ROBERT M. FRIEDMAN, JOHN M. MARSHALL, AND OMAR S. AKBARI

G E N E
DRIVES
NEW AND IMPROVED

As the science advances, policy-makers and regulators need to develop responses that reflect the latest developments and the diversity of approaches and applications.

It is now more than three years since the National Academies of Sciences, Engineering, and Medicine released their influential report *Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values*. The 2016 report, responding to a series of early demonstrations of gene-drive applications in yeast, fruit flies, and mosquitoes during 2015, identified important issues for policy-makers to consider regarding the technologies envisioned at the time. Though genetically modified organisms have been introduced into the environment for decades, organisms modified with gene drives are specifically designed to spread and may persist in the environment for years, with possible irreversible, unintended consequences.

Put simply, gene drives are engineered snippets of DNA that can be introduced into an organism's genome to significantly increase the chance that a desired genetic trait will spread through a population faster than would normally happen through sexual reproduction. In the few years since the National Academies report, the technology landscape has progressed to offer a richer set of alternatives that regulators and policy-makers may soon be hearing about and, as product development advances, asked to review and approve. The vision of the early approaches to gene drives was to start with a small number of organisms carefully engineered in the laboratory, release them into the environment, and rely on the engineered construct itself to rapidly spread a desired trait throughout the wild. Although this idea had been contemplated for over half a century, the pace of development dramatically quickened when scientists started using CRISPR gene-editing technology to engineer organisms. Today, though the term "gene drive" is most often used as if it were a single technology, it is more accurate to consider it as a suite of approaches that can be tailored to the needs of specific applications. Research continues on gene drives designed to spread widely, but scientists are also working to develop new types of gene-drive organisms designed to be geographically localized or designed with limited life spans. Each brings different strengths and weaknesses for specific applications.

Our goal here is to describe the various options under development in nontechnical terms for a policy-making audience, review how far along each is, and examine the broader context of how this new suite of technologies compares with other available alternatives. Early engagement by the policy and regulatory communities will be of great help to product developers, and thus ultimately to society through better and more appropriate products. Our hope is that this improved understanding of what is in the development pipeline will enhance the dialogue between the policy community and developers.

But first, we should review some basics. Why consider using gene drives at all given the difficulties of even field testing an organism designed to spread and persist in the environment? How should scientists design and regulators evaluate field trials that might become the equivalent of a full-scale release? The Convention on Biological Diversity, a United Nations multilateral convention with 196 Parties (member countries), focuses on, among other things, risks to natural ecosystems from genetically modified organisms. The full Convention meets every two years to review many biodiversity-related topics. In 2016 and again in 2018

representatives of the member nations discussed a possible moratorium on field release of engineered gene drives. Fortunately, in our view, the Parties rejected a moratorium, opting for a cautious set of preconditions to be met prior to experimental field trials. The 2016 National Academies report, as well as a 2017 report from the Australian Academy of Science and a 2018 report from the Royal Society in the United Kingdom, examined the risks and potential benefits from applications of engineered gene drives. All recommended continued research and development, again with a careful series of steps to be followed.

The vast majority of research on gene drives to date has been devoted to developing new methods for controlling pests that have been highly resistant to other control measures. These pests fall into three major categories: insect vectors (such as mosquitoes) that transmit diseases to humans and animals, invasive species (such as mice) that threaten native species on islands, and insect agricultural pests (such as spotted wing drosophila) that devastate crop production. The toll of unchecked human suffering, loss of biodiversity on islands, and lowered crop productivity is extensive. According to the World Health Organization, malaria affects 230 million people in 87 countries annually, and 405,000 people died from the mosquito-borne disease in 2018 alone, two-thirds of whom were children under the age of five. The mosquito-borne viral disease dengue affects about 100 million people per year across even more countries. Some 80% of known species extinctions have occurred on islands, many due to the spread of invasive species. About 10% to 15% of potential global food production is lost to insect pests every year.

That controlling such significant pests using organisms engineered with gene drives would also pose environmental risks should come as no surprise. Current control methods that rely primarily on chemical insecticides and rodenticides are also not without harm. Regulators must consider, on a case-by-case basis, the risks and potential benefits from any new approach to pest control compared with the benefits and harms from currently available methods.

