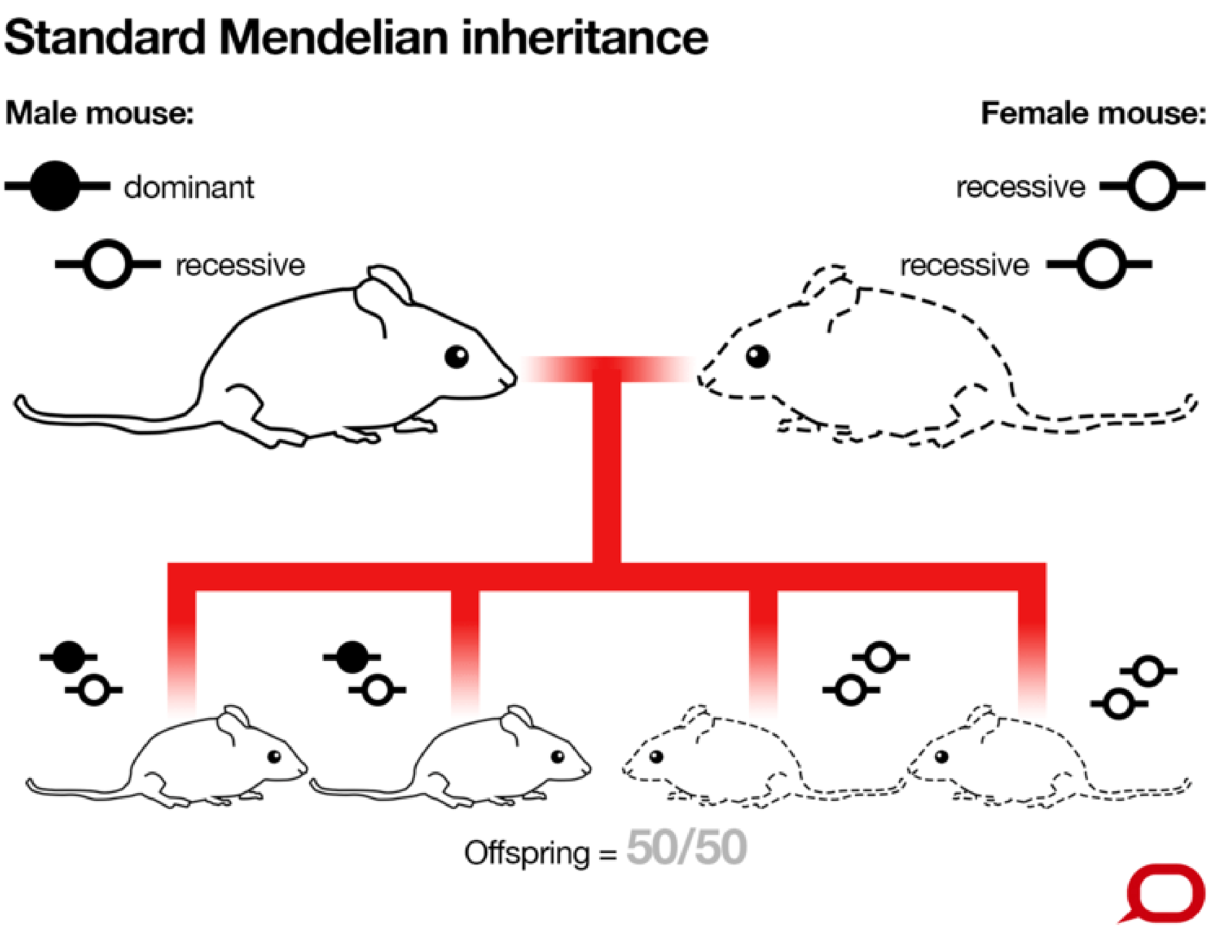
Now we can edit life itself, we need to ask how we should use such technology

November 24 2016, by Charles Robin



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Imagine a world where mosquitoes no longer pass on the deadly malaria parasite, where invasive species such as cane toads are wiped out from Australia, and agri-chemical resistant pests revert back to their original susceptible state.

Scientists are currently energised about such prospects, thanks to advances in what's known as gene drive technology.

