Keeping up with the fast-moving science of gene drives

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Credit: North Carolina State University

The emerging science of gene drives is drawing attention for its potential to help with critical health issues such as mosquito-borne diseases and environmental concerns such as agricultural pests and invasive species. At its most basic, a gene drive operates outside the traditional realm of genetics, in which an offspring has a 50-50 chance of inheriting a trait from one of its parents. A gene drive introduces a trait that will spread –

or drive – through a population. In effect, a gene drive stacks the deck in favor of a trait being inherited, even if that trait doesn't help the species survive.

Examples of gene drives exist in nature, but recent laboratory research with CRISPR-Cas9, a targeted gene editing system, has shown that scientists can engineer a gene drive that would allow a targeted trait to spread through nearly 100 percent of a population of yeasts, fruit flies or mosquitoes.

The National Academies of Sciences, Engineering, and Medicine just released a report, "Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values," to explain the state of gene drive science and discuss next steps for scientists, stakeholders, regulatory agencies and the public.

The 15-person committee of experts who developed the report over the past year includes NC State's Jason Delborne, associate professor in the College of Natural Resources and the Genetic Engineering and Society cluster. Delborne, who has expertise in science and technology policy and public engagement on controversial scientific issues, helped introduce the report on Capitol Hill and during its public presentation in Washington, D.C.

We sat down with Delborne to learn more about the gene drive report and its recommendations.

Why is this report timely?

The science of gene drives is moving very fast. Our committee was formed in July 2015, and major scientific papers have come out since that time showing new proofs of concept in the laboratory with fruit flies and mosquitoes. As our report shows, our ability to assess the risks of gene drives, to oversee them with regulatory agencies and to have a public discussion around gene drives is falling behind the science. It's not keeping pace. So it's important that we do this analysis now before we're faced with a yes or no question. When we have a technology that's ready to deploy, the question becomes, do we do it or not? We don't want to wait until we have the technology in front of us to have discussions about regulation, oversight, ethics and engagement.

Why is gene drive science at a turning point?

What makes gene drive science worthy of study at this moment is that we can design a gene drive with a targeted trait and a mechanism of drive that is under human control. And so we can essentially genetically modify a sexually reproducing organism and then drive that trait through a population in a way that we've never been able to do before – with intention. It's theoretically more precise and potentially much more powerful.

Gene drives do occur in nature, so the mechanism isn't something that's completely unfamiliar. But until the development of molecular technologies like CRISPR-Cas9, designing a targeted gene drive hasn't been feasible.

What are some of the possible applications for a gene drive?

You can either use a gene drive to decrease the numbers of a population or you can use it to change their characteristics.

Some of the examples proposed include using a gene drive to create a population of mosquitoes that's not able to transmit diseases such as dengue, human malaria or avian malaria. You could also use a gene drive to crash an invasive pest population by biasing the sex ratio of offspring to the point where too few females exist to sustain the population.

Could gene drive technology be used to fight the Zika virus?

Our committee was not tasked with identifying what problems gene drive should be applied to. What we did say is there may be a temptation to develop and deploy a gene drive quickly, when there is a crisis. Our message as a scientific committee is that we need to be aware of the level of uncertainty that surrounds gene drives at this moment, and it's still very high. The advent of Zika is scary. There's a lot of uncertainly around how Zika works and how it's transmitted, so we don't know exactly the best way to intervene and take care of that public health problem and potential crisis.

The uncertainty around Zika and how it works and the uncertainty around the stability, functionality and safety of gene drives means that these two things probably don't go together right now.

What are the limitations of using a gene drive?

A gene drive doesn't work in every type of organism. It only works in organisms that sexually reproduce. You need a short generation time for a gene drive to be realistically useful. You need the genetic elements to be stable after environmental release, and that's not something that's been proven yet. We have research to know that gene drive works in a lab with some different organisms, but we don't know yet how this works through multiple generations in natural contexts.

Could a gene drive be used with a human population?

Because human generation time is quite long, unlike a mosquito or yeast, gene drives are not likely to be considered a tool for use in driving a trait through a human population. It just would take too long. And the bad news is that probably means we can't think about gene drives as a tool for addressing inherited diseases or things like that. The good news is that we probably don't need to worry about a nefarious use of gene drive affecting human reproduction.

The kinds of potential harms that we talked about as a committee in terms of human health were more related to how we might transform existing organisms, and how that would impact human health. As a hypothetical example, if we were to create a gene drive mosquito that didn't transmit malaria, is it possible that another more efficient vector would take its place in spreading the disease? Is it possible that the modified mosquito might transmit a different disease and affect human health? So there are those kinds of potential for harm to human health that accompany any sort of intervention into the natural world.

That's one of the reasons we say as a committee that we don't know enough yet to release a gene drive modified organism into the environment. Instead, we recommend a phased testing approach that would reduce the chances of potential unintended consequences.

Some critics have asked whether gene drive technology gives us the ability to "play God." How did the committee handle that issue?

As one example, the ability to use gene drives raises the question of whether or when we should eradicate a species. We have public calls for eradicating mosquitoes because they are vectors for spreading multiple diseases. That's not an easy question to answer. It's incredibly complex, from a biological standpoint, to even attempt to answer that. Also, from an ethical perspective, I think there are important questions about when and how to intervene in natural processes.

