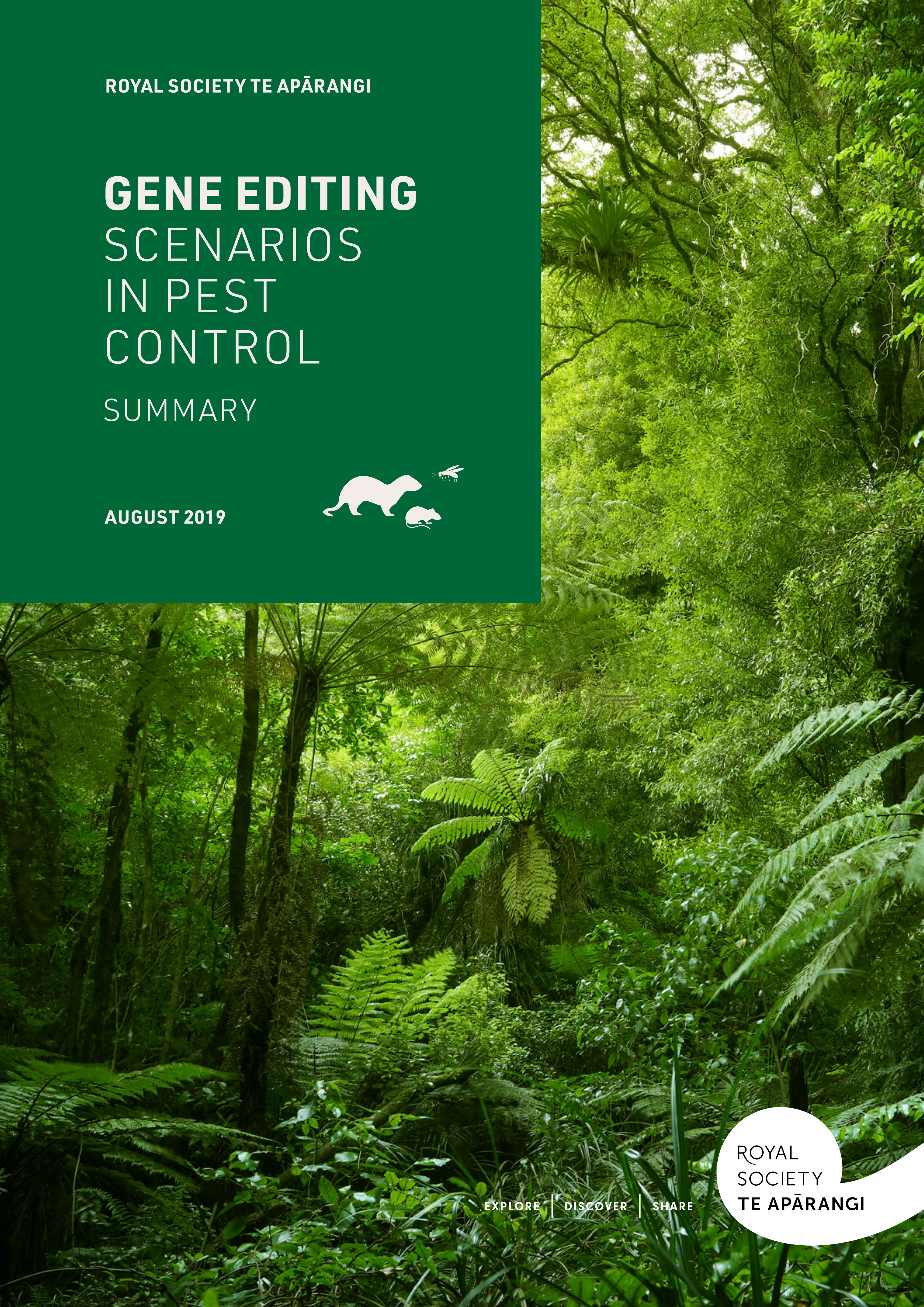
ROYAL SOCIETY TE APĀRANGI

GENE EDITING SCENARIOS IN PEST CONTROL

SUMMARY

AUGUST 2019



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ROYAL SOCIETY TE APĀRANGI

INTRODUCTION

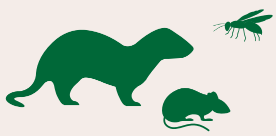
The revolution in gene editing technologies is making it easier to change genetic material with potential benefits in many sectors, including healthcare, agriculture and conservation. However, as a technology, gene editing is moving ahead of any consensus on how it should be used.