While the concept of gene drives has been around since the 1960s, it is new developments in gene editing technology, supported by lab-confined proof-of-concept experiments in flies and mosquitos that has sparked their imagination.

The Australian Academy of Science is running a public consultation process on gene drives. It's time for society, regulators and various tiers of governments to also start thinking about the application and hazards of the technology.

We need to talk

The revolutionary gene editing technology known as CRISPR/Cas9 can be used for many different purposes.

For instance, it was in the news recently because it is being used to edit the genome of a living human in an effort to fight cancer.

Gene drives take gene-editing technology down a distinctly different path where whole populations of organisms have their genomes edited.

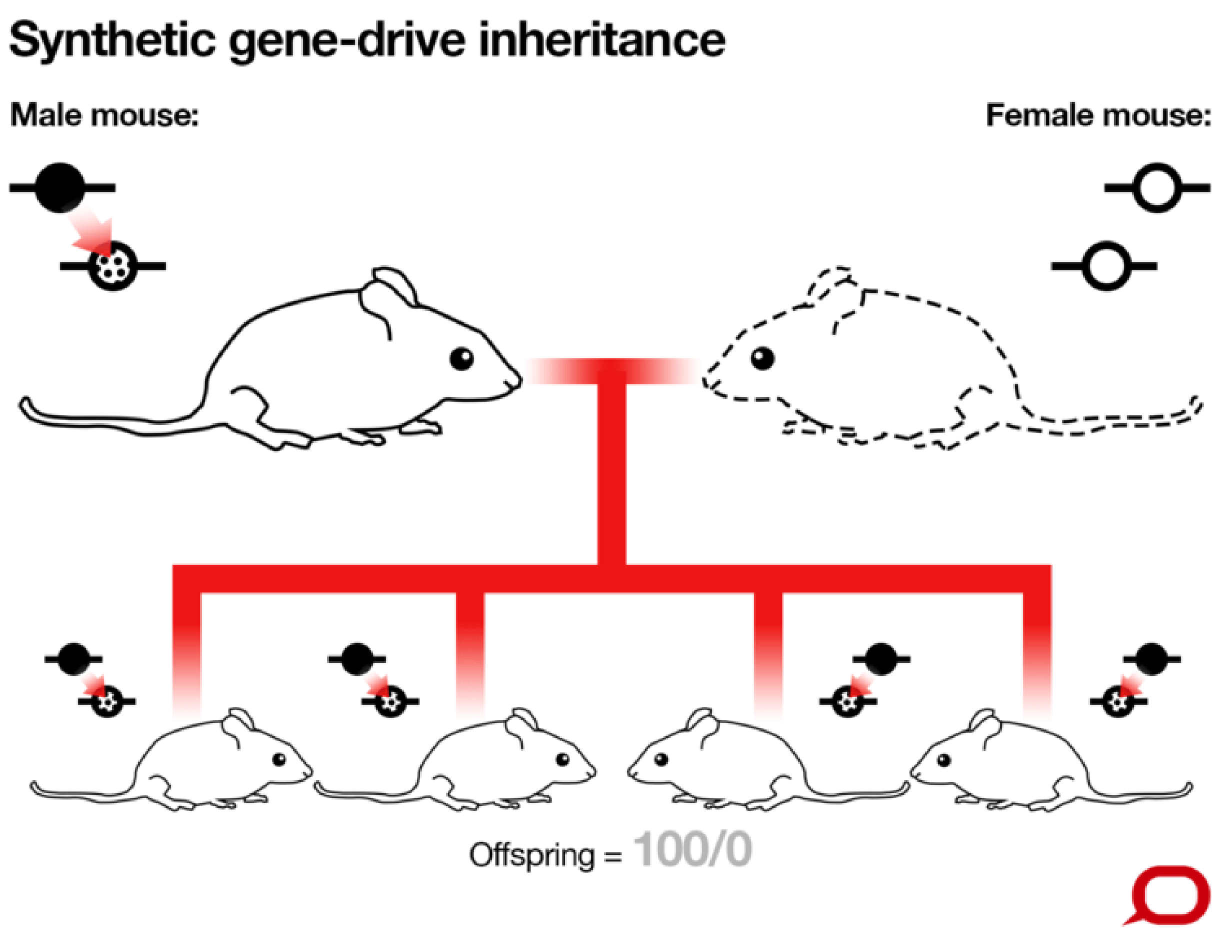
Self-propagating genetic elements can be designed to target specific genes in the population and either disrupt them or replace them with transgenes, which are genes taken from other creatures.