Let's examine the notion of case-by-case evaluation a bit further. In a regulatory context, this typically means evaluating risks and benefits of a single technology for a specific application, and essentially arriving at a "yes or no" decision. But as we stated earlier, the term gene drive refers to a suite of technologies under development, each with differing performance characteristics and outcomes. From a policy perspective, then, rather than thinking about evaluation as a yes-or-no exercise, we believe it is more appropriate to approach any potential application of a gene-drive organism as a *design challenge*. What

performance characteristics and outcomes are the product developers attempting to achieve? What outcomes should the developer and product regulators be trying to avoid? Robust design dialogues among product developers, regulators, and other societal players, combined with an R&D portfolio intended to meet a variety of outcomes, are the best bet for producing gene-drive organisms matched to the characteristics of, and desired societal outcomes from controlling, current pest management challenges.

Performance outcomes

Gene-drive organisms intended to spread a desired trait into a population contain two linked sets of genetic modifications. The first set includes the genetic modifications that encode the new trait. The second set imparts the ability to "drive" the trait into a wild population with far higher probability than would normally occur. In some cases, when the intention is to suppress a population, a single set of modifications may suffice; say, when a gene drive disrupts a gene required for female mosquito fertility, viability, or both.

For example, scientists are attempting to use gene drives to genetically modify a mosquito to include a new trait that would no longer allow it to transmit the pathogen that causes malaria. Most sexually reproducing organisms pass genetic traits to their offspring following well-understood principles of heredity. Such a trait, if engineered alone into a batch of mosquitoes in the laboratory and then released to the wild, would linger at a low frequency and quite possibly be lost as the engineered mosquitoes mated with the overwhelming number of wild mosquitoes that can transmit malaria. To be successful, it would be necessary to introduce an enormous number of engineered mosquitoes, a feat that would be nearly impossible to achieve on the scale of the geographic distribution of the species.

However, by adding "drive-inducing" genetic modifications to the engineered mosquito, once it is released to the environment and mates with a wild mosquito, the offspring will almost always maintain the genetic modification that prevents it from transmitting malaria. In addition, those offspring, once they mate with wild mosquitoes, almost always maintain and pass on the desired trait to their progeny, and so on. It is the combination of these two sets of genetic modifications that drive through the population of mosquitoes.

Thus, a scientist designing a gene-drive organism has two sets of desired performance outcomes from which to choose: the characteristics of the new trait and the characteristics of the drive. Below, we briefly describe the variety of alternative performance outcomes currently under development in each category. In Box 1 we describe the current state of development for each.

To date, scientists have focused on three general classes of traits or "effectors" to control the types of pests discussed

Box 1

UPDATE ON PROGRESS

NONLOCALIZED GENE DRIVES

Of the several applications under development, research on nonlocalized gene-drive modified mosquitoes to control malaria is perhaps the most advanced.

Target Malaria, a not-for-profit research consortium based at Imperial College London with partner institutions around the globe, aims to suppress the population of malaria-transmitting *Anopheles* mosquitoes in sub-Saharan Africa. The group is developing a nonlocalized suppression drive to reduce the number of female biting mosquitoes. Given that females lay eggs and hence have the largest influence on population size, if such an engineered mosquito were deployed into a wild population, the resulting lack of female mosquitoes remaining for reproduction would induce a population crash. Target Malaria is making significant progress, with the most compelling example being the recent development of a drive targeting a gene, known as *doublesex* (*dsx*), that is important for sex determination. In several tests in which multiple generations of mosquitoes were raised in containment cages in a laboratory, the *dsx*-drive spread to every individual, resulting in complete eradication of the caged mosquito populations. Efforts are now under way to demonstrate effectiveness in larger, more genetically diverse populations. If successful, and if regulatory approvals are granted, these gene drives may enter testing in the field within a decade.

A second effort, by teams at the University of California, Irvine Malaria Initiative and the Tata Institute for Genetics and Society at the University of California, San Diego, is focusing on a gene drive to modify *Anopheles* mosquitoes. In contrast to Target Malaria, these teams aim to develop a nonlocalized replacement drive linked to genes that prevent mosquitoes from transmitting Plasmodium, the pathogen that causes malaria. These teams are also making significant progress in multigeneration laboratory-contained trials, replacing the original population of mosquitoes with one containing genes that prevent the transmission of the malaria-causing pathogen. As with Target Malaria, rigorous laboratory-contained tests are under way to measure performance of these drives, and if performance is maintained and regulatory approvals are granted, these may be tested in the field in the coming years.

LOCALIZED GENE DRIVES

Several groups are developing localized gene drives in a variety of organisms, including mosquitoes, though the research is not as far along as with nonlocalized gene drives.

