BOSTON TECH HUB FACULTY WORKING GROUP

FALL SESSION 3 • NOVEMBER 19, 2019

# Gene Drives


PREPARED BY:

**Mike Miesen**
Research Assistant, Belfer Center for Science and International Affairs



HARVARD Kennedy School
BELFER CENTER
for Science and International Affairs
TECHNOLOGY & PUBLIC PURPOSE PROJECT

Harvard John A. Paulson
School of Engineering
and Applied Sciences

**The Boston Tech Hub Faculty Working Group**, hosted by former Secretary of Defense and Harvard Kennedy School Belfer Center Director Ash Carter and Harvard SEAS Dean Frank Doyle, will convene its third session of the fall semester on the topic of gene drives. The session will examine current applications, capabilities, limitations, and ongoing debates regarding acceptable use, regulation, and governance of the technology.

# Context

- **Gene Drives** are pieces of DNA that are inherited by offspring more frequently than 50% of the time. While gene drives exist in nature, this session will focus on engineered gene drives inserted into a species, with the intent of spreading a specified change through a specified population.[1]

- Currently, gene drive systems use CRISPR-cas9 (Clustered Regularly Interspaced Short Palindromic Repeats), a tool to precisely identify a section of DNA, make a cut, and insert desired DNA.[2] The CRISPR system can also be included in inserted DNA, so that any offspring—which inherit one chromosome from the edited parent and one from a 'wild' unedited parent[3]—will be 'self-edited' and therefore will pass the gene drive system on to their own offspring. In this way, a gene drive "allows humans to change the genetic makeup of a species by changing the DNA of a few individuals that then spread the modification throughout an entire population."[4]

- Engineered gene drives could be made to be endlessly reproducible or temporary. Endlessly reproducible gene drives would, if successful, transmit through each subsequent generation of a species, because "they carry everything they need to copy themselves."[5] Temporary gene drives—sometimes referred to as '**daisy drives'**—would theoretically cause a gene drive system to fail after a certain number of reproductions;[6] the change would be self-limiting. Certain non-driving technologies can also affect wild populations and shared environments, but because they do not increase in frequency in the wild, they can only affect much smaller areas.

# Applications

1 We are grateful to Naomi Silverstein for research assistance with this brief.

2 Researchers discovered CRISPR as a simple immune system in bacteria meant to identify and disrupt viral 'attackers.'

3 Assuming that the other parent has not also been genetically modified.

4 Matthews, Dylan. "A genetically modified organism could end malaria and save millions of lives — if we decide to use it." Vox. September 26, 2018. https://www.vox.com/science-and-health/2018/5/31/17344406/crispr-mosquito-malaria-gene-drive-editing-target-africa-regulation-gmo

5 "Daisy Drive Systems." Sculpting Evolution. MIT. http://www.sculptingevolution.org/daisydrives

6 Ibid. Theoretically, this same system could be used to restore a target species to its original state.

- In **agriculture**, gene drives could be developed to control pest populations without pesticides or to eliminate parasites like the New World Screwworm that cause economic losses and animal suffering in cattle (and other non-livestock animals). In **human health**, gene drives could be developed to reduce the spread of diseases like malaria, schistosomiasis, and Lyme. In **ecosystems**, gene drives could be used to remove invasive species from a geography or to add beneficial traits to threatened species, like coral. In **animal welfare**, gene drives could reduce the fecundity of rodent pests currently controlled through inhumane poisons.

- Gene drives could be used to **disrupt transmission of certain diseases** by either *making a vector or reservoir species immune* or by *suppressing* the population. For example, mosquitoes that transmit malaria could either be engineered to pass on immunity to the parasite or engineered to produce disproportionately sterile male offspring, crashing the population and disrupting transmission of the disease.[7] In either case, the mosquito would be unable to act as a vector of disease, reducing transmission and potentially eradicating a disease from a given area.

## Public Purpose Concerns and Considerations

- **Ecological Impact.** Self-propagating gene drive systems cannot be tested in the field due to their extreme invasiveness; any trials would require a daisy drive or equivalent. If a gene drive is used to reduce or eliminate a species, the full ecological impact throughout the range is unlikely to be known prior to use. This concern is somewhat tempered by the ability to precisely target certain species; three species of mosquito (out of 3,500) are mostly responsible for transmitting malaria, for example.[8] However, ecological impacts remain an important consideration for scientists, advocates, and governments.