Royal Society Te Apārangi convened a multidisciplinary panel to consider the social, cultural legal and economic implications of gene editing in Aotearoa New Zealand, incorporating Māori perspectives and broader cultural contexts.

To help you consider the potential use of gene editing for pest control in New Zealand, this paper highlights three scenarios of using gene editing to create gene drives to control three types of pests:

- wasps
- possums
- rats and stoats.

The characteristics of all living organisms are determined by their genetic material, or DNA.



WHAT IS GENE EDITING?

The characteristics of all living organisms are determined by their genetic material, or DNA. Genes are segments of DNA which provide the code for particular functions or characteristics.

Normally, when one strand of DNA is cut or damaged, it is repaired by enzymes which use the information in the other strand as a template. Gene editing uses this process but provides new repair information to change the DNA strand. By editing genes it is possible to make changes to organisms, such as changing the version of a gene from one that causes disease to one that does not.

A technique called CRISPR has increased the speed, ease and accuracy of gene editing. Modified from a system found in bacteria to cut up invading virus DNA, CRISPR is much more precise than earlier gene editing techniques. However, this ability to edit genes is, in many cases, ahead of our understanding of everything that different genes do, resulting in the possibility of unintended effects.

HOW COULD GENE EDITING BE USED FOR PEST CONTROL?

Gene-editing tools have not been used to date in the conservation of wildlife, but their use in the control of non-native invasive organisms is being explored in the laboratory with the creation of sterile insects, and the use of 'gene drives'.

In 2015, researchers demonstrated how CRISPR could be used to develop gene drives, where edited genes 'drive' themselves and nearby genes through populations of organisms over many generations. In normal sexual reproduction, offspring inherit two versions of every gene, one from each parent. Each parent carries two versions of the gene as well, so chance (50:50) normally governs which particular variant of the gene that will be passed on. Gene drives ensure that the genetic changes will almost always be passed on, allowing that variant to spread rapidly through a population.

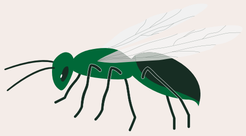
So far, gene drives are being developed in yeast, the fruit fly, mice, and two mosquito species, and could be used to drive a naturally occurring, or introduced, gene for sterility through a population.

SCENARIO ONE

INVASIVE WASPS IN NEW ZEALAND

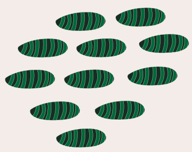
SPECIES

Vespula wasps



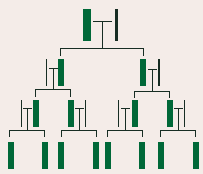
GOAL

Reduce fertility



CELL TYPE TARGETED

Germline cells (hereditary)

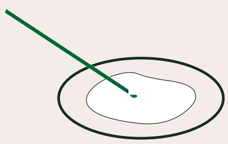


GENE EDIT

Gene switched off

MECHANISM

Embryo direct injection



OUTCOME

Pest numbers reduced

Environmental

Invasive wasps predate on native species such as caterpillars and spiders.

Technical / scientific considerations

Genetically modifying wasps has not been done before.

Legal considerations

Release of wasps with gene drives would require approval by the Environmental Protection Authority, under HSNO Act.

Ethical considerations

Risk that altered wasps could find their way back to Europe.

Two social (*Vespula*) wasps have been accidentally transported to New Zealand and become established here.

- The common wasp was first recorded in New Zealand in 1921 and became abundant in the 1970s.
- The German wasp became widespread and abundant in New Zealand after a major incursion in 1945.

They are both now distributed throughout New Zealand, with the common wasp as the dominant social wasp in beech forests.

The world's highest recorded densities of these wasps are observed in New Zealand, with up to 40 nests per hectare. Densities of workers have been observed to exceed 370 wasps per square metre of tree trunk.

The biomass of these wasps in honeydew beech forests has been estimated as similar to, or greater than, the combined biomass of birds, rodents and stoats. Their large densities exert intense predation pressure on native invertebrates. The direct economic impacts of wasps are largely associated with their predation of bees and associated hive robbing, with flow-on effects associated with lower rates of pollination in nitrogen-fixing clovers, which are important for the productivity of New Zealand pastures. In 2015, approximately 20% of beehive losses in the North Island were due to wasp attack.