The laboratory of one of us (Akbari), located at the University of California, San Diego, is developing localized gene-drive modified mosquitoes of a different species, *Aedes aegypti,* which is the principal vector for dengue, chikungunya, yellow fever, and Zika virus transmission. The lab recently developed a self-limiting drive system with the intended goal of population replacement. This group has also developed potent antiviral effectors that can block transmission of dengue or Zika viruses. In the coming years, the researchers will work on linking antiviral effectors to this drive system and begin laboratory-contained testing.

Researchers at the lab have also been developing gene drives to suppress populations of major agricultural pests. They are focusing on spotted wing drosophila (*Drosophila suzukii*), an invasive fruit fly originally from Southeast Asia that is now present all over the world. This fly poses significant economic threats to production of soft summer fruit such as cherries, blueberries, and strawberries. Prior to the introduction of this significant pest in California, cherry farms did not need pesticides. Today, farmers spray an arsenal of pesticides to combat the fly populations, which have already developed resistance to these chemicals. As an alternative, the team is developing a localized, high-threshold drive system and has demonstrated its ability to maintain itself at high frequency over multiple generations of the flies in laboratory-contained populations. The researchers are now working to link this drive system with an effector that when spread into a population would make the flies susceptible to a developmental or environmental stimulus, such as exposure to high temperatures, resulting in population suppression.

The Genetic Biocontrol of Invasive Rodents (GBIRd) program is a partnership of several universities, governments, and nonprofit organizations in the United States, Australia, and New Zealand. The program is trying to develop population suppression gene-drive technologies to combat the spread of invasive rodents that threaten native wildlife on islands, among the leading causes of biodiversity loss. To minimize the risks associated with the spread of the engineered rodents to areas where they are not wanted, GBIRd intends to develop a

localized drive that is geographically confined to an island. Even as this work proceeds, recent studies led by Kimberly Cooper at the University of California, San Diego, have demonstrated that the development of a confinable drive system in mice is possible. However, the system had only moderate efficiency at biasing transmission and functioned only in females, indicating that significant optimization would be required to further develop a system robust enough to spread into a wild mouse population.

Kevin Esvelt of the MIT Media Lab is developing a form of localizable drive referred to as a "daisy drive." Unlike high-threshold drive systems that are localizable, this system has a low threshold for spread, but its spread is transient. This leads to it spreading and then falling out of the population, with its spatial spread being limited by its transience. Development of this system is proceeding in yeast and nematodes; however, due to the multicomponent nature of the system, this may take some time.

REVERSAL GENE DRIVES

Research is under way in several groups, including Andrea Crisanti's laboratory at Imperial College London, Ethan Bier's laboratory at the University of California, San Diego, and Amit Choudhary's laboratory at the Broad Institute, to develop tools for controlling and countering previously introduced gene-drive organisms, if necessary.

The Crisanti and Bier labs are developing genetic remediation systems intended to remove previously introduced gene-drive organisms from the environment in the event of unwanted consequences. Their goal is to be able to design a second gene-drive-modified organism of the same species as the unwanted gene-drive organism to reverse the changes made to the first. The new organisms would be designed to affect only the unwanted modified organism, not the native species. The hope is that if a gene-drive organism were to produce unwanted consequences, then a reversal gene-drive organism could be released to remove or prevent the spread of the original organism. Development of these genetic systems is proceeding in flies and mosquitoes, and their potential use in the environment is being explored with population genetic models.

The Choudhary lab is developing small organic molecules that can easily enter cells and are designed to either turn on or turn off gene-drive activity. Thus, the drive component of a gene-drive organism would be activated only in the presence of a very specific small molecule so that the organism could not spread without the presence of that chemical. Alternatively, the gene-drive organism could be designed so that drive activity is terminated when a specific small molecule is present. This has great potential to increase the safety of field trials of nonlocalized gene-drive organisms, which, for instance, could be conducted in the presence of a small molecule activator of gene-drive activity, thus limiting the spread of the organism to the trial area. Proof of concept of this technology has been demonstrated, and development is proceeding in flies and mosquitoes.

in the first section. These include genetic modifications to suppress pest populations, to alter a characteristic so that the modified organism is no longer a disease vector or pest, or to reverse the effects of previously introduced gene-drive organisms.

