**Should gene drives be considered a conservation strategy in New Zealand?**

***For instructors:*** *The goal of this case study is for students to evaluate both the biology and ethics behind the use of synthetic genetics and gene drives to potentially solve a conservation problem. Currently, this is the most realistic proposal that involves genetic manipulation of a vertebrate animal. Some questions do not have a single correct answer, but logical suggestions are detailed below (in italics). The IUCN concluded that each proposal will have its own benefits and risks, and the technology should not be reviewed as one technique, but as individual applications. Hopefully, the students will reach a similar conclusion and discuss the pros and cons of this approach. (The presentation should be delivered prior to handing out the case study and be made available for reference).*

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**Overview**

One of the best detailed proposals to use gene drives for conservation purposes suggests using this technology to exterminate non-native, European rats (*Rattus rattus* and *Rattus norvegicus*) from New Zealand. New Zealand is a very unique land mass, as it has no native species of mammals except for bats. Therefore, many species - including plants, reptiles, insects, and bird - have declined dramatically due to herbivory and predation by introduced rats, stoats, and possums. In particular, New Zealand has a very rich avifauna - including such birds as the forest-dwelling parrot (kakapo), kiwi, and many others (Fig. 1) - some of which have only been saved from the brink of extinction due to captive breeding and release on mammal-free, offshore islands. While stoats and possums also pose a significant threat, these are less acceptable targets of genetic manipulation due to more limited genetic sequencing and their importance to other ecosystems. For example, the species of possum that is invasive in New Zealand is protected in Australia, and accidental escape of genetically modified individuals to this nearby continent could be devastating. In contrast, rats are commonly used as a laboratory species and are invasive in many parts of the world.

The purpose of this case study is to discuss the benefits and costs of using this technology to restore the altered ecosystem of New Zealand. One of the reasons we focus on New Zealand is due to a large initiative called “Predator-Free 2050” which was initially started as a lobby group by Les Kelly. Kelly lived abroad for many years before returning to New Zealand. He was struck by the huge decline of birds within the span of his own lifetime. As the idea won support from conservation biologists, the government, and the public, it has caught on as a goal to restoring some of the former ecology of the country by the year 2050.

**Proposed use of gene drives to eliminate rats**

Two types of gene drives have been proposed to eventually eliminate populations of rats. One is a gene drive to turn all offspring into females (all gametes will possess an X chromosome), which should lead to a skewed sex ratio and eventual local extinction of populations. Another proposed mechanism is to reduce fertility in homozygous female offspring (gene drive depicted in the presentation), which again would cause populations to decrease. These mechanisms first spread the gene drives and then causes reduced population growth within generations (both are “daisy-chain gene drives”, which are explained in more detail below).

**Risk: If local release becomes global invasion:**

1. What happens if these genetically modified rats escape to different parts of the globe?

*One threat is the extirpation of native populations in other countries, in which they play an important role in the ecosystem. Other human communities have not approved this technology and may not be in favor of it - which could be seen as an infringement of rights.*

2. Rats have not been studied as species of conservation-concern. But what do you think ecological effects of complete extermination would be in areas where they are native?

*Extirpation could cause ecosystem-level effects. Rats may provide food sources to other mammals. Rodents have been shown to be important as seed dispersers. Alternatively, the impacts may not be severe, if other rodents in those areas perform similar ecological roles.*

3. In sexually-reproducing species, how are the effects of gene drives different from the introduction of a genetically-modified animal without the use of gene drives?

*Gene drives are self-perpetuating and the gene of interest is passed on to all the offspring. If a genetically-modified animal (without the use of gene drives) mates with a normal animal, only half of the modified genes would be expected to be passed down to the offspring.*

4. Given many of these risks, why might New Zealand be a good place for the release of gene-drive engineered rats?

*New Zealand is an island, so it is easier to contain a genetically-modified organism.*

**Proposed safe-guards:**

Currently, New Zealand has closely-monitored safe-guards against importation of invasive species. These safe-guards were not in place in the past, when many of these mammals were intentionally or accidentally introduced. The IUCN (International Union for the Conservation of Nature) report on this project suggests that these safe-guards can also be used to limit exportation of potentially invasive species as well. However, two of the experts of gene drive technology in this example also note that there are economic incentives for smuggling engineered rats to different parts of the world for rodent control, as these same two species are introduced/seen as pests in large parts of the world.

A second safe-guard has been proposed by Esvelt, which are called “daisy-chain gene drives” and are self-limiting gene drives. For example, a gene C would drive (or perpetuate, via CRISPR/CAS) a gene B, which drives a gene A. Gene A produces the phenotype, but does not have its own gene drive. After multiple generations, these gene drives should die out. This happens because gene C does not drive, or perpetuate itself - and is eventually lost. As C is lost, gene B will also be reduced and eventually lost in the population, with the same thing happening to A as B is lost.

1. How do you think mutations might affect the gene-drives and daisy-chain gene drives?

*Mutations in general, might cause gene drives to not work properly. For example, loss- of-function mutations in any one of the three genes would not lead to the expected phenotype spreading throughout the population. Other possible answers: Mutations could cause unexpected changes to be driven into the population. Other genes might become linked to the drives and also become fixed in the population.*

2. Many models of spread of gene drives include the idea of panmixis (i.e. complete mixing of a population). Can you think of reasons why a rat population might not be in panmixis, as barriers to gene flow or mate-selection?