Effective wasp control options currently are limited to small-scale operations involving pesticides or other chemicals (e.g. petrol). The use of toxins over large areas such as the 1 million hectares of beech forest currently overwhelmed with huge wasp numbers, is untenable. Prior attempts at biological control have been unsuccessful.

The development of a gene-drive to spread an infertility gene within the wasp population could be an additional tool that could be used to dramatically reduce their numbers.

Technical / scientific considerations

This has not been done before. It would require genetic changes, including the insertion of a CRISPR sequence into the genome of common or German wasps. Suitable genes for sterility would need to be identified.

Genetic modification of honeybees has been carried out, and given the similarities of social wasps and bees, it seems likely that this would be possible.

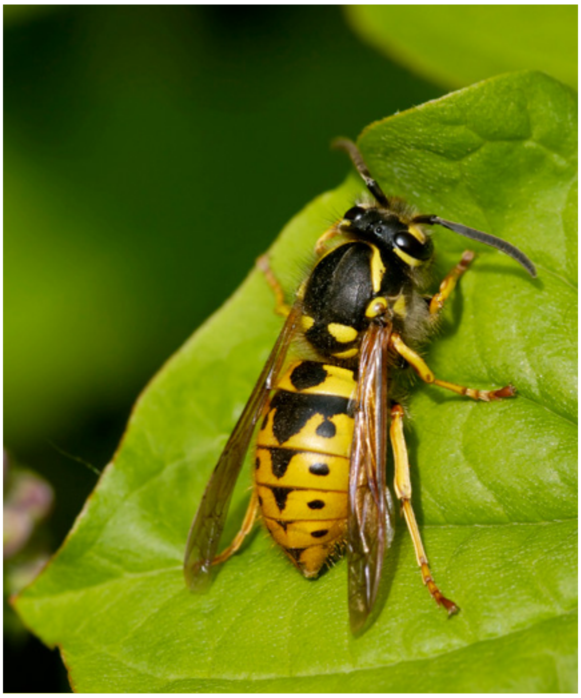
Wasps have a division of labour dependent upon whether they are reproductive or not. These features may have significant, unknown consequences for the inheritance of a gene drive system. In addition, over time resistance to the gene drive could develop in the wasp population, reducing its impact on their population.

Legal considerations

Inputs and outputs of gene drive techniques will be regulated by the Hazardous Substances and New Organisms Act (HSNO Act) if they come within the definition of an 'organism' and 'new organism' in this Act.

'Organism' is widely defined in the Act and includes a genetic structure (other than a human cell) that is capable of replicating itself. The definition of 'new organism' includes organisms belonging to species that were not present in New Zealand prior to July 1998 and Genetically Modified Organisms (GMOs).

The definition of a GMO is very broad (organisms whose genes or genetic material have been modified by *in vitro* techniques). Genetically modified animals are defined as new organisms under the HSNO Act, and therefore gene edited wasps would be classified as 'new organisms'.



Ethical considerations

While *Vespula* wasps in New Zealand are a critical pest, in their native European home areas they are valued and important components of the ecosystem.

Social wasps were not introduced deliberately to New Zealand, but have hitchhiked here, presumably in imported cargo. Given this route of introduction, any gene drive system must take into account the possibility that gene edited wasps might be transported to regions where these wasps are valued.

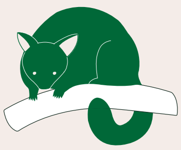
For Māori, considerations relate to various Māori values including whakapapa (of the organism, as well as the relationship/kinship between humans and other species), tika (what is right or correct), manaakitanga (cultural and social responsibility/accountability, for example to other nations who value wasps), mana (justice and equity), tapu (restrictions), kaitiaki (guardianship) and whanaungatanga (valuing and supporting whānau).

SCENARIO TWO

BRUSHTAIL POSSUM IN NEW ZEALAND

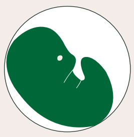
SPECIES

Brushtail Possum



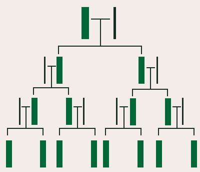
GOAL

Reduce fertility



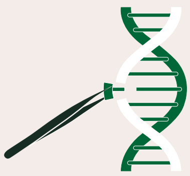
CELL TYPE TARGETED

Germline cells (hereditary)



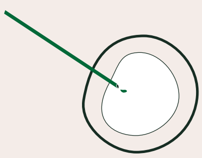
GENE EDIT

Gene switched off



MECHANISM

Egg cell direct injection



OUTCOME

Pest numbers reduced

Environmental

Possums are New Zealand's most significant mammalian pest.