Suppression drives employ genetic modifications that reduce or eliminate pest populations—for example, to reduce the number of disease-carrying mosquitoes or eliminate rats on an island. *Replacement drives* modify pest populations so that they are no longer disease vectors or pests—for example, by adding a gene that renders mosquitoes unable to transmit malaria. The number of mosquitoes remains the same; only the number of malaria-causing parasites is reduced. *Reversal drives* include genetic modifications that are designed to disable or reverse the effects of a previously introduced gene-drive organism if something goes wrong.

Within each of these general classes of traits, scientists are working to be able to "tune" the characteristics or strength of the drive/trait combination. Perhaps the most important of these characteristics are geographic reach and persistence in the environment.

Again, people who have heard about gene drives commonly equate the term with what might be better described as *nonlocalized drives*. These are gene-drive organisms designed to spread a trait widely and rapidly from a small number of introduced modified organisms. Nonlocalized gene drives might be most appropriate for controlling malaria, for example, where the intent is to control the disease over a wide geographic area.

Scientists are also working on gene drive designs that are geographically confined. *Localized drives* are engineered to limit the spread of an introduced trait. This might be done in two different ways: a *high-threshold drive* that can spread only when a large number of modified organisms are introduced, or a *self-limiting drive* that lasts for only a limited period. A high-threshold gene-drive organism used to control, for

example, an agricultural pest in one region of the country would be unlikely to migrate to another region in sufficient numbers to be successful. On the other hand, a self-limiting gene-drive organism would be designed to lose its ability to drive after several generations. It still might require only a modest number of released individuals to start spreading, but would not survive in the wild for very long.

Which brings us to the second important characteristic of an engineered gene-drive organism: persistence of the introduced trait in the environment. Survival of a gene-drive organism in the wild depends on both how well it can compete with its wild relatives and its susceptibility to mutations that lead to loss of either the desired trait or the ability to drive. Some gene-drive organisms might persist for only a limited number of generations. Others may persist for years. Persistence in the environment can be considered either a feature or a bug, depending on intent or perspective. Geographic spread is of course related to persistence. Even a gene-drive organism that has been designed to spread will not get very far unless it can persist in the wild.

Public attitudes

What does the US public thinks about gene drives? Researchers at North Carolina State University recently conducted a nationwide survey of US adults to determine their attitudes about the use of gene drives for agricultural pest control, when conventional controls were not adequate. After being informed about the potential risks and benefits of two applications currently under development, respondents' support versus opposition depended heavily on whether the spread of drives can be limited, whether they were replacement drives or suppression drives, and whether the target species were native or nonnative.

Support was strongest for use of an agricultural gene drive targeting a nonnative pest when the spread of the drive can be limited. When asked about localized suppression drives, 61% of respondents supported use of the drive and 14% were opposed. Results were similar for localized replacement drives, with 57% supporting and 16% opposed.

When asked about an agricultural application of gene drives lacking controls for spread, support was mixed, both for suppression drives (33% supported, 34% opposed) and replacement drives (37% supported, 34% opposed). In all cases, support for use of gene drives to control native species was lower than for controlling nonnative agricultural pests.

Researchers at the University of California, San Diego, conducted 18 online focus groups throughout California—a state where the presence of invasive mosquitoes is expanding—to explore public opinions about the use of gene drives to control mosquito-borne disease. The researchers first displayed a narrated slideshow outlining the health threats from invasive mosquitoes and then compared control methods, both existing and those under development.

When asked about three alternative types of gene drives, about 75% of respondents found self-sustaining (nonlocalized) drives acceptable, 60% found high-threshold drives acceptable, and 54% found self-limiting designs acceptable. Based on qualitative comments during the focus groups, the researchers concluded that the higher acceptability for nonlocalized drives was due to participants seeing these drives as more cost efficient.

We are not aware of similar public opinion surveys or focus groups about use of gene drives to control invasive species on islands.

Expanding the portfolio of pest control alternatives

Currently, chemical pesticides are the most widely used method for controlling insect vectors of human disease, invasive species, and agricultural pests. Well over 500 chemicals in commerce are classified as insecticides, and over 50 as rodenticides. Responsible use of pesticides, in which the choice and method of delivery are carefully tailored for a specific application, tries to minimize effects on human health and the environment. Nevertheless, there is a clear need for alternatives that are both more effective and less harmful.

As discussed in Box 1, nonlocalized, low-threshold gene drives—that is, those intended to spread a trait widely and rapidly from a small number of introduced modified organisms—are at a more advanced state of development than ones designed to be localized or to have limited persistence. The two most advanced research efforts are to help control malaria. Both are approaching the point when they might advance to carefully designed field testing. Localized drives and those designed with limited persistence, though perhaps acceptable for a wider variety of applications, are a bit further behind in development.

