potato disease. Potato farm gate price losses due to late blight in Europe have been estimated at 15.8% based on a Dutch investigation (Haverkort et al. 2008). If this figure was to be applied to Scotland it would equate to ca £39.5 m losses pa based on Scottish production figures (Scottish Government, 2020a; 2020b). Moreover, ca 37% of Scottish production is for the higher value seed market, compared with 24% in the Netherlands, which may increase the cost of losses still further. Most farm gate losses come from the cost of crop protection chemicals and their application (ca 92%), with the remainder from actual crop losses (ca 8%). Losses due to late blight in the Dutch organic market have been estimated at ca 32%, such that if potatoes are grown organically, losses due to late blight are twice that of conventionally produced crops (Haverkort et al. 2008).

A potato leaf showing late blight infection caused by *Phytophthora infestans*. Howard F. Schwartz

GE has been applied successfully to late blight caused by *P. infestans*, in tomato and potato, in both cases by disabling different sets of plant genes co-opted by the pathogen to help it infect the host (Hong et al. 2021). Such genes are often referred to as 'host susceptibility genes' since despite being part of and used by the plant, they may also be exploited by a pathogen(s) to aid infection (Koseoglou et al. 2021). Further examples of their use will be described below. This is significant as these genes are widely present in all land plants (Hong et al 2019) and therefore provide a huge opportunity for GE across many different plant species and are likely to offer resistance against different pests and pathogens.

Cisgenic approaches have also been used to generate potato plants with durable resistance (long-lasting resistance that has a reduced chance of being overcome by the pathogen) to late blight disease, e.g., through the transfer of multiple late blight resistance (R) genes from crossable wild potato species. In this case, an antibiotic resistance gene marker was initially used to validate entry of the genes into the potato plants, after which the marker was removed to leave a marker-free cisgenics variety. It was shown that stacking two or three R gene in this way in different combinations could reduce fungicide use by over 80% (Haverkort et al. 2016). Selected genes were used in a similar cisgenics approach by the company BASF who produced a late blight resistant potato names Fortuna that stacked two resistance genes. However, the Fortuna potato failed to make it to market. Following this, the company Simplot developed a late blight resistant potato called Innate, which also contained the same two genes plus a third, offering further stability against the disease (Halterman et al 2016). Innate is sold commercially in the USA (simplot.com/plant_sciences/innate_potatoes).

2.1.2 Potato virus Y (PVY)

PVY belongs to the potyvirus family, is the most damaging potato virus worldwide, with field losses of up to 80% and infects tobacco, pepper, tomato and eggplant (Lacomme and Jacquot 2017; Quenouille et al. 2013). PVY is a major cause of downgrading and failure of potato seed crops in Scotland (McCreath, SASA 2020). Nolte et al (2004) calculated that a 1% increase in PVY in Idaho, USA resulted in a loss of 0.18 tons / ha (equivalent to 0.2 metric tonnes / ha). If such a loss was to impact the whole of potato production in Scotland, this would equate to a 5.6% yield loss or £14 m based on the current value of potato production in Scotland (Scottish Government, 2020b).

To date, there appears to be no published examples of GE being used (under the definition used in this report) to develop PVY resistance in potato. However, Cas has been used to create transgenic potatoes (cv Desiree), actively targeting PVY particles as they enter plant cells rather than evading them through lack of recognition (Zhan et al 2019). Although this technology is outside the scope of this review GE deletions, which are in scope, have also been used to increase resistance to PVY in other crops by targeting plant host susceptibility factors used by the virus to replicate and / or spread. For example, a gene *eIF4E* in tobacco, required for PVY infection was mutated leading to PVY resistant tobacco plants (Ren et al. 2021). Other examples include mutations in *eIF4E1* in tomato to reduce susceptibility to PVY^N but not PVY^O (two variants of PVY), and to cucumber mosaic virus (Atarashi et al. 2020; Hameed et al. 2019). While the use of GE for PVY resistance in potatoes has not been published to date, work is ongoing both in the UK and elsewhere. GE has also been used to control a wide range of other viruses on crops, including others belonging to the potyvirus family, e.g., zucchini yellow mosaic virus and papaya ringspot mosaic virus (Chandrasekaran et al. 2016).

GE techniques used to improve resistance against viruses have highlighted the issue of

potential negative effects when mutating plant host genes, e.g., reduced crop yields (Akhter et al. 2021). This is because such genes play one or more functions in the host and removal can, in some instances, affect the hosts overall well-being. However, this issue can be overcome by using GE to precisely target a gene(s) to change its sequence so that it is no longer recognised by the virus but retains its function in the plant and thereby retains its yield potential (Bastet et al. 2019). Another strategy in developing resistance using GE is to induce general resistance mechanisms in the plant that are only switched on during an attack thus allowing the plant to divert energy away from growth only when required to defend itself (Hameed et al., 2019).

2.2 Cereals

Barley is Scotland's most grown crop with an output of 1.94 m tn valued at £249 m, while other major cereal crops include wheat (Scotland's No. 3 crop in terms of value) with an output of 937,000 tn value of £132 m and oats at 189,000 tn valued at £26 m (2019 figures from Scottish Agricultural Tables – economic report 2020 edition). The main pests and diseases to affect cereals in Scotland include Ramularia (*Ramularia collo-cygni*), Rhynchosporium (*Rhynchosporium commune*) and Septoria (*Septoria tritici*) (F Burnett, SRUC pers comm).