Technical / scientific considerations

Genetically modifying possums has not been done before.

Legal considerations

Release of possums with gene drives would require approval by the Environmental Protection Authority, under HSNO Act.

Ethical considerations

Non-lethal means of pest control. Risk that altered possums could find their way back to Australia.

Perhaps New Zealand's most significant mammalian pest is the brushtail possum. This marsupial was first brought to New Zealand from Australia in 1837 with the aim of setting up a fur industry.

In New Zealand, the possum found an environment with few of the challenges of Australia and grew to plague proportions.

The possum eats plant matter, native birds and invertebrates, and is a carrier for bovine tuberculosis, and thus possum control is carried out for conservation and agricultural purposes.

Possum control costs the New Zealand government approximately $110 million/year, much of this spent on aerial distribution of poison baits. Other approaches, such as traps and bait stations, are also used. These methods are effective when animals are at high densities but become less effective as densities drop.

Gene drives and other genetic solutions may provide an opportunity to add another tool to the pest control 'toolbox' to achieve national eradication.

Technical / scientific considerations

Over the last twenty years knowledge of possum reproduction and genetics has increased.

One key challenge is the ability to genetically change the organism, a feat never achieved in a marsupial. To do so would require the generation of reasonable quantities (hundreds or thousands) of immature egg cells. Techniques for superovulation and implanting embryos into possums have been developed as part of a reproductive control approach to possums, and could be used to generate egg cells for manipulation.

If genetically changing possums were possible, there would be a need to identify what genes or processes should be targeted for a gene drive system. Little is known about functional genetics in marsupials. Several marsupial genomes have been sequenced, providing a resource for further genetic work, but understanding the function of marsupial genes is only making slow progress.

Over time, resistance to the gene drive could develop in the possum population, reducing its impact. The use of gene edited possums for gene drives to control wild possum populations would require very large numbers of altered animals to be bred and released (between 1 – 10% of the wild population).

Legal considerations

As for wasps, genetically modified animals are defined as new organisms under the HSNO Act, and therefore possums containing gene drive would be classified as 'new organisms'. As with wasps, risk assessments of organisms produced through gene drives are carried out under the provisions of the HSNO Act on a case-by-case basis by the Environmental Protection Authority.

Ethical considerations

From the perspective of the individual animal, some may argue that it has a fundamental right to respectful treatment, while others could argue that ecosystems and species have value in themselves and ought to be protected, even if it means violating the rights of individual animals to do it. Much hinges on the ecological impact of the removal of the pest animal.

One area of concern is around the control and containment of a possum gene drive. In Australia, brushtail possums are a protected species and an important part of many Australian ecosystems, so the spread of a gene drive that reduced possum fertility there would be most unwelcome.

To avoid such an incident we may require the means to turn off a gene drive, possibly through the introduction of a resistance gene, or the use of a 'daisy-chain' gene drive that runs out after a number of generations. However, the development of evolutionary resistance to a gene drives would also serve to diminish its impact over time.

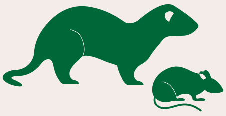
For Māori, the ethical considerations would be similar to the previous scenario: whakapapa, tika, manaakitanga, tapu, whanaungatanga and mana. Implicit in those considerations would be the question of who stands to benefit from the introduction of a gene drive in this scenario; what the risks are to the ecosystems of other nations; and where Māori accountabilities lie in terms of the outcomes. There are also economic considerations: some Māori (and non-Māori) currently obtain income from possum control and/or fur sales. Such benefits will need to weighed against other outcomes, and are a potential consideration for Māori whose whānau are engaged in such activities (whānaungatanga).