As gene drive research progresses, product developers will have to demonstrate both safety and effectiveness. Moreover, these new products will have to prove their superiority to chemical pesticides, as well as to other biological approaches. In particular, two biological control approaches are worth considering as alternatives: one has similar characteristics to engineered gene drives, but does not involve genetic engineering; the other is not a gene drive, but can use genetic engineering. The current state of development of these other biological approaches is summarized in Box 2. Not only may these prove useful in their own right, but they also may provide opportunities to learn about the potential ecological effects of novel approaches and, perhaps more important, how to engage both regulators and local communities in the decision of whether, when, and how to adopt novel approaches to pest control.

Given the magnitude of remaining pest challenges—to

Box 2

OTHER BIOLOGICAL APPROACHES

Engineered gene drives are not the only biological control methods being developed. Two other promising approaches are discussed below; one uses a bacterium called *Wolbachia* and one uses what is called the sterile insect technique (SIT).

Research groups in Australia and the United States are experimenting with infecting *Aedes aegypti* and *Aedes albopictus* (mosquitoes that can transmit dengue and Zika, among other diseases) with *Wolbachia*, a bacterium naturally found in many insect species. Depending on the *Wolbachia* strain and how the mosquitoes are bred and released, the bacteria can either reduce the ability of mosquitoes to transmit the pathogens that cause disease or suppress their populations.

A research team based at Monash University in Australia, the World Mosquito Program (formerly the Eliminate Dengue Program), releases both male and female mosquitoes infected with *Wolbachia*, repeatedly and at high concentrations, into populations of uninfected mosquitoes. When the proportion of infected mosquitoes exceeds a threshold, the infection spreads through the rest of the population and remains relatively stable, but may occasionally require additional releases of infected mosquitoes. When the bacteria are used in this manner, the number of mosquitoes remains about the same, but their ability to transmit disease is reduced. Though no genetic engineering is used, this is essentially a replacement drive. The program currently has test sites in Australia, Brazil, Colombia, India, Indonesia, Mexico, Sri Lanka, Vietnam, and the Pacific Island nations of Fiji, Kiribati, New Caledonia, and Vanuatu.

MosquitoMate, a private company based in Kentucky, uses a different approach. Its researchers release only male mosquitoes infected with *Wolbachia*. When the infected males mate with wild, uninfected females, those females lay eggs that do not hatch. The company releases enough infected males in small enough regions that a wild female is more likely to mate with an infected male than a wild, uninfected male. The result is that the population of mosquitoes in that small region is suppressed. Because this approach has no drive component, it does not persist for very long, and thus must be repeated throughout the mosquito season. The company has tested its product in Kentucky and California, and the Environmental Protection Agency has now given it clearance to use the product in some 20 states. MosquitoMate is also collaborating with Verily—the life sciences arm of Google's parent company, Alphabet—to improve methods for selecting only infected males for release.

MosquitoMate's approach is a variant of the widely used sterile insect technique, first developed in the United States in the 1950s. SIT has been used in many countries around the world to control fruit flies, tsetse flies, screwworm, moths, and mosquitoes. The most common method uses radiation to produce sterile insects, but these do not compete well with wild insects, so the sterilized insects must be released repeatedly, and in very large numbers, to be effective.

Another company, Oxitec, has improved the SIT approach using genetic engineering to target *Aedes aegypti* mosquitoes. Using an approach similar to that of MosquitoMate, Oxitec releases only male mosquitoes, engineered to include a gene that upon mating with wild females is inherited by their offspring. The gene prevents offspring from surviving to adulthood, suppressing the population. The engineered mosquito has been tested in Brazil, Panama, and the Cayman Islands. Additional tests are proposed for the Florida Keys and India. Oxitec is also testing this approach on an agricultural pest, the diamondback moth, that feeds on cabbage, broccoli, cauliflower, and canola. In addition, the company is working on implementing a second-generation technology that enables males that inherit the gene to survive, which would mean that the effect of each release would remain for a few generations but soon disappear as neighboring wild mosquitoes dominate.

