gene ethics — working for a GM-free future

Friends of the Earth Australia

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House of Representatives
Environment and Energy Committee
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Submission to the House of Representatives Environment Committee Inquiry into the problem of feral and domestic cats in Australia

Many thanks for the opportunity to contribute to the Committee's inquiry into the problem of feral and domestic cats in Australia.

While invasive species such as feral and domestic cats are clearly an important contributor to our current extinction crisis, it needs to be stressed that habitat loss remains the number one threat to Australia's species.[1] Most habitat is lost through land clearing for agriculture and urban development. Furthermore, powerful agriculture and development lobbies have ensured that successive Federal and State Governments - almost without exception – have failed to address this critical problem.

The key role of habitat destruction in driving species extinctions must be the primary consideration when considering conservation funding priorities and policy settings. Without strong measures to halt the further destruction of critical habitat, other conservation measures such as culling feral cats will fail to halt our current species extinction crisis.

Importantly, habitat destruction makes rare and endangered species much more vulnerable to threats such as predation. When habitats are intact, large and in good natural condition, the species that depend on them are much better equipped to withstand the multiple threats to their survival and rehabilitation. But as habitat is destroyed and chopped into smaller fragments, species' populations become smaller, more isolated, less genetically diverse and more vulnerable.[2]

Specific comments addressing the Inquiry's Terms of Reference

Our submission will focus predominantly on:

e. the efficacy (in terms of reducing the impact of cats), cost effectiveness and use of current and emerging methods and tools for controlling feral cats, including baiting, the establishment of feral cat-free areas using conservation fencing, gene drive technology;

There is now broad consensus that a network of large, feral predator-free fenced areas must form part of any strategy to prevent further extinctions of Australian wildlife. A range of direct and indirect methods will also be necessary if the impact of feral cat populations on native animals is to be mitigated. Direct control includes a range of techniques such as trapping, shooting, and Indigenous tracking. Indirect control includes managing ground cover (for example through de-stocking and prescribed burning) to promote shelter for wildlife and reduce the impact of predation.[3]

Importantly, studies suggest that eliminating feral cats from certain ecosystems may increase the activity or abundance of co-existing invasive predators such as foxes and/or invasive prey such as mice. It is therefore important to have mitigation strategies in place.[4]

Gene drives

Engineered Gene Drives are a new form of genetic modification that uses the gene editing technique CRISPR/Cas. To create gene drives, this bacterial defence system is transferred into animals – creating organisms that could never occur in nature. Unlike previous genetically modified organisms they are deliberately designed to spread their genes far and wide into wild populations of the target species. They offer the potential to permanently modify or to eradicate local populations - or even entire species - in the wild.[5]

Gene drives have been suggested as a potential way to control feral cats in Australia. CSIRO is one of the main organisations researching and promoting such a strategy, and is being funded by the US military's Defense Advanced Research Projects Agency (DARPA) to do so.[6]

Because of their potentially irreversible consequences, a comprehensive joint report on gene drives by Critical Scientists Switzerland (CSS), the European Network of Scientists for Social and Environmental Responsibility (ENSSER) and Vereinigung Deutscher Wissenschaftler (WDF) argued that:

> *"This means no mistakes must be made, neither concerning the target species nor the affected ecosystems. They must not go where they are not intended to go, nor accidentally escape from cages in laboratories, nor have any unintended effects on the target species, ecosystems biodiversity or human health."*[7]

Given the inherent unpredictability of gene drives this is unlikely to be achieved. The scientists observed that:

> *"there are also serious limitations with the functioning of this technology, such as its inefficiency in many organisms, the quick emergence of resistance, and with its control, such as irreversibility and the impossibility of containment or recall once released."*[8]

There is a concern that gene drives could potentially spread to populations that they are not intended to – or to related species. These concerns have led scientists to come up with ideas such as 'local gene drives', 'reversal drives' and 'self-limiting drives'.[9] Importantly though, these are just theoretical concepts – there are no examples of them having been successfully developed.[10]

Because of the high level of unpredictability, the lack of knowledge and the potentially severe negative impacts on biodiversity and ecosystems, both scientists and over 200 global NGOs have called for a moratorium on the environmental release of gene drives.[11]

No one knows if gene drives will work in mammals

As CSIRO themselves point out – scientists still don't know if they can make gene drives work in mammals. Any potential deployment in feral cats – if it is even technically feasible - is likely to be many years away:

"The current focus of research is assessing whether it's viable in mammals like mice, which will require many years of work. Only then could it be considered for feral cats, and many more years of research into the genetics and ecology of feral cats in Australia would be required."[12]