SCENARIO THREE

STOATS AND RATS IN NEW ZEALAND

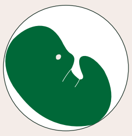
SPECIES

Stoats and rats



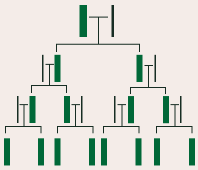
GOAL

Reduce fertility



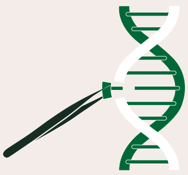
CELL TYPE TARGETED

Germline cells (hereditary)



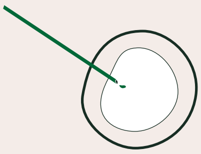
GENE EDIT

Gene switched off



MECHANISM

Egg cell direct injection



OUTCOME

Pest numbers reduced

Environmental

Rats and stoats predate on native species, such as birds.

Technical / scientific considerations

International efforts exist looking into rat gene drives, but less known for stoats.

Legal considerations

Release of rats and stoats with gene drives would require approval by the Environmental Protection Authority under HSNO Act.

Ethical considerations

Non-lethal means of pest control. Risk that altered rats and stoats could find their way back to Europe.

Stoats are ferocious predators that do significant damage to many of our native bird populations, and have contributed to the extinction of five native species. There are three rat species in New Zealand: the ship or common rat, the Norway or brown rat and the Polynesian rat or kiore. Of the three, the ship rat is of greatest conservation concern, but they all predate native species

These pests are controlled in many different ways depending on the target species, including the widespread use of 1080 poison (sodium fluoroacetate), a metabolic poison most effective against mammalian pests. The use of this toxin remains controversial in some sections of the community, however, it is relatively cheap and able to be distributed from the air, providing a pest control tool for the rugged, heavily forested terrain that makes up much of New Zealand's conservation estate.

Other pest control measures include innovative new approaches to trapping, and the development of self-resetting traps. Current pest control measures are relatively expensive and take a lot of planning. Gene-drive solutions could provide another avenue for pest control.

Technical / scientific considerations

While New Zealand researchers have spent decades understanding the ecology, reproduction and, more recently, the genetics of possums, we are less well informed about many of these key issues for stoats.

One potentially promising avenue to explore is to harness the significant efforts made in understanding the reproduction and genetics of mink, a species valued for its fur, that is farmed in parts of the Northern hemisphere.

Unlike possums and stoats, rats are global pests and active efforts are underway to tap into international initiatives now aimed at establishing gene drive methods for the control of invasive rodents.

Rats are one of the best-studied mammals, so there is no shortage of knowledge on reproduction or genomics, although most of this knowledge comes from the Norway rat, a well-established model animal studied in laboratories that was among the first mammals to have its complete genome sequenced. Less is known about the ship rat, although it has just had its genome sequenced by a New Zealand team.

As with possums, the use of gene drives to control wild populations of rodents and stoats would likely require the breeding and repeated release of very large numbers of altered animals over large areas.

Legal considerations

As for wasps, genetically modified animals are defined as new organisms under the HSNO Act, and therefore stoats and rats containing a gene drive would be classified as 'new organisms'. As with wasps, risk assessments of organisms produced through gene drive are carried out under the provisions of the HSNO Act on a case-by-case basis by the Environmental Protection Authority.

Ethical considerations

Gene drives offer a control method that is less harmful at an individual level than conventional pest control methods, which usually involve killing the animal. However, this is dependent upon being as harmless as possible in its effects on any ecological changes the gene drive brings.

Globally, while rats are pests in many contexts, they are also important providers of key ecosystem services such as pollination or as critical elements of ecosystem food webs.

Eradicating rats in New Zealand, where our ecosystems were free of rodents up until human arrival around 800 years ago, may have few knock-on effects. However, in other parts of the globe the effects on natural systems might be very different. Rats are very good invaders, disperse well, and hybridise with closely related species, making accidental release and spread of gene drive modified rats a serious consideration.

Similarly, stoats are an important animal in northern European ecosystems, so even the prospect of such an incident will mean the need for a means to turn off any gene drive.

The key ethical considerations for Māori in this scenario will overlap with those in the previous scenario, with the exception of the kiore, which for some iwi at least, is a taonga. As such, the kiore has a whakapapa (relationship) involving humans that predates European arrival and thus is of significance for Māori. Efforts to eradicate this particular species would not be accepted by at least some hapū and iwi.

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For further information on the use of gene editing in pest control, a reference paper on the topic prepared by the Panel is available from the Royal Society Te Apārangi's web page along with links to a panel discussion chaired by RNZ's Kim Hill: **royalsociety.org.nz/gene-editing-pests**

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