The Akbari lab has recently developed another improvement to SIT that the researchers call a "precision-guided sterile insect technique" (pgSIT). Carefully engineered breeding insects are kept in a lab or other contained facility to produce eggs to be released to the environment. When the eggs hatch, only sterile males make it to adulthood. The lab has demonstrated the method in flies, and hopes to transition the technology to both crop pests and disease vectors. Releasing eggs that produce sterile males is far simpler than releasing adult insects, as is done in the other SIT approaches. This could lead to better suppression results in the field as SIT is essentially a numbers game: the more sterile males the better.

human health, island biodiversity, and agriculture—options in addition to chemical pesticides are sorely needed. Biological alternatives hold great promise, but to be successful, developers must be able to match the performance characteristics and outcomes of biological alternatives to the needs and challenges of the specific problems they are attempting to solve. Continued development of many different approaches will be required, including some that use nonlocalized gene drives, localized gene drives, or no gene drives at all; some that suppress pest populations and others that replace them with characteristics that prevent transmission of disease; and some that can remain in the environment for only a few generations or persist far longer. Clearly, one size does not fit all.

Given the current stage of these new technologies, we urge policy-makers to support and encourage this diversity of technology development. Research to date has been funded primarily by private philanthropies such as the Bill & Melinda Gates Foundation, while government funding has come primarily from the US Defense Department's Defense Advanced Research Projects Agency. Regulatory agencies, in the United States and other countries around the world, will be challenged to review gene-drive organisms, particularly nonlocalized-drive designs. In the United States, the Environmental Protection Agency's Office of Pesticide Programs and the Department of Agriculture's Animal and Plant Health Inspection Service should offer guidance to help product developers collect the information they will need to obtain permits to field test gene-drive organisms under development, both nonlocalized and localized.

Regional organizations are also beginning to consider these new technologies. For example, in 2018 the New Partnership for Africa's Development issued a series of recommendations to its member countries to encourage phased testing of gene-drive modified mosquitoes for control of malaria, and the European Food Safety Authority is currently reviewing the risks and potential benefits of gene-drive organisms for control of agricultural pests. Because at least some gene-drive organisms might cross national boundaries, continued involvement by regional organizations is crucial.

Finally, international organizations must continue to provide guidance. The World Health Organization's Vector Control Advisory Group is working with product developers to review two different gene-drive-modified mosquitoes (one a suppression drive, the other a replacement drive) for control of malaria, as well as several of the other biological control alternatives discussed above. We anticipate that this process will be extremely useful to individual country policy-makers.

The International Union for Conservation of Nature, whose members include both governments and civil society organizations, will be considering the use of gene drives and other synthetic biology tools for conservation purposes at its next World Conservation Congress, to be held in France in June 2020. The Convention on Biological Diversity has set into motion a series of intersessional online discussion forums and meetings to review gene drives, and in particular methods for environmental risk assessment, in preparation for its next major biennial meeting, to be held in China in October 2020. An international online discussion forum will take place in January 2020; interim meetings will be held in March and May.

Continued development of a rich portfolio of design alternatives is key to the success of new approaches to biological pest control. Only then will product developers, national regulators, regional organizations, local communities, and other societal players be able to work together to match the characteristics of, and desired societal outcomes from, current pest management challenges.

Robert M. Friedman is vice president for policy at the J. Craig Venter Institute and a policy consultant to the Tata Institute for Genetics and Society at the University of California, San Diego. John M. Marshall is an assistant professor in residence at the University of California, Berkeley, School of Public Health and the Innovative Genomics Institute. Omar S. Akbari is an associate professor in the Section of Cell and Developmental Biology and the Tata Institute for Genetics and Society at the University of California, San Diego. He has a pending patent application for pgSIT and equity interest in Agragene.

Recommended reading

Sarah R. Carter and Robert M. Friedman, "Policy and Regulatory Issues for Gene Drives in Insects: Workshop Report," J. Craig Venter Institute and the University of California, San Diego (2016).

Michael S. Jones, Jason A. Delborne, Johanna Elsensohn, Paul D. Mitchell and Zachary S. Brown, "Does the US public support using gene drives in agriculture? And what do they want to know?" *Science Advances* 5, no. 9 (2019): eaau8462.

National Academies of Science, Engineering, and Medicine, *Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values* (Washington, DC: National Academies Press, 2016).

The Royal Society, "Gene Drive Research: Why It Matters" (2018).

Kent H. Redford, Thomas M. Brooks, Nicholas B. W. Macfarlane, and Jonathan S. Adams, *Genetic Frontiers for Conservation: An Assessment of Synthetic Biology and Biodiversity Conservation* (Gland, Switzerland: International Union for Conservation of Nature, 2019).