Our committee wasn't trying to silence critics or critical questions, and I don't want to either. I want to respect the fact that there might be many people who have grave concerns about this research, who would demand a very high threshold for certainty and safety around any sort of field trial or release of gene drive organisms. I can understand that.

What makes a gene drive different from a genetically modified organism (GMO)?

A gene drive gives a trait the ability to spread and persist in a population. Because this trait is driving through a population, even if it makes the organism less competitive or fit, the trait is likely to persist and spread in the environment. Because of the properties of gene drive, there's the potential to cause irreversible ecological change. In contrast, if you introduce a genetically modified organism into the environment, the expectation is that over time it's likely to dissipate or disappear, unless it confers a fitness advantage.

What are some of the ethical, practical and social considerations of using a gene drive?

A major message of our report is that responsible science isn't just a research issue. One of the things that's amazing about gene drives is that their potential applications tie into challenges of public health and conservation. And so in deciding how these might be used, we're making values-based decisions and we're making political decisions, not just scientific decisions.

Science raises issues of governance, values, research practice, risk assessment and public engagement. For responsible science, all of these different factors have to be considered. It's not just a technical scientific question of whether gene drives work or not.

How should stakeholders and members of the public be involved in the gene drive discussion?

One of the important messages of the report is that public engagement cannot be an afterthought. The outcomes of engagement may be as crucial as the scientific outcomes to decisions about whether and when to release a gene drive modified organism into the environment. We place a greater emphasis on communication, on finding out what stakeholders value and incorporating that feedback into how we should approach gene drive research and development.

It's a big deal for a National Academies committee to say this, and it's telling that there are a number of social scientists and humanists on the committee, in addition to experts in biology, entomology, population genetics, ecology, and risk assessment.

One of our tasks was to come up with criteria for selecting sites for potential field testing. Our recommendations include engaging with relevant publics – a mix of the community of people who live near where this may happen, other stakeholders and wider publics. There's a whole chapter on community, stakeholder and public engagement, which is a novel aspect of this report.

What guidance does the report contain for researchers?

The committee's recommendation is that we should move forward with laboratory research and contained field trials, but that we have insufficient evidence to support release of a gene drive outside highly controlled conditions. We call for coordinated research to reduce gaps in knowledge.

We recommend that whenever possible researchers should include a visible marker with a gene drive that would distinguish it in that organism to facilitate research and monitoring. That may not always be possible, but that's a recommendation because you can't look at an organism and know whether it's a wild type, regular GMO or a gene drive modified organism. If there's a visible marker, that helps with surveillance.

There's been some talk about so-called reversal drives, which is using the same kind of molecular technique to sort of recall a gene drive that went wrong or that you want to reverse. Our committee, looking at the existing evidence, judged that we should not solely rely on a reversal drive as a strategy for mitigating the effects of a gene drive. It's problematic if we're talking about an unintended consequence of the technology, to rely on the same technology to protect us.

Which agencies will help oversee gene drive research?

Gene drives don't respect political boundaries. The way they're designed and their potential for spread has no respect for boundaries, which means that international governance and international cooperation and collaboration is even more important for gene drive modified organisms than for regular GMOs.

Up until now, regulation of GMOs and other biotechnologies are predicated on containment. And in a sense gene drives are meant to overcome boundaries – they're meant to spread – and they're a new challenge to our existing frameworks of how we govern biotechnologies. At the international level, we have the United Nations Convention on

Biological Diversity, specifically the Cartagena and the Nagoya protocols. At the national level we have the Coordinated Framework for the Regulation of Biotechnology, which is already under a review process and partly why these National Academies studies are happening right now. The White House has asked the agencies involved in the Coordinated Framework to meet and consider how these agencies can adapt to emerging biotechnologies. Gene drive is certainly part of that challenge.

There's a lack of clarity about which of these agencies would have primary responsibility for regulating a gene drive modified organism. It depends on how you classify the organism. Is a gene drive a plant pest or an animal drug or a rodenticide? There are already challenges with existing biotechnologies, but the gene drive organisms could challenge it further.

One of the recommendations of our report is advocating for a change from an environmental assessment to an ecological risk assessment that would take into account the characteristics of the gene drive, its effects on the population, and local values and governance.

We also identify concerns around misuse and the idea that someone could use gene drive technology for nefarious purposes. Even though there's no evidence anyone's tried to do that, it's something we have to pay attention to.

What lessons can we draw from GMOs?

There's some mistrust among the public about the science behind biotechnology. There has been a perception that GMOs have private benefits instead of public benefits, that safety hasn't been taken seriously, that GMOs have been introduced stealthily. Some of the public backlash against GMOs in Europe and in this country could be understood as being suspicious of the fact that these things have been at play, not just about health risks or environmental impacts. It's about the perception that the technology is invisible and being privately controlled, so that we're eating genetically modified food but we don't know it. Because of these kind of concerns, the committee recognized that more transparency and more engagement is good for science and for the technology.

There has been too little communication about GMOs among public audiences and stakeholders that's been respectful and productive. If that's repeated with gene drives, that would be a shame. Hopefully this report is moving us in the direction of having more transparency and open communication about an emerging technology – its potential benefits and its potential harms.

More information: Gene Drive Research in Non-Human Organisms: Recommendations for Responsible Conduct. nas-sites.org/gene-drives/

Provided by North Carolina State University