Examples where GE has been used to enhance resistance in major cereals include resistance to the *Blumeria graminis* (powdery mildew) in wheat, *Fusarium graminearum* (Fusarium head blight) in barley and *Magnaporthe grisea* (rice blast) in rice (Zhang et al. 2017; Low et al. 2020; Wang et al. 2016). In all cases, mutagenesis of host susceptibility genes improved or showed the potential to improve resistance. Cas-based transgenic techniques, akin to those described for PVY above, have also been used to improve barley resistance by direct targeting of wheat dwarf virus (Kis et al. 2019). While there are few other examples of GE for resistance in barley, it has been used for other purposes, including the improvement of biofuel production through reduced lignin content (Lee et al. 2021) and increased starch, amylose and beta-glucan content (Yang et al. 2020). Other uses in wheat include reduced gluten (Sanchez-Leon et al 2018), herbicide tolerance (Zhang et al. 2019) and enhanced weight and shape of grain (Wang et al. 2019). Currently, cisgenic transfers in wheat are limited but new species hybrids have opened new possibilities, e.g., transfer of the glutenin gene, involved in bread-making quality, from bread wheat to Durum wheat (Gadaleta et al. 2008). A cisgenic approach has also been used to improve phytase activity in barley (Kerr et al. 2010) but there is little evidence for this approach having been used to develop pest or disease resistant plants.

2.2.1 Ramularia leaf spot on barley

Ramularia leaf spot is caused by the fungal pathogen *Ramularia collo-cygni* and is one of the most damaging disease of barely in Scotland, causing annual yield losses of ca £10 m (Neil Havis, SRUC pers comm). The disease also reduces grain size, causing uneven germination of grains during the malting process (Havis et al., 2015), which is a concern for the Scotch Whisky Industry (Gurr et al., 2020).

A significant issue with Ramularia is that it is capable of rapid mutation and has quickly overcome the fungicides used to control it. Therefore, GE will be important as a medium to long term control strategy in combination with other methods. Whole genome sequences are now available for barley and *Ramularia collo-cygni* (Stam et al., 2018), which has enabled some early research on plant genomic regions important in the pathogen-host interaction that could ultimately be edited to increase resistance to this pathogen (Neil Havis, SRUC pers

comm).

2.3 Fruit crops

Strawberries, raspberries and other soft fruits are major crops to Scotland with outputs of 29,800 tn (valued at 95.1 m), 2, 000 tn (valued at £15.6 m) and 12.5,000 tn (valued at £33.5 m), respectively (2019 - Scottish Agricultural Tables – economic report 2020 edition).

While there are few examples of the use of GE to increase resistance in soft fruit to pests and diseases, GE studies have looked at yield and quality traits. For example, the main breeding targets in strawberry are fruit quality (Martin-Pizarro et al. 2019), the control of flowering (for fruit yield) and other traits (Gaston et al, 2020). Likewise in raspberry, studies have mainly looked at fruit quality (Miller, 2019). There appear to be no publications describing the use of cisgenics to improve soft fruit crops, although a PhD thesis describes its successful use in strawberry against *Botrytis cinerea* (Schaart 2004).

2.3.1 Raspberry root rot

Raspberry and strawberry crops succumb to several important pests and diseases, including root rot of raspberry (*Phytophthora fragariae* var. *rubi*) and strawberry (*P. fragariae* var. *fragariae*) (Schumann and D'Arcy, 2006). Breeding facilitated by genomic markers for raspberry root rot resistance is underway in Scotland (JHI, 2021) but so far GE technologies have not been utilised anywhere for this purpose. Given the knowledge of both the raspberry and *Phytophthora* genomes, and of the plant genes that could act as targets for GE, e.g., based on knowledge from *P. infestans* – see above, it seems likely that GE could provide a route to producing resistant raspberry plants in the future.

2.4 Oilseed rape and Vegetables

Scotland producers 130,000 tn of oilseed rape (OSR - valued at £38.9 m) and 432,000 tn of vegetables (excluding potato – valued at £164.5 m) each year. In Scotland, the main diseases affecting oilseed rape are clubroot (*Plasmodiophora brassicae*), sclerotinia (*Sclerotinia sclerotiorum*) and powdery mildew (*Erysiphe cruciferarum*) (Farm Advisory Service, 2021), with a wide range of pests and diseases in vegetable production including slugs, weevils, pollen beetles and flea beetles (Oerke, 2006). Most breeding for OSR and vegetables is carried out in the Netherlands, with limited vegetable breeding in the UK.

While there are few examples of GE use in OSR and vegetables important to Scotland, or in controlling pests and diseases, it has been used to improve OSR seed oil content and protein levels (Karunarathna et al. 2020; Sashidhar et al. 2020). GE has also been used in the UK to tackle the problem of pod shatter in Brassica crops (Lawrenson et al. 2015).

2.4.1 Club root

Club root is an infection of the roots of brassicas and related plants by a fungal-like organism called *Plasmodiophora brassicae*. It causes swelling, distortion and severely retarded growth, but some cultivars do show increased resistance to some pathotypes (Schwelm and Ludwig-Müller, 2021). In Scotland ca 50% or arable land is infested with the pathogen and yield losses

are currently managed using resistant varieties. This resistance is failing in areas where the only available resistance gene has been deployed often in the rotation. Losses can be ca 50% where resistance has failed (F. Burnett, SRUC pers comm).

There is currently no chemical control for club root and cultural practices, such as long crop rotation times, limit but do not remove *P. brassicae* from the infestation soil (this pathogen can live in the soil for at least 20 years). Therefore, the development of resistant cultivars is considered the most economical and efficient method for clubroot control (Peng et al., 2014). Early-stage research has been undertaken and two resistance genes have been identified against club root (Dakouri et al., 2018). GE could build on this work to provide a means of speeding up traditional breeding of club root resistant plants.

2.5 Land use, pesticide withdrawals and organic production

2.5.1 Land use

Crops are grown on ca 503,000 ha of land in Scotland, representing 10.4% of agricultural land (Scottish Agricultural Census: June 2018). Cereals are grown on 86% of this land, with Spring barley most widely grown at 48%, while potato is grown on only 5.5% of the land (Fig. 3). However, when considering economic value, potato (£250.5m) is approx. equal to barley (£249.5m), while soft fruit and vegetables also have a more prominent position (Fig. 4).

