Current CRISPR gene drives are too strong for outdoor use, studies warn

Heritable gene-editing tools need reliable brakes to prevent them from spreading worldwide

BY **SUSAN MILIUS** 3:00PM, NOVEMBER 16, 2017

SO CUTE, SO WRONG No one has a genetic way of getting rid of invasive brushtail possums (shown) in New Zealand, but now is the time to debate whether CRISPR gene drives are too strong to be considered, two researchers argue.

Gene-editing tools heralded as hope for fighting invader rats, malarial mosquitoes and other scourges may be too powerful to use in their current form, two new papers warn.

Standard forms of CRISPR gene drives, as the tools are called, can make tweaked DNA race through a population so easily that a small number of stray animals or plants could spread it to new territory, predicts a computer simulation released November 16 at bioRxiv.org. Such an event would have unknown, potentially damaging, ramifications, says a *PLOS Biology* paper released the same day.

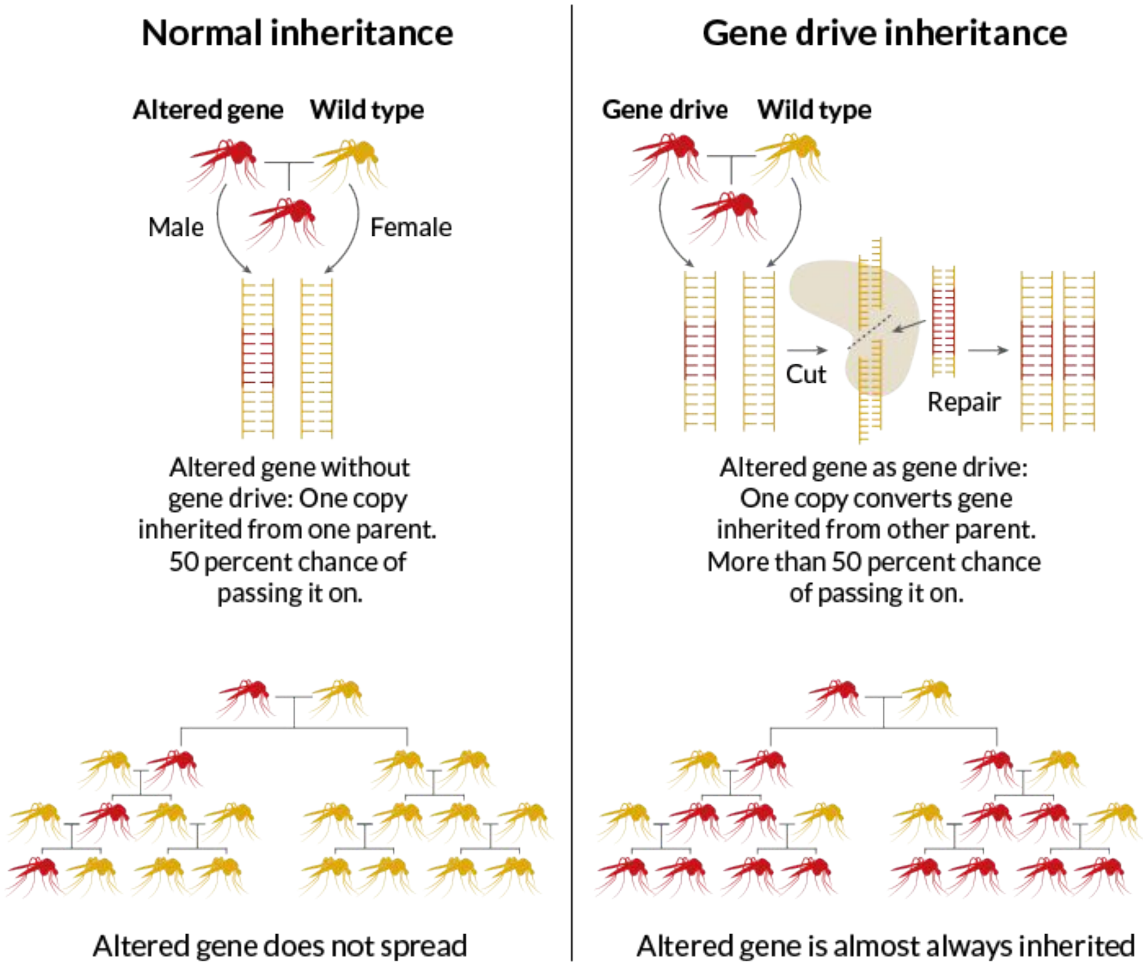
“We need to get out of the ivory tower and have this discussion in the open, because ecological engineering will affect everyone living in the area,” says Kevin Esvelt of MIT, a coauthor of both papers who studies genetic solutions to ecological problems. What’s a pest in one place may be valued in another, so getting consent to use a gene drive could mean consulting people across a species’s whole range, be it several nations or continents.

