Playing God with mosquitoes? We humans have loftier aims

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'Franken Mozzie' goes under the spotlight. Credit: Phil, CC BY-NC-SA

In a startling development in "gene-drive" technology, a team of researchers at the University of California has succeeded in creating genetically modified mosquitoes incapable of spreading the malaria parasite to humans, and which could potentially spread this trait rapidly throughout mosquito populations in the wild.

This success has the potential to be translated into a huge global health benefit. Although global malarial deaths have been in decline over the past decade or so, the WHO estimates that malaria has been responsible for over 400,000 deaths this year alone.

The *Anopheles* genus of mosquito, when infected, transmits Plasmodium parasites to humans via their bites, and it is these parasites that cause malaria. It is possible to cure the disease (often through artemisinin-based combination therapy) if diagnosed early enough. There are also preventative measures that can limit the spread of the disease. However, not all such treatments and preventative measures are readily available, particularly in sub-Saharan Africa, where malaria is most prevalent, and nearly half of the world's population remains at risk of this potentially fatal disease. Preventing transmission would save hundreds of thousands of lives a year.

The moral status of mosquitoes

Gene-drive technology essentially creates genetically modified organisms to stimulate the inheritance of certain genes throughout entire populations. The idea of using gene-drive technology to combat malaria is not new. Last year, Anopheles gambiae mosquitoes were successfully modified to produce 95% male offspring by a team at Imperial College, a trait that was inherited by the modified mosquitoes' offspring. The long-term effect of this modification would be the eradication of this mosquito species.

The Californian team reported the success of a different kind of genetic modification. Rather than modifying the species to alter the sex of the mosquitoes' offspring, they modified the mosquitoes to carry genes for antibodies that target the Plasmodium parasite. The results of early tests are highly promising. In the laboratory, the anti-malarial gene was inherited by 99.5% of the modified mosquitoes' offspring. The hope is that these mosquitoes would then breed with non-modified mosquitoes in the wild and pass the anti-malarial genes on to their offspring, ideally leading to all future generations being resistant to the malaria parasite.

For those who believe that there is something morally problematic about eradicating an entire species of mosquito, the Californian team's gene-drive strategy is morally preferable to that of the Imperial team. The former wouldn't eradicate *Anopheles stephensi*, but would prevent them from carrying the parasite.

This is an important difference even for those who believe that mosquitoes have no moral status. A number of scientists have raised concerns about hybridisation between closely related animal species, and that gene-drive technology could lead to a modified gene "hopping". In the case of gene-driven species eradication, this could lead to the unintended extinction of the "wrong" species. In contrast, the possibility of such "gene-hopping" in anti-malarial genes could be useful for malaria control, since a modified gene in one parasite-carrying mosquito species could spread it to the other seven that carry the Plasmodium parasite.

'Playing God'

Yet, there has been a degree of moral concern about genetically modifying mosquitoes. This is perhaps in part due to the use of the same Crispr-Cas9 gene-editing procedure that was controversially used to edit genes in human embryos this year.

However, many of these criticisms of gene-editing in embryos are less readily applied to using the procedure to modify mosquitoes. For instance, one prominent objection in the former context is that the Crispr-Cas9 procedure is unsafe and can lead to unexpected mutations that would harm the embryo. While this is a salient concern for human embryos, it is less clear that an individual mosquito might be harmed in so far as we believe that mosquitoes lack significant moral status.

Plasmodium: the real enemy. Credit: NIAID, CC BY

A more common objection is that the procedure amounts to 'playing God', displaying the same sort of hubristic attitude of mastery over nature that Victor Frankenstein displayed in creating his monster in Mary Shelley's famous novel. It is not a persuasive argument.

A response to the "playing God" objection is familiar from the GM food debate. Humans have been selectively breeding both plants and animals for hundreds of years, and this can be viewed as an indirect form of genetic modification that we do not find morally problematic.

In seeking to find solutions to world hunger by genetically modifying crops, it is misguided to claim that we as a society are displaying the hubris of Frankenstein. Similarly, it seems ridiculous to claim that humans were overly hubristic in eradicating the variola virus responsible for smallpox through the development of vaccinations, and even more problematic to claim that such 'hubris' was morally wrong; the 'wrong' of the supposed hubristic attitude here is surely morally outweighed by the value of the many lives that were saved by eradicating smallpox.

The playing God objection does, however, point towards a morally relevant consideration. Unlike the Gods, humans are not omniscient and we might overlook the possibility of devastating unintended and unforeseen consequences. It might be claimed, for example, that releasing genetically modified organisms could potentially have dramatic effects on the ecosystem.

This objection was voiced by Helen Williams of Gene Watch against the idea of eradicating the *Anopheles gambiae* mosquito. But there is room for scepticism here. In 2010, Nature ran a feature asking researchers what would happen if mosquitoes were eradicated. Entomologist Joe Conlon captured a common response:

Mosquitoes don't occupy an assailable niche in the environment. If we eradicated them tomorrow, the ecosystems where they are active will hiccup and then get on with life. Something better or worse would take over.

So if scientists doubt that the eradication of mosquitoes would have bad effects on the ecosystem then it is unclear why removing their capacity to transmit malaria would. This does not rule out the possibility of bad ecological effects; the scientific consensus on this issue might be wrong, or perhaps gene-drive technology might lead mosquitoes (or the Plasmodium parasite) to develop other catastrophic capacities – a possibility made all the more worrisome by the irreversibility of gene-driven changes – but we ought to bear in mind not only the badness of a worst case scenario, but also the likelihood of it occurring.

With great power…

Although gene-driven technology could be used to combat disease, it could also plausibly be developed into a bio-weapon if it fell into the wrong hands. This technology is not alone in its potential to be used for nefarious as well as honourable ends; for instance, similar concerns have been raised against the development of synthetic biology, and studies into H5N1 flu transmission, among many others. It is a legitimate concern. Conversely though, it might also be argued that gene-drive technology might not even be effective.

The objections raised show that we face a great deal of uncertainty when we consider the implementation of gene-drive technologies: will the technology work or will it lead to unforeseen catastrophe?

However, this does not mean that we must prohibit the future use of such technologies, even for morally weighty goals. We can take steps to minimise the risks, and increase the likelihood that the technology will bring about intended good effects. Research can increase the likelihood that modified mosquitoes would lead to the prevention of malaria and sophisticated modelling can increase the reliability of our predictions.

We can also look to implement safeguards that are strong enough to minimise the risk of the technology being used by malign groups. How to do so is very much a hot debate – some researchers argue that precise information about generating gene-drives should be classified, while others argue for transparency.

With any novel technology, it seems that at some point we must make a decision about whether to advance or not based on whether the expected value of doing so is greater than that of refraining.

This is the same sort of leap that we have historically made in releasing GM crops into the ecosystem, and deploying other novel technologies that could have had unintended and unforeseen consequences, such as IVF, the internet and mobile phones.

Now is the time for cool, honest, rational reflection on the expected harms and benefits of gene-drive technology so that we can make an informed choice on this matter, rather than scaremongering claims about playing God and "Franken-mozzies". Then our task will be to think about how we should make adequate preparations to cope with the ensuing population increase that gene-drive success in eliminating disease would inevitably lead to.

Source: The Conversation

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