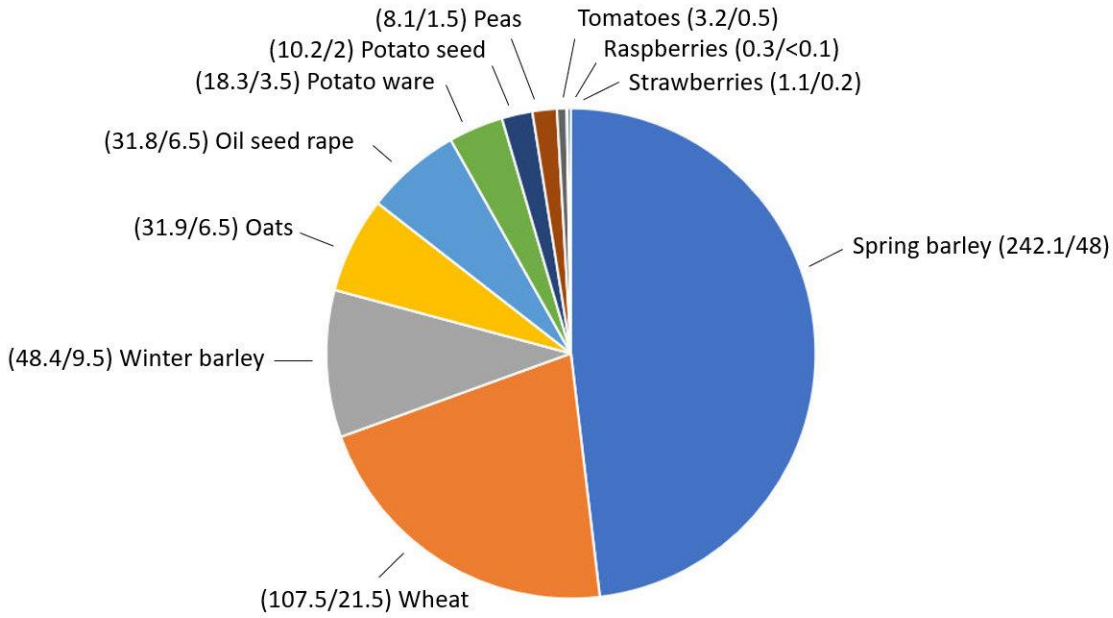


Figure 3 - Crop production land use in Scotland (2019) based on data from Scottish Agricultural Tables – economic report 2020 edition. Figures = 000 ha / % crop production.

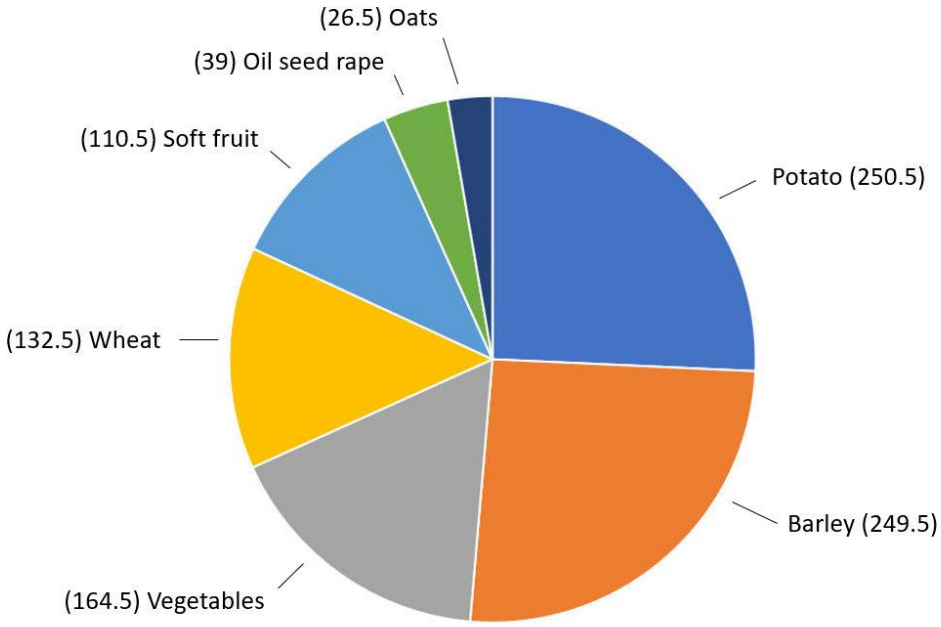


Figure 4 - Crop value in Scotland (2019) based on data from Scottish Agricultural Tables – economic report 2020 edition. Figures = £ millions.

2.5.2 Pesticides

In the UK, crop yield losses of 4-50% have been estimated where there is a high likelihood of plant protection products (PPP) being lost or restricted via pesticide withdrawal (Anderson Report 2011). This would lead to changes in cropping patterns, including an increase in spring cropping, fallow and temporary grass, and overall food output from farming and horticulture would decline. The UK would therefore have more reliance on food imports and reduced self-sufficiency. Some foodstuffs would be severely affected, e.g., peas, apples and carrots. Livestock feed costs would rise and, overall, there would be a Gross Value-Added fall of ca £1.6bn per annum, a drop of 20% based on a 5-year average (2009-2013), with much wider economic impacts of downstream food production, employment etc. This study is supported by two recent pesticide reports for Scotland produced by the Plant Health Centre (PHC pesticide reports PHC2018/15 and PHC2020/09), with loss of high-risk PPP leading to economic losses of ca £50 m for cereals, ca £30 m for potatoes and £50 m for strawberries and raspberries combined. This would escalate significantly if medium and low risk pesticides were to be withdrawn.