Researchers have constructed this kind of drive in yeast, a fruit fly and several mosquitoes, but none of the tools have been deployed yet in the wild (*SN: 12/12/15, p. 16*). Meanwhile, some researchers are already working to add brakes or off-switches into a new generation of gene drives.

Story continues below graphic

Natural vs. driven

Normally, organisms have a 50 percent chance of passing along a gene to an offspring (left). A gene drive (right) copies and pastes itself into chromosomes from both parents, ensuring it gets passed on more often.



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The major concern is that current gene drives "are probably too powerful for us to seriously consider deploying in conservation," says geneticist Neil Gemmell of the University of Otago in Dunedin, New Zealand. Gemmell is a coauthor of the *PLOS Biology* paper.

This opinion could prove especially controversial in New Zealand. In 2016, the government resolved to protect the nation's imperiled biodiversity by exterminating invader rats, stoats and possums that are wreaking havoc on native species. Gene drives just might make that possible.

Though warning of perils, the researchers also propose some solutions. A weaker system, which Esvelt calls a daisy drive, splits up components of the drive called guide RNAs. These guide RNAs direct the gene-editing machinery to its DNA target, where molecular scissors then snip and swap genetic material. As genes get inherited or not in the chancy jumbling of sexual reproduction, descendants in later generations become less likely to inherit all the spaced-apart pieces needed to operate the gene drive.

Esvelt's lab is working to create a daisy drive in two kinds of nematode worms and is looking at other species as well. Other labs are now working on tamer gene drives, too.

Anthony A. James of the University of California, Irvine says that the disease-carrying *Anopheles* mosquito species that he and his colleagues have equipped with gene drives are self-limiting. When females end up with two of the genes he's inserting, they don't "survive very well after they have fed on blood." Researchers are now raising these mosquitoes to see whether the genes spread and then dwindle away. "We don't need our genes to last forever," James says, "only long enough to contribute to getting rid of malaria."

Another lab's current version of disease-fighter mosquitoes already has a touch of the daisy. *Aedes aegypti* mosquitoes engineered with some built-in parts of the gene editor have their guide RNA split into two parts and put on different chromosomes, says molecular biologist Omar Akbari of the University of California, San Diego. Pictures of many weird mosquitoes created this way — all yellow or with three eyes or forked wings — attest to the fact that the drive system works. Akbari's research appears November 14 in the *Proceedings of the National Academy of Sciences.*

Akbari is not very worried about the risk of accidentally wiping out disease-carrying mosquitoes. "A thousand children die every day," he says. It would be unethical not to use a tool that could lessen the loss, he says.

He does recognize that the case for caution could be different for other species. “A lot of pet owners would be sad,” he says, if a gene drive went wrong and escaped worldwide during some future attempt to rid, say, Australia of its terribly destructive feral cats.

Citations

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Further Reading

T.H. Saey. Gene drives spread their wings. *Science News*. Vol. 188, December 12, 2015, p. 16.

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