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CAS9 Mediated Gene Drive Might be the Best Way to Eradicate Malaria Worldwide

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CAS9- MEDIATED GENE DRIVE MIGHT BE THE BEST WAY TO ERADICATE MALARIA WORLDWIDE

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ABSTRACT

Malaria is a disease caused by a protozoan parasite that is transmitted by the Anopheles female mosquito. Some parts of the world, such as the US, have successfully eliminated malaria, but malaria is still an enormous threat in many African countries. Although efforts exist to prevent and control the spread of malaria, the rate of death it causes is still higher in the poorest countries. The use of impregnated mosquito nets and insecticides do not seem to be enough to stop it. This review of the literature will discuss some genetic approaches to controlling mosquitoes. One such approach has been to release sterile male mosquitoes to suppress a population of mosquitoes. Another approach has been to release male mosquitoes that are carriers for a gene designed to cause flightless females. CRISPR/Cas9 gene-editing systems are powerful new tools to delete, replace, or insert specific DNA sequences in living organisms. The CRISPR technology also provides a way to create an effective gene drive, a technology that could be used to genetically modify an entire mosquito population. Advancements in genetic technology provide more powerful tools to combat disease vectors for a better world. However, there will be ethical, environmental, and political issues that must be considered since powerful genetic modifications will spread beyond national boundaries.

Before the Crisp/Cas9 technology, researchers have discovered many ways, natural and synthetic, such as the use of naturally occurring selfish elements to synthetic gene drives in mosquitoes, the use of the endosymbiont Wolbachia to gene drive in mosquitoes, and many more genetic techniques as ϕ C31, HEGs, ZFNs, TALENS, to eradicate and genetically modify mosquito population. Despite these strategies, researchers still lacked the ability to target specific sites in a mosquito genome. The use of Cas9 protein to gene editing in mosquitoes made mosquito gene-editing very cheap, more targeted, and more efficient. Cas9, defined in the reviewed article, is an endonuclease borrowed from the CRISPR biology of the bacteria *Streptococcus pyogenes*; and this endonuclease targets a specific location using a small guide RNA. This gene-editing is delivered to mosquitoes and other insects by the embryo injection.