The European Parliamentary Research Service report (2019) on farming without plant protection products estimates that, if all PPP are lost from agriculture, potential crop losses across Europe would be ca 20-40% varying between crops, e.g., ca 80% for potato and 55% for wheat (approx. half of which is due to the impact of weeds). However, actual losses (involving the use of other often less effective control methods) would reduce these values to ca 38% and 28%, respectively. NW Europe is likely to have the largest overall potential losses (71%), due to the more intense use of PPP, fertilisers, and higher overall yields, but lower actual losses (18%) due to more adequate alternative crop protection methods. Reduced crop yields would also be associated with an increase in yield instability based on differences in pest, pathogen and weed pressures impacting on food security (Table 2).

Crop	% losses with PPPs*	% losses without PPPs ** (own estimation)	% potential losses ***	Yield gain by PPPs
Wheat	21% (10.1-28.1)	40%	50%	19%
Rice	30% (24.6-40.9)	62%	77%	32%
Maize	22% (19.5-41.1)	55%	69%	33%
Potato	18% (8.1-21)	60%	75%	42%
Soybean	21% (11-32.4)	48%	60%	27%

*: Savary *et al.*, 2019; **: estimated at 80% of the potential losses; ***: Oerke, 2006

Table 2 - European Parliamentary Report (2019) showing potential crop losses with and without Plant Protection Products (PPP) and potential gains from using PPP. Losses are calculated at a global scale. Column 3 is estimated actual losses following use of alternative crop protection methods including crop rotation, biological control, soil management and resistance varieties etc.

2.5.3 Organic production

In the UK (2020) there are 489,000 ha of land used for organic farming, 95,700 ha (20%) of which is in Scotland. Most of this land (62%) is permanent pasture, with 20% for temporary pasture, 3% for woodland and 11% for crops (9% for cereals and ca 2% for all other crops, including potato). Organic crop production therefore represents only ca 1.2% of the total crop area.

Based on a report by Kirchman (2019), yields in Sweden of organically grown legumes were 20% less and non-legumes 40% less compared to conventionally grown crops (organic / conventional yield ratios of 0.8 and 0.6 respectively). Overall, for all crops the organic yield gap was 35%, requiring 50% more land to produce the same yield as conventional production. Yield ratios for crops important to Scotland include cereals (0.60), oilseed rape (0.66), potato (0.64), peas / beans (0.76) and forage (0.8). Failed harvests also occurred as follows: Cereals (0.7%), oilseed rape (1.8%), potato (0.6%) and peas / beans (0.9) (Table 3).

Type of crop and land use	Organic/conventional yield ratio	Arable land allocated to different crops: Organic arable land (368,800 ha; %)		Conventional arable land (2,210,800 ha; %)	
Nonlegumes					
Winter wheat	0.58	23,160		351,220	
Spring wheat	0.60	12,460		62,430	
Rye	0.53	2140		14,470	
Winter barley	0.57	400		18,680	
Spring barley	0.62	18,950		280,930	
Oat	0.66	33,330		139,590	
Triticale	0.67	4060		26,200	
Maize	—	120		1660	
Failed cereal harvest	—	630		2900	
	0.60 mean	∑ 89,600	24.2	∑ 928,400	42.0
Winter oil seed rape	0.71	5370		78,050	
Other oil seed crops	0.61	1040		16,650	
Failed oil seed harvest	—	120		850	
	0.66 mean	∑6530	1.8	∑95,550	4.3
Food potato	0.64	1680		15,630	
Starch potato	—	3		2900	
Failed potato harvest	—	10		130	
	0.64 mean	∑1690	0.5	∑18,660	0.8
Sugar beet	—	—		30,700	1.3
Legume/legume mixture					
Pea	0.72	3240		21,970	
Bean	0.79	10,710		19,170	
Failed harvest pea	—	70		270	
Failed harvest bean	—	60		140	
	0.76 mean	∑ 14,080	3.8	∑41,550	1.9
Grass clover forage	0.85	183,120		622,340	
Green legume forage	0.73	5120		13,310	
Grain-legume forage	0.74	7090		7,180	
Green cereal-legume forage	0.88	16,560		23,140	
	0.80 mean	∑211,890	57.4	∑665,970	30.1

[a]Certain crops (vegetables, energy forest, etc.), green-manured and fallowed land were not included. Data derived from agricultural statistics of Sweden (SCB, 2017a, 2017b, 2017c).
Note: Bold figures refer to an area-corrected mean yield ratio of a group of crops.

Table 3 - Organic over conventional crop yield ratios and arable land allocated to different crops in Sweden 2016 (Kirchmann 2019).

From the above, PPP play a vital role in crop production in terms of yield (due to reduced loss from pests, diseases and weeds), economic impact, minimising land use (increasing yield on a set area of land), national self-sufficiency and food security (Fig. 5). Many PPP have already been lost and others are currently being phased out with more to follow (see PHC reports PHC2018/15 and PHC2020/09). While alternative methods of crop protection are available and research is underway to develop more, often as part of an integrated pest management (IPM) approach, these methods are not currently sufficient to fully protect crops in the increasing absence of PPP.

The most promising alternative method to PPP is the use of resistant crops. Breeding resistant crops is often a slow process, sometimes taking decades, although alternative methods, e.g., dihaploids breeding and use of molecular markers in potato, are reducing this time (see section 2.1). However, even after many years of development, pests and pathogens may overcome the resistance within a few years. Based on increased yield losses, and therefore the need for increased land use, an organic approach to crop production in the absence of resistant crops is highly unlikely to replace conventional production following reduction in the use of PPP. GE, therefore, could potentially play a major role in limiting actual losses, highlighting the need for the next generation of new, improved and timely disease resistant crops.