- **Improper Use.** Gene drive systems can be created and released unilaterally. An unsanctioned use of an engineered gene drive could cause harm to a geographic area and could set back the use of engineered gene drives for other purposes— effectively 'scaring off' society from using the technology. This concern is compounded by the troubling history of the "Global North" testing medicines and treatments on the "Global South" and the inherent power imbalance between organizations like Target Malaria, which is based in London, and the communities it seeks to work in, often in sub-Saharan Africa.

7 There are other ways to suppress a population, like spreading a gene that causes female sterility.

8 Matthews, Dylan. "A genetically modified organism could end malaria and save millions of lives — if we decide to use it." *Vox*. September 26, 2018. https://www.vox.com/science-and- health/2018/5/31/17344406/crispr-mosquito-malaria-gene-drive-editing-target-africa-regulation- gmo

- **Security**. Because they are slow, obvious to sequencing, and can be reliably overwritten, gene drive technology inherently favors defense. However, adequate defense requires monitoring at-risk species and/or environments, which will be challenging for most nations, and the technology could be used as a social weapon to deepen societal divisions and incite trade wars and border controls.[9]

- **Resistance.** Organisms may become resistant to one or more aspects of engineered gene drives, rendering them less useful and potentially making it more difficult to use gene drives in the future. While resistance can likely be engineered around, gaining approval or multiple drives in a given locality may be difficult.

## Regulatory Proposals

- **Self-Governance.** Most scientists, researchers, and organizations working on engineered gene drives approach their use cautiously. For example, Target Malaria—which seeks to use gene drives to eliminate malaria-carrying mosquitoes in endemic areas—created an ethics advisory committee and works closely with civil society organizations and governments in the four countries where it seeks to eventually release edited mosquitoes.

- **Local, National, and Regional Governance.** Many countries have prohibitions in place against the use or sale of genetically modified organisms. Some researchers argue for an interdisciplinary task force to create a deliberative framework that can help local communities decide whether and how to allow the use of engineered gene drives in their geographies.[10]10

- **International Governance.** In a 2018 meeting of the United Nations Convention on Biological Diversity, nations rejected a moratorium on the release of species engineered with gene drive systems. The nations did, however, include language about informed consent and local involvement. Various protocols (e.g., Cartagena Protocol on Biosafety, Nagoya Protocol) exist to regulate the movement of living organisms produced by genetic editing and the access to genetic resources.

  Many individuals (including Kevin Esvelt, an inventor of CRISPR-based gene drive) and organizations have called for all proposed experiments involving gene drive to be made public, allowing those affected to have a voice in critical early- stage decisions that will determine the form of the eventual application. They have advocated for the World Health Organization or another international

---

9 Esvelt, Kevin. "The thing to fear is fear itself." http://mars.gmu.edu/handle/1920/11337

10 Kofler, Natalie and Kevin Esvelt et al. Editing nature: Local roots of global governance." Policy Forum. American Association for the Advancement of Science. November 2018. https://research.ncsu.edu/ges/files/2018/11/Editing-nature_Local-roots-of-global- governance_Science_Kuzma_11.2.18.pdf

organization to host a registry that would require sponsorship of proposals byan interested local community.

## Discussion Questions

- Should gene drive technology be reserved for only certain issues afflicting humanity? What is the threshold of severity that warrants gene driveuse?
- At what level should governance be considered? (i.e., should a local village have the ability to consent to gene drive use, or should an international treaty govern its use?)
- Are existing governance frameworks appropriate for regulating the use of engineered gene drives? If not, what else is needed?

## Readings

"Gene Drive FAQ." Sculpting Evolution, *MIT Media Lab.* 2019.

Natalie Kofler, Kevin Esvelt et al. "Editing nature: Local roots of global governance." *Policy Forum. American Association for the Advancement of Science.* November 2018.

Winterberg, Susan, Carmel Shachar, Jeantine Lunshof, and Joshua Grolman. "Genome Editing." *Technology Fact Sheet Series. Technology and Public Purpose Project*. 2019.