TARGET MALARIA

The Science: What is gene drive?

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Gene drive is a genetic phenomenon that occurs in nature and causes a selected trait to spread rapidly through a species via sexual reproduction over several generations. Gene drive works by increasing the likelihood that a modified gene will be inherited by its offspring. Normally, genes have a 50/50 chance of being inherited, but gene drive systems could increase that chance to upwards of 99 percent. This means that over the course of several generations, a selected trait could become increasingly common within a specific species.

Researchers have been studying how to harness gene drives to solve some of society's most intractable problems for a long time. Public health and ecosystem conservation are two of the main areas where research has focused, although other uses are also possible.

What are gene drive applications in public health?

In public health, several proposals have been made which would use gene drive to limit the spread of diseases, particularly those spread by insect vectors, such as malaria, which affect several hundred million people a year. For malaria, this could be done by inserting a trait which makes the mosquitoes unable to host the malaria parasite, or one which affects the local population dynamics of the mosquitoes to reduce their numbers.

Gene drive approaches to vector control represent a potentially highly effective, long term and cost-effective tool that could, in the context of integrated approaches, help eliminate malaria.

How is Target Malaria using gene drive technology?

We aim to tackle malaria at the source. Target Malaria is using gene drive approaches to insert a modification in malaria mosquitoes that would affect the mosquito's ability to reproduce. By reducing the population of malaria mosquitoes, we aim to reduce the transmission of the disease.

Worldwide there are more than 3,500 species of mosquito, with 837 of them in Africa. Of these, a single cluster of three very closely related species are responsible for most of the malaria transmission – *Anopheles gambiae, Anopheles coluzzii* and *Anopheles arabiensis.*

The project is investigating the use of genes that produce enzymes (called nucleases) that cut specific sequences of DNA. The concept for these nucleases is based on Homing Endonuclease Genes (HEGs) which are a class of nuclease genes, found in simple single celled organisms, which are capable of copying themselves from one chromosome to another.

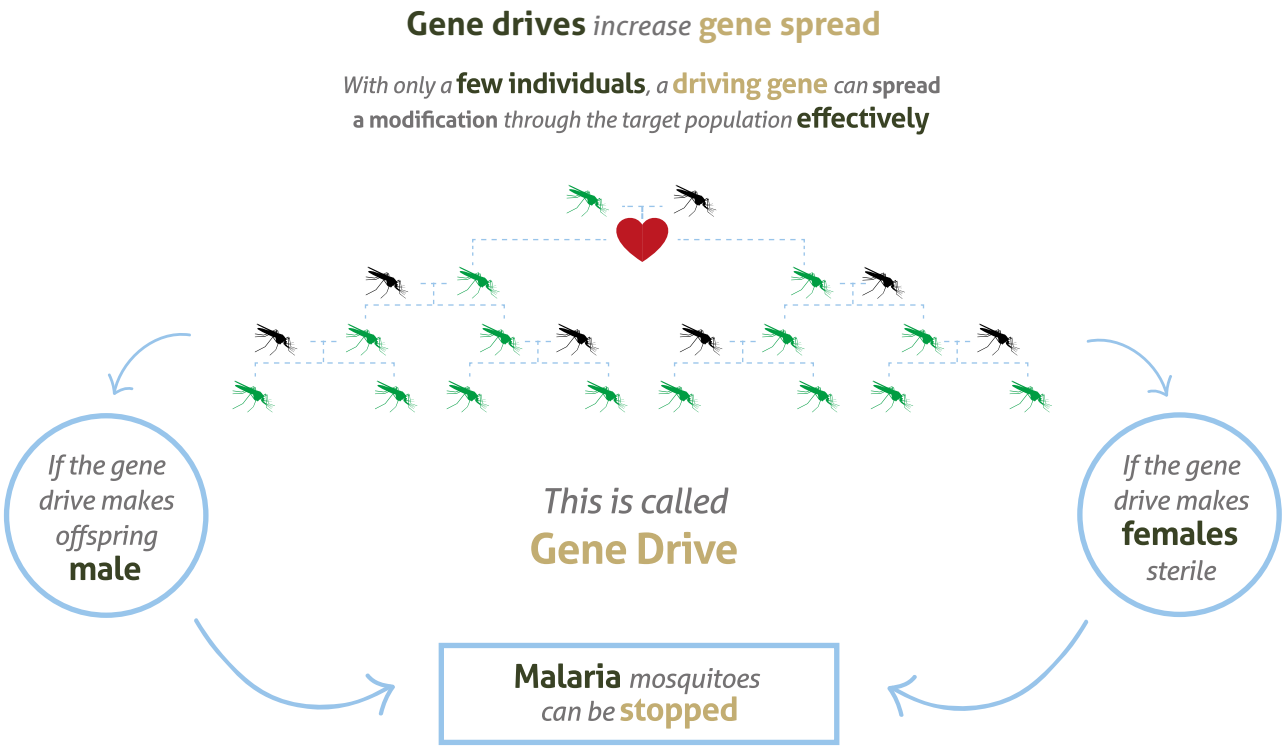
> **Two of the main areas we are currently focusing on are biasing the sex ratio of mosquito populations and reducing female fertility.**

When introduced in the malaria mosquito, the nuclease work by identifying and cutting through essential genes targeted by our researchers, such as fertility genes. The interrupted gene will no longer function, and modified mosquitoes will be affected according to the nature and importance of the gene.

The ultimate goal is to produce modified malaria mosquitoes that can pass these genes on to a disproportionately high percentage of their offspring, so the modification is spread throughout the specific population relatively quickly and is effectively "self-sustaining". This makes the reduction of the malaria mosquito vector population relatively cost effective and simple to implement because the mosquitoes themselves do the work.

What is the timeline for gene drive applications for malaria control?

Current research on gene drive is at an early stage, and so definitive decisions about gene drive-based products is premature at best. Based on current progress, products ready for field testing are 5 years out, possibly longer. This gives scientists and stakeholders, particularly those from countries where gene drives might one day be employed, time to consider the important questions of regulation, risk assessment, ethics, and engagement, and to prepare for assessing an actual application.



For more information go to our website:
www.targetmalaria.org/ourwork