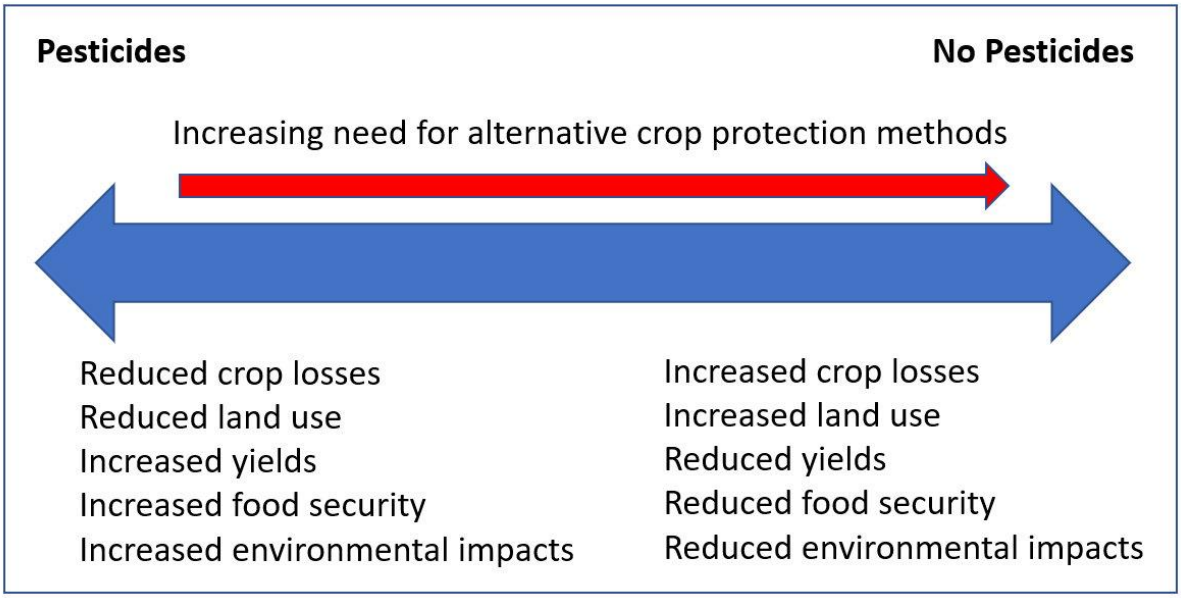


Figure 5 - Representation of consequences of crop production with and without pesticides, with the increasing need for alternative crop protection methods as the arrow moves to the right.

3 Trees and Forestry

Tree pests and diseases have become an increasingly significant issue in the last few decades. The development of resistant trees has therefore become much more relevant. However, the successful development and utilisation of resistant trees is far from simple (Woodcock et al., 2018). Selection of beneficial traits has been common practice in tree breeding for decades, particularly in commercial forestry to increase the quality of the most commonly grown species (Forest Research, 2021a). However, this has not been without its challenges, particularly given the long generation times of trees and the effects of climate change (Pretzsch et al., 2018). Given these challenges it has been argued that there is a role for new gene technologies in timber-producing forestry to improve traditional breeding of disease resistance by targeting appropriate genes and speeding up the breeding process (Dort et al., 2020). In addition to this, tree species are not pure lines and often exhibit a range of resistance levels through a population, from highly susceptible to resistant individuals (French et al., 2016). They are also highly variable in their yield, the cause of which is hard to assess given their longevity, and the large land areas involved. Identifying genes responsible for such variation is a priority but is in the early stages, nevertheless, the potential for GE to modify relevant genes and speed up the selection of more resistant individuals is there. Equally important is the possibility of using GE to induce rapid life cycles for experimental and breeding purposes, which can then be precisely reversed using the same GE processes.

It is clear from the literature that, at the very least, our understanding of tree genomics, and the translation of genomics into phenotypic effect, should be improved so that new technologies could be utilised as they arise.

3.1 Increasing disease resistance

With the advent of several serious tree diseases in the UK, research projects are underway to identify healthy looking material in order to propagate from it, in the hope that the resulting plants can be grown on to eventually produce a more resistant population (e.g., the living ash project - Forest Research, 2021b). Clarity on the genetic basis of this resistance is continually increasing (Stocks et al., 2019), but material is generally selected on a physical (phenotypic) basis rather than on an understanding of the DNA (genotype). GE may therefore have a role to play in the manipulation of disease resistance-related genes in trees going forward rather than relying on phenotypic selection. For example, ash dieback, caused by the fungus *Hymenoscyphus fraxineus*, is having a profound impact on the ecologically important native ash tree (*Fraxinus excelsior*). Whole genome data is now available for ash (Sollars et al., 2017), which has so far been used to identify genes that may confer resistance to ash dieback (e.g., Sahraei et al., 2020). Given that the economic, environmental and cultural cost of ash dieback has been estimated at £15 billion over coming decades (Hill et al., 2019), comparative genomics could be used to identify genes suitable for GE mutations, and this could make ash more resistant to ash dieback disease. However, such research is in its early stages (Queen Mary University, 2021).

Ash dieback disease (*Hymenoscyphus fraxineus*). Sarang, Wiki Commons

3.2 Controlling invasive conifer species

Tree species selected for forest plantations in Scotland often originate from other regions with

a similar climate and high growth rates, two factors which also contribute to enhanced invasiveness (Richardson and Rejmánek 2004). Introduced species are also grown in large-scale plantations, which creates a massive propagule pressure, increasing the probability of them escaping from cultivation (Pyšek et al., 2014). In Scotland, "escaped" exotic conifers have had an ecological impact, particularly on the uplands (Bunce et al., 2014). GE could be used to prevent future commercial species becoming invasive by manipulating their reproduction, e.g., so that they do not produce cones (Fritsche et al., 2018). This could also benefit forestry because the GE trees would put their energy into growth rather than cone production, thereby potentially speeding up growth. This approach has been suggested in New Zealand where invasive conifer species have become a significant issue (Fritsche et al., 2018), but research is yet to get underway.

