What if we genetically engineered an entire species?

'Gene drive' is best known for its capacity to suppress malaria by eradicating mosquito populations. However, its applications reach even further, including through its potential to eliminate other insect-transmitted diseases, erase herbicide and pesticide resistance in weeds and pests, and remove invasive species from ecosystems. It is worth looking into these potential benefits, while also weighing the significant risks involved in gene drive use.

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A gene drive is a technique for manipulating ecosystems by introducing self-propagating custom genes among a population of sexually reproducing organisms, using the CRISPR-Cas9 gene-editing technology. This recent revolutionary technology grants scientists nearly endless possibilities for manipulating genes and genomes with high efficiency and ease, and at a low cost. The specific CRISPR-Cas9 set-up used can subvert normal inheritance rules in order to bias a custom gene so that it is inherited at a frequency higher than the normal 50 % (sometimes up to 100 %) – an effect produced by other genetic mechanisms in nature as well. Researchers can then insert this set-up into the genome of a number of initiator organisms and release them into the wild, causing the custom gene to spread and perform its function throughout a growing fraction of the population. This gene may induce a variety of effects on the targeted organism, such as fatal development problems, change of sex, sterility, increased resistance to parasites, decreased resistance to pesticides or herbicides, etc. Instead of introducing a custom gene, the drive may also alter the organism by disrupting a natural gene, such as one that performs a critical development role.

While the idea of gene drives has been around since 2003, they only became practicable in 2013 with the advent of CRISPR-Cas9. Gene drives have proven to be successful in lab tests on mosquitoes and fruit flies, but less so on mice, showing room for improvement. So far, no gene drives have been released into wild populations. Current research focuses on combating malaria by reducing mosquito populations or their ability to transfer the malaria parasite, and on eradicating rodents that cause major damage to the endemic flora and fauna on the islands they invade.

Since the above-mentioned technology modifies the germline of the species, i.e. the genetic material that passes onto the next generation, this practice raises a host of ethical considerations. Are we willing to take on the risk of introducing irreversible and unintended changes in the genome of a species, or even of unleashing an environmental catastrophe through carelessness? Is assuming such a risk justified by the fact that in so doing we could eradicate insect-transmitted diseases and thereby prevent 700 000 deaths per year? Or by the fact that we could manipulate ecosystems to better withstand invasive species – eradicating them in a humane way – and thereby increase productivity of farmland? Many feel that using gene drive technology to eradicate species or populations of organisms is wrong, but others argue that it can help us prevent the extinction of others. In any case, an open, well-informed debate including all stakeholders is crucial before deciding on regulation and implementation.

Potential impacts and developments

Potential gene drive applications include reducing or eradicating insect-transmitted diseases such as malaria, dengue, Zika, Lyme, schistosomiasis and others; removing herbicide resistance in weeds or pesticide resistance in insects; inserting pesticide or parasite resistance in vulnerable populations (think of bees suffering from Varroa mites and pesticide use, and the decline of amphibia due to Chytrid fungus);

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inserting vulnerabilities to harmless molecules in pests, making (local) eradication easier; and suppressing populations of invasive species, weeds and pests (e.g. fruit flies, aphids). However, these potential benefits are not free of hazards. Ecologists are very unsure about the potential impact of suppressing or eradicating populations of organisms on ecosystems. The gene drive may spread globally and cause unwanted extinctions; accidental releases from research labs are likely; failure of the drive to eradicate a population may leave genetic residues such as a skewed sex ratio; and the still significant off-target effects of CRISPR-Cas9 may cause unwanted mutations. Furthermore, harmful mutations could occur in the gene drive itself that would ride along and spread, and possible non-target effects may cause the gene drive to spread horizontally to other species. Lastly, drives might be used as a biological weapon or in bioterrorism.

As an answer to these risks, scientists are developing safeguards and preventive measures in the form of temporally and locally limited gene drives (known as daisy drives); reversal drives that use a second gene drive to reverse effects of a first drive; and immunising drives that spread through a population of organisms and immunise them against other drives. Future research may also produce drives that respond to certain environmental stimuli that are triggered, for example, when the targeted pest eats certain crops. In addition, nature has its own defences in the form of evolution. Resistance to drives will often already be present in wild populations or will occur after some time, by rapidly spreading through populations and stopping the drive systems. With this in mind, gene drives may be better suited as an additional tool alongside traditional approaches to fighting diseases and conservation, with new drives designed whenever resistance is acquired. There are ways to increase the potency of a drive so as to make resistance unlikely to evolve in the first place, but this may bring along consequences we are not willing to face.

So what are the potential positive impacts for the EU? There are currently 49 invasive alien species of Union concern causing damage worth billions of euros to the EU economy. Suppressing or eradicating these species from EU soil would improve ecosystem services crucial to many sectors. Drives may also reduce our reliance on herbicides and pesticides in agriculture, by removing tolerance in weeds and pests. Among the diseases within the EU that are targetable by gene drives, Lyme disease occupies a prominent place, given that more than 360 000 cases of persons suffering from it have been reported over the past two decades. When it comes to negative impacts for the EU, hostile nations could use gene drives as a biological weapon to target keystone species in order to damage European ecosystems (e.g. pollinators such as bees). As gene drives are so inexpensive and relatively easy to engineer, bioterrorism is also an issue the EU should consider. As a side note, no major risks are attached to gene drives being released in crops and livestock or humans, since these are slow to spread and easy to monitor due to the long reproduction cycles.

Anticipatory policy-making

There are concerns that the privatisation of gene drive technology without strict regulation could lead to an ecological cacophony of drives targeting whatever insects or plants industry labels as 'pests'. Agribusiness incentives tend to focus on the short term and are of a profit-driven nature. Mainstreaming the use of gene drives will therefore likely happen through the prevalence of economic interests over those of local communities, which will have to face the potential harms or side effects. In this context, one of the inventors of the CRISPR-based gene drive calls for the exclusive non-profit exploitation of the technology.

Gene drives fall under EU GMO legislation, which includes Regulation (EC) 1946/2003. The latter translates the UN Cartagena Protocol on Biosafety to the Convention on Biological Diversity into EU law, and details procedures for handling transboundary movements of GMOs. In November 2018, the convention refrained from establishing a moratorium on gene drive, instead building stronger precautions in terms of research. Risk assessment/management and the consent of involved communities are now central to regulation.

As regulation will always lag behind technological developments, researchers' responsibility is important, making sure there are possibilities for cooperation among them, rather than incentives to conceal results and information for fear of being ‘scooped’ and of missing the chance to see one's work published.

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