*Rats are small and geographic barriers (rivers, mountains, etc.) would be obstructions to gene flow. Roads with high traffic may limit gene flow. Rats may also inbreed within family group, also reducing gene flow. Some rats favor human establishments, so gene flow may actually be limited across large expanses of natural areas.*

3. If there are barriers to gene flow, do you think the gene drives would spread more quickly or die out more quickly?

*They would spread more slowly. Multiple introduction of manipulated rats might be needed for population sizes to shrink.*

4. If gene drives die out too quickly, can you think of an argument against their use in eradicating a species?

*This technology might be more expensive than other means of control. Public opinion might change if gene drives do not work as well as promised.*

**Reducing widespread application of rodenticide**

Currently, rats and other invasive mammals are controlled by various means, but include the widespread application of toxic chemicals. These are also toxic to pets and livestock.

1. How might gene drives be considered more humane than poisoning live animals?

*Gene drives reduce fertility, but do not kill adult animals. Gene drives would also reduce accidental poisoning of non-target mammals.*

2. Do you think the risks (stated so far) outweigh the benefits of potentially saving species from extinction and reducing pollution?

*Yes: Gene drives seem humane and clean. We have an ethical obligation to reverse risks of extinction that humans have caused.*

*No: Gene drives are too risky. Humans should not change the genomic signature of a species. We cannot risk the chance of causing the complete extinction of one species that happen to be invasive in some parts of the world.*

**Communities (including indigenous communities) rightfully feel skeptical about new technology being used for conservation**

Humans - especially from industrialized nations - have a bad track record in biocontrol and causing more harm than good in the name of economic or environmental benefits. Examples include the introduction of cane toads to Australia to limit pests in sugar fields. Cane toads outcompete some native species, are toxic to native predators, and spread disease. In fact, stoats and possums were intentionally introduced to New Zealand to limit introduced rabbit populations and as part of the fur industry, respectively. Finally, the use of genetically modified crops has been criticized in some regions as disenfranchising local communities, leading to an increase in monocultures, poor local nutrition, and widespread application of herbicides.

In New Zealand, the Maori (native population of Polynesian descent) have lived in New Zealand for roughly 800 years and have a strong ethic for preservation of the land. Luckily, open forums about the clear problem of invasive mammals and the risks of genetic modification have led to thoughtful debates, and some community support, mixed with concern and a cautionary view towards conservation. Esvelt and Gemmel (2017) specifically address the importance of open conversation and only using this technology with approval of the local communities in New Zealand.

1. As part of the local community, what might some of your concerns be about the release of gene-drive rats?

*This is just another release of a non-native species. Unpredictable ecological ramifications may occur - such as a disruption to predator-prey relationships, increased populations of stoats, etc.*

2. The kiore rat (*Rattus exulans*) was brought to New Zealand by Maori people and is culturally important. While it might still be considered a threat to some native species, this species of rat is relatively localized in the southern parts of the South Island and causes much less damage than the two more common species. Do you think hybridization with the other species and spread of gene drives could negatively affect these small populations?

*Hybrids of most species of mammals are not fertile, and therefore would not spread the gene drive. Studies should be done on interbreeding among all three species, to rule out a risk to the kiore. Gene drives may actually benefit the kiore, if less rodenticide poisons are spread on the landscape.*

3. One worry is that this new technology will be seen as a “cure” to species extinctions and more traditional conservation strategies, such as preserving habitat and land stewardship, will no longer be emphasized. Do you agree or disagree with this sentiment?

*Agree: usually there is limited money for conservation. It might make more sense to continue with trapping rodents and also fund other types of land conservation. Public sentiment might also stop favoring more traditional conservation.*

*Disagree: New Zealand has a good track record for caring about conservation and Maori culture also favors land stewardship. I do not think the additional use of genetic manipulation will change that sentiment. New Zealand also has strong tourism industry, due to natural features and unique species: there is also economic pressure to preserve the ecosystem.*

**Pro/Con: What is our ethical obligation?**

Finally, two other questions emerge from this debate. These are entirely based on your opinion/world view:

1. Is it ethical to fundamentally change an organism?

*Various answers.*

2. If we have the means to save species that we, as humans, have driven to the brink of extinction, is it not ethical to use technology and science to reverse those extinctions?

*Various answers.*

**Regulations**

While the IUCN reviewed the potential use of gene drives for conservation, they proposed a cautionary look at this new technology, the need for new regulations (beyond those now in place for agricultural genetically modified organisms), the need for international as well as national agreements and laws, and the review of proposals on a case-by-case basis. In short, all biological and ecological effects cannot be predicted, but the hope is that scientists can use lessons learned in the past from both failed and successful manipulation of the ecosystem to use this technology only with great care and full community support.

**Read more here (click on links or ask your instructor for these resources):**

**Websites (Predator Free 2050):**

<https://predatorfreenz.org/big-picture/pf-2050-vision/>

<https://www.doc.govt.nz/nature/pests-and-threats/predator-free-2050/>

**Popular science article:**

Young, E. 2017. New Zealand’s war on rats could change the world. Atlantic Daily. https//www.theatlantic.com/science/archive/2017/new-zealand-predator-free-2050-rats-gene-drive-ruh-roh/546011

**Peer-reviewed publication:**

Esvelt, KM, NJ. Gemmell. 2017. Conservation demands safe gene drive. PLOS Biol. 15:e2003850.

**IUCN Report:**

Genetic frontiers for conservation: an assessment of synthetic biology and biodiversity conservation. IUCN Task Force on Synthetic Biology and Biodiversity Conservation. 2019. [doi: 10.2305/IUCN.CH.2019.04.en](https://portals.iucn.org/library/node/48409); available at <https://portals.iucn.org/library/node/48408>

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