3.3 Disease resistant fruit trees

Deletions / mutations in susceptibility genes for fire blight (bacteria – *Erwinia amylovora*) disease have been achieved in apple protoplasts (Malnoy et al., 2016; Pompili et al. 2020). This could potentially allow for the generation of disease-resistant plants.

3.4 Rapid breeding in fruit trees

It can take more than 20 years to get a new apple variety to market, therefore shortening the juvenile stage has been the subject of intensive research (Flachowsky et al., 2007). GE has been used to delete an apple gene to produce an early flowering phenotype (Kotoda et al., 2006). This would allow rapid breeding of new cultivars through several cycles, after which the edited gene could be crossed out to restore the non-engineered flowering phenotype without any trace of the modification. This process is not only applicable to fruit trees but is also relevant to productive forestry species (Pers. Comm. Richard Buggs, Kew).

3.5 Cisgenics

Research on cisgenics in fruit trees has also been carried out. For example, Kost et al. (2015) produced a cisgenic apple line using a gene from wild apple, which was significantly more resistant to fire blight (*Erwinia amylovora*). In addition to fire blight, cisgenic apple scab (caused by *Venturia inaequalis*) resistant apple lines have been produced in this way (Chizzali et al., 2016).

4 Horticulture

GE research in ornamental horticulture is yet to gather momentum, and only a few studies using GE have been reported in ornamental plants. Species under examination include roses (Raymond et al., 2018) and chrysanthemums (Su et al., 2019). This lack of take-up is perhaps due to the wide range of species available to horticulture, i.e., if a species is being grown and a disease causes a significant loss, the grower can change to another species rather than invest in new technologies to solve the problem. Not many species are profitable enough to warrant significant investment in new gene technologies. In addition, ornamental species are often grown in carefully controlled automated systems where pests and diseases can be successfully

managed, including with the use of fungicides. There are several significant turfgrass diseases that impact on sports and amenity sites and cost money to manage (Vargas, 2018). There could, therefore, be the potential to use GE to make turf more resilient to pests and diseases, thereby reducing reliance on chemical controls.

5 Natural environment

Managing pests and diseases in the natural environment is challenging because of the distribution of the species involved, the different management practices employed by landowners, and the natural processes that take place. Deploying GE into this system is complicated because the approach would require that the GE-manipulated gene spreads through a natural or semi-natural landscape. This is in contrast with agriculture where the genetic changes are contained within the crop.

GE research has so far concentrated on short-lived crop species in tightly controlled systems (e.g., agriculture). The gene changes in these studies are likely to be tightly controlled and in Scotland, with few crop relatives, these changes would have a low likelihood of spread to species outside of the target crop. Conversely, if GE was used on a species to improve disease resistance in the natural environment or on a species such as a turf grass, with close wild relatives, genetic changes would be required to help new trait spread naturally through wild populations once they were introduced. For example, if resistant ash trees were produced through GE and placed into the natural environment, the genetic changes would need to spread through the existing ash population for wider ash resistance to be increased.

Research in this area in the UK and Europe is very much in its infancy, possibly because current regulations prohibit deliberate release even in experimental setting. If this type of research is to get underway, a revised regulatory framework would need to consider the appropriateness of such deliberate releases.

6 Existing international regulations for GE governance

As discussed above, new GE technologies make it is possible to make small, targeted changes to a plant genome without having to insert foreign DNA into the gene. This means that GE (which may include cisgenics), unlike transgenics (defined in this report as akin to GMO), is seen as equivalent to traditional breeding techniques. As a result, this has intensified the debate as to whether the existing GMO regulations do and should apply to GE and other new breeding techniques.

6.1 European policy

The European GMO Directive 2001/18/EC does not prohibit the cultivation of GMO crops but does regulate the release of GMO crops into the environment. The licencing procedure in place aims to ensure a high level of protection to the health and wellbeing of animals and the environment (EU, 2001). Crops bred with conventional mutagenesis methods are exempt from the Directive but still require tests for distinctness, uniformity and stability (DUS-testing), and for value to cultivation and use (VCU) (APHA, 2014; APHA, 2015).

Some agrochemical and plant breeding companies, and many research organisations, have argued that GE can and should be viewed as a modern form of mutagenesis. Mutagenesis is exempt from the GMO Directive, so it could be argued that new GE techniques should also be, so long as no foreign DNA is present in the end product (Macnaghten & Habets, 2020), i.e., it is the product that should be regulated rather than the process.

On 29 April 2021, the European Commission published a study regarding the status of New Genomic Techniques under Union law. It concluded that EU legislation on genetically modified organisms should be updated to allow for the use of targeted GE in crops (European Commission, 2021). This has been welcomed by industry and researchers, but it is likely to take some time to produce new regulations (Zubaşcu, 2021).

6.2 International examples of GE regulation

Europe is not alone in its attempts to clarify the regulations for gene technologies. The United States, Australia, New Zealand and Japan are also tackling this complex issue.

6.2.1 United States

The US Department of Agriculture (USDA) revised its biotechnology regulations by promulgating the Sustainable, Ecological, Consistent, Uniform, Responsible, and Efficient (SECURE) rule (Hoffman, 2021). Specifically, the SECURE rule 1) establishes exemptions for plants modified by genetic engineering where the modification could otherwise have been made through conventional breeding, 2) uses risk posed by the introduced trait to determine whether an organism is regulated, rather than relying on how the organism was developed, and 3) provides a mechanism for a rapid initial review.

6.2.2 New Zealand

In New Zealand, the government has decided that all GE applications are regulated according to the national biosafety framework (Eckerstorfer et al., 2019). This means that GE is considered to be genetic modification and is subject to an approval process under the Environmental Protection Authority (EPA). This process requires decision makers to consider Māori perspectives (Hudson et al., 2019).