At its essence, a gene drive distorts the standard segregation law of

Mendelian inheritance. Consider a typical gene in a male mouse, say a gene determining coat colour. Under Mendelian inheritance, that mouse would have inherited a version (or allele) of the gene from its mother and a version from its father.

A sperm cell produced by that mouse will only carry one of those two versions, and the probability that it derived from its father is equal to the probability that it derived from its mother.

If this gene were not a typical gene, but instead it had a version that increased the odds of its own inheritance above 50%, it would have the potential to spread – or "drive" – through the population.



Natural gene drives do occur and approaches to exploit them for population control have long been discussed, and even employed.

But the CRISPR/Cas9 technology is game-changing because it enables a scientist to design a synthetic gene drive that targets a specific character in an organism of choice.

Size matters

The organism needs to be one that reproduces sexually, is amenable to transgenic manipulation and has a short generation time (determined by the age of reproduction).

This latter criteria means that gene drives are not suitable to humans (or, indeed, elephants) because their generation time is too long.

But scientists have proposed various types of synthetic gene drives. Some aim to suppress a population, whereas others would alter a population with a new character (such as the inability of a mosquito to carry human pathogens).

An example of a suppression strategy would be to drive a gene through a population that results in an overabundance of one sex. If mothers carrying the element only give birth to sons, then the population will decrease as the gene drive increases in relative frequency.

Such a strategy is being suggested to rid islands of feral rodents that are endangering rare native species.

Gene drives may also replace more conventional insect population control strategies, such as the Sterile Insect Technique, which is used to control fruit flies in Australia and mosquitos around the world.

Gene drive strategies will not require that insects are continually bred and released from factory scale insectaries in an attempt to inundate pest populations.

The synthetic gene drives spread themselves, potentially doubling every generation, so that only relatively small numbers of gene-drive bearing insects would need be to released to inoculate a pest population.

What to target?

The exact design and nature of the gene drive will depend on the specific organism and problem, and there could be many options.

For example, would it be better to have a gene drive targeting female fertility or male fertility? Would it be better to make cane toads sterile or to alter them so they do not produce toxins?

In the latter case, the toad population would be suppressed indirectly because predators would find them more palatable.

Or myxomatosis resistance alleles that have arisen in Australian rabbits could be targeted so that that this control agent becomes more effective again.

Similarly, we could reverse the evolution of pest weeds or insects that have become resistant to agri-chemicals by making them susceptible again.

The hazards

There are, of course, many hazards with gene drives. For example, a gene drive introduced into a pest species could spread back to that animal's native territory, where it is not a pest but valued as an important part of the ecosystem.

Imagine if New Zealanders decided to release a gene drive against brush tailed possums, considered an introduced pest in that country, and it jumped the Tasman sea. How would such drives be contained to regions or international boundaries?

Will there be trade implications with countries that have differing legislation around the technology? And how do we best assess the ecological costs of a gene drive before it is released?

There is also the ethical question of whether the deliberate elimination of an entire species, even a disease-bearing mosquito, is conscionable given the ravages humans have already made on biodiversity. More significantly: who gets to make such decisions?

Generations of Australian research has aimed to protect Australia's unique ecosystems and agriculture from unwanted pests.

Perhaps the targeting of invasive species is where gene drives would be best applied. While much of these earlier control strategies have been successful, there are notable ones, like the introduction of cane toads that have worsened rather than improved the situation.

But much can be learnt from the successes and failures of past biological control efforts, and gene drive technologies have enormous potential to protect and preserve biodiversity.

For these reasons, and for the reasons of disease control, the gene drive route is worth mapping out to determine whether there is a way to navigate the potential hazards.

That's why it's important people get chance to read and comment on the Australian Academy of Science's discussion paper on gene drives. All feedback must be in by Sunday November 27, 2016.

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