Attempts to develop a gene drive in mice have so far been unsuccessful. Experiments have shown that whilst a CRISPR/Cas9 gene drive can work in mice, it does so with only very limited efficiency.[13] In the study, the gene drive was designed to spread a mutation which changed coat colour from grey to white. When inherited through the female germline, the gene was transmitted to 73% of offspring, exceeding the 50% expected from Mendelian inheritance. However super-Mendelian inheritance was not observed when the CRISPR/Cas9 construct was passed through the male germline, for reasons that are not yet understood. The researchers state that levels of transmission efficiency fall short of what is needed to rapidly drive a gene through a wild population without resistance arising, and comment that "both the optimism and concern that gene drives may soon be used to reduce invasive rodent populations in the wild is likely premature."[14]

CRISPR is prone to unintended impacts

Studies have shown that the gene-editing tool CRISPR used to create gene drives can result in significant mutations – such as large deletions and complex rearrangements of DNA.[15] According to scientists:

"such rearrangements constitute a clear risk, as they can alter gene expression, give rise to further mutations during reproduction, as well as disable or alter the sequence of genes at the site of rearrangement."[16]

Another recent study found that CRISPR produced foreign mRNAs or proteins in about 50 per cent of the cell lines studied – raising serious questions about the safety and predictability of this gene editing technique.[17]

The potential for CRISPR to edit unintended regions of DNA – so called off-target effects – is well recognised. An extremely good and accurate knowledge of the DNA sequence of an organism is therefore important in order to predict off-target effects. This will pose serious challenges when applying the technique to wild and diverse populations, where genetic variation within a species could render the gene drive ineffective.[18]

As scientists observe:

"Thus far, only laboratory data has been generated, and it can be anticipated from the findings, that unintended on-target effects as well as off-target effects will take place. This is a serious concern, as it adds additional risks to the release of GDOs [gene drive organisms] into wild populations."[19]

Species are likely to evolve resistance to gene drives

Studies in mosquitoes suggest that the chances of species developing resistance to gene drives that render them ineffective is high.[20] Modelling in mice has confirmed that this presents a serious problem.[21]

Gene drives are likely to be ineffective in cats

Studies suggest that gene drives are likely to be most effective in species with short generation times, large numbers of progeny, that mate randomly and that are not genetically diverse.[22] None of these factors are true of feral cats.

Moro *et al.* observe that spreading gene drives through feral cat populations would be challenging due to the size and primarily solitary habits of these species. They also note that "feral cats are problematic to maintain as they are a solitary-living species whose physiology and behaviours have been shown to change in captivity."[23] It is not clear if cats modified with gene drives and bred in captivity would be able to successfully breed with feral cats after release.

Rode *et al.* also raise the concern that "the release of gene drive individuals might transiently increase population size with potentially long-lasting ecological consequences".[24]

The opportunity cost of gene drives

Proponents and the science media often portray the purported benefits of gene drives as unquestionable, with the risks played down as not being proven or demonstrated. However, the reality is really quite different. As scientists observe:

> *"the ability of engineered gene drives to perform according to plan and to deliver the envisaged benefits is still largely hypothetical, the associated risks to biodiversity, human health and agroecosystems, on the other hand are very real."*[25]

Researchers also report that:

> *"Failure to properly include alternatives and exaggeration of the effectiveness of gene drives can lead to significant opportunity costs (mis-spending of money), especially if large sums of money – and other resources, as well as time – are wasted on unrealistic future promises rather than implementing existing interventions effectively and conducting more cost-effective, diverse and appropriate R&D."*[26]

Gene drives are an unpredictable, expensive and unproven techno-fix that must be viewed in the context of other potential approaches to solving the same problem e.g. fencing or employing indigenous rangers to cull cats. As scientists observe:

> *"Many of these alternatives may carry fewer risks, may be more actionable in the short term, more sensitive to local needs and resources and/or may better align with a diverse range of worldviews"*.[27]

Gene drives have dual use potential

A number of scientists have raised serious concerns about the potential military application of gene drive technology. As Rode *et al.* observe:

> *"Gene drive organisms can be seen as an efficient technology for population control but also as potential bioweapons".*[28]

Gurwitz raises concerns that:

> *"just as gene drives can make mosquitoes unfit for hosting and spreading the malaria parasite, they could conceivably be designed with gene drives carrying cargo for delivering lethal bacteria toxins to humans. Other scary scenarios, such as targeted attacks on major crop plants, could also be envisaged."*[29]

It is significant that the US military's Defense Advanced Research Projects Agency (DARPA) provides the majority of funding for gene drive research globally, including the research into gene drive mice being conducted by the University of Adelaide and CSIRO.[30] Viewed in this context, the University of Adelaide and CSIRO's current gene drive research program is a dangerous and irresponsible misuse of public resources.

Recommendations

The Federal Government should take urgent action to:

- prevent the further erosion of threatened species habitat, which remains the number one threat to Australia's species.[31]
- fund proven solutions to the feral cat problem such as predator-free fenced areas; direct control processes such as trapping, shooting, and Indigenous tracking; and indirect controls such as managing ground cover (for example through de-stocking and prescribed burning) to promote shelter for wildlife and reduce the impact of predation.[32]
- legislate a moratorium on the environmental release of gene drives.
- prohibit the use of public money, personnel, or institutions in gene drive research.

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