6.2.3 Australia

In contrast to New Zealand, Australia has opted not to subject GE techniques to the Gene Technology Act 2000 provided no new genetic material is introduced (Mallapaty, 2019). However, with specific regards to GE and foods, Australia is still considering how to regulate.

6.2.4 Japan

Japan will not regard organisms as Living Modified Organisms (LMOs) if they don't contain remnants of inserted nucleic acids (DNA or RNA). However, information must be submitted to the relevant authorities (and to be made public, bearing confidentiality considerations) on aspects that include the method used, the trait changed, the modified gene and its function,

and a discussion of the possible influence on biological diversity when the organism is used (Ministry of the Environment, 2018). The Japanese government are considering a case-by-case approach for GE technologies used in food production, i.e., whether a notification or safety assessment is required. GE products intended to be placed in the market need to undergo a prior consultation (Ministry of Health, Labour, & Welfare, 2019).

6.2.5 The Norwegian Gene Technology Framework

The Norwegian Biotechnology Advisory Board has set out a progressive regulatory framework aimed at harnessing the potential of GE (and future technologies), while at the same time protecting health and the environment, and promoting societal benefit, sustainability and ethics (Figure 6) (Bioteknologirådet, 2018). The Norwegian approach is seen by many as a good example of a gene technology framework because it stipulates that plant production through gene technologies is done in an ethical and societally responsible manner, in accordance with the principle of sustainable development and without harmful effects to health and the environment. Broader socio-economic and sustainability considerations have thus been integrated into a biotechnology regulatory framework (Macnaghten & Habets, 2020).

Specifically, the approach describes several levels based on the manner of the genetic change:

- **Level 0** – Organisms with temporary, non-hereditary changes. For certain types of organisms, genetic material has been used during parts of the production process without causing permanent changes in the final product, and thus could be exempted from the Gene Technology Act based on the proposed criteria.
- **Level 1** – Organisms with changes that correspond to those achieved by conventional methods. A notification to the relevant authorities would be sufficient.
- **Level 2** – Other genetic changes within the same species that could not be achieved using conventional breeding methods (e.g., removing large DNA segments). These would be subject to an expedited risk assessment and approval requirement.
- **Level 3** – Organisms with permanently added genetic material from different species or synthetic (not naturally occurring) DNA sequences (transgenes). In cases where new DNA is permanently added to an organism, either from other species or synthetic DNA sequences (which do not naturally exist), the current GMO regulations and requirements for approval and impact assessment should be used.

7 Conclusion

This paper provides many examples of where GE research on pest and disease resilience could be focussed on Scotland. To date, of all sectors, agriculture has been the main beneficiary of GE approaches due to the importance of food security. However, GE could be utilised across a wide variety of applications throughout all sectors in Scotland should there be willingness to do so. It is therefore important that agricultural applications are considered but that horticulture, forestry and the natural environment sectors are not left behind. Work on understanding plant genomes and how they interact with their environment should continue across all sectors so that opportunities can be taken to increase the resilience of important species as GE technologies develop. Critical to the advancement of GE technologies in

Scotland will be the development of a new governance framework. This framework will need to provide clarity to all stakeholders on Scotland's direction of travel so that investment can be made with confidence, focussing on the safety of different technology as well as their potential economic advantages.

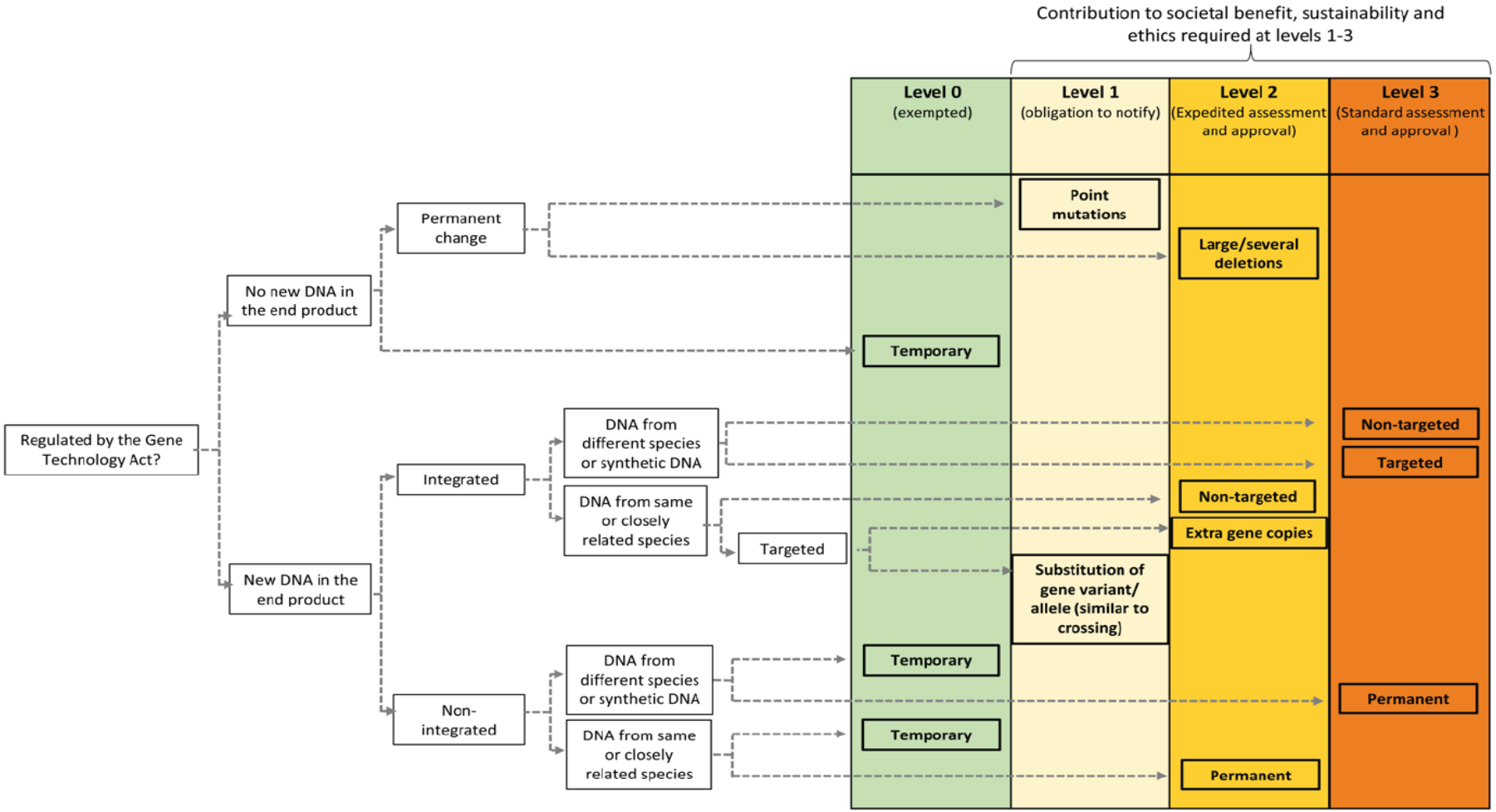


Figure 6 - Example of a level-based model which is based on genetic change (from Bioteknologirådet. (2018).

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9 Glossary

Backcrossing – A breeding method used to move one or a few desirable genes from an agronomically poor crop line to an elite line.

Cas – Abbreviation for "CRISPR Associated protein". There are numerous Cas proteins with various functions: Cas9 is an enzyme that cuts specific sites in DNA.

Cisgenics – A term for organisms that have been engineered using a process in which genes are artificially transferred between organisms that could otherwise be conventionally bred.

CRISPR – Acronym for "Clustered Regularly Interspaced Short Palindromic Repeats." A segment of DNA involved in the defence mechanisms of prokaryotic organisms to viruses, which can be used as a genetic engineering tool along with its associated protein (Cas) to edit a gene.

DNA – Acronym for "deoxyribonucleic acid". DNA encodes the heritable genetic information for an organism.

Durable resistance - long-lasting resistance that has a reduced chance of being overcome by the pathogen.

gRNA – Acronym for "Guide RNA". A two-piece molecule that Cas9 binds and uses to identify a complementary DNA sequence. Scientists have also formed a version of the guide RNA that consists of a single molecule, the single-guide RNA (sgRNA).

Genes – The regions of DNA that encode the physical and inherited characteristics of an organism.

Genetic Modification (GM) – Altering the genetic composition of an organism by the insertion of a new gene encoding a desired protein that is expressed. The resulting organism is known as a genetically modified organism (GMO).

Genome – The complete set of genes or genetic material present in a cell or organism.

Genomics - The branch of molecular biology concerned with the structure, function, evolution, and mapping of genomes.

Genome editing (GE) – Intentionally altering the genetic code of a living organism. Can be done with ZFNs, TALENs, or CRISPR. These systems are used to create a double-strand break at a specific DNA site. When the cell repairs the break, the sequence is changed. Can be used to remove, change, or add DNA.

Genotype – The genetic constitution of an individual organism.

Hybrid breeding – The cross breeding of two genetically different parental lines.

Inbreeding – Breeding of plants more closely related than the average relationship within the population.

IPM – Integrated pest management.

Introgression breeding - A crop species that contains genetic material artificially derived from a wild relative population through repeated backcrossing.

Knock-out mutations – To mutate the DNA in a way that stops the gene's expression permanently.

Marker-assisted selection - An indirect selection process where a trait of interest (e.g., productivity, disease resistance, abiotic stress tolerance, and quality) is selected based on a marker (morphological, biochemical or DNA/RNA variation) linked to a trait of interest rather than on the trait itself.

Mutagenesis – The production of genetic mutations.

Mutation – A change in the nucleotide sequence of an organism's genome.

Mutation breeding – The process of exposing seeds to chemicals, radiation or enzymes in order to generate mutants with desirable traits for breeding with other cultivars. Plants created using mutagenesis are sometimes called mutagenic plants or mutagenic seeds.

Natural variation – The within-species phenotypic variation caused by spontaneously arising mutations that have been maintained in nature by an evolutionary process.

Nucleotide – The building blocks of DNA or RNA.

Phenotype – The set of observable characteristics of an individual resulting from the interaction of its genotype with the environment.

PPP – Acronym for 'Plant Protection Products'.

Progeny – A descendant or descendants of a plant.

RNA – Acronym for "ribonucleic acid". There are several forms of RNA, including messenger RNA (mRNA) which conveys the genetic information from genes (encoded by DNA) to proteins (encoded by amino acids).

Resistance – The ability to prevent or reduce the presence of diseases in otherwise susceptible hosts.

Resistance genes (R-Genes) – Genes in plant genomes that convey plant disease resistance against pests or pathogens by producing R proteins.

Susceptibility genes (S-Genes) – A natural gene in and used by a plant which may also be exploited by a pathogen to aid infection.

sg/RNA – Abbreviation for "Single Guide RNA". Adaptation of the bacterial CRISPR-Cas system for genome editing purposes.

TALEN (Transcription activator-like effector nuclease) – A genetic engineering tool wherein one portion of the protein recognizes a specific DNA sequence and another part cuts DNA.

Tolerance – Plants that exhibit little disease damage despite substantial pathogen levels, e.g., when a crop maintains yield in the presence of a pest or disease.

Trait – A distinct variant of a phenotypic characteristic of an organism.

Transformation - the process by which exogenous DNA is transferred into the host cell.

Transgenic – When one or more DNA sequences from another species have been introduced into an organism by artificial means.

ZFN (Zinc-finger nuclease) – A genetic engineering tool wherein one portion of the protein recognizes a specific DNA sequence and another part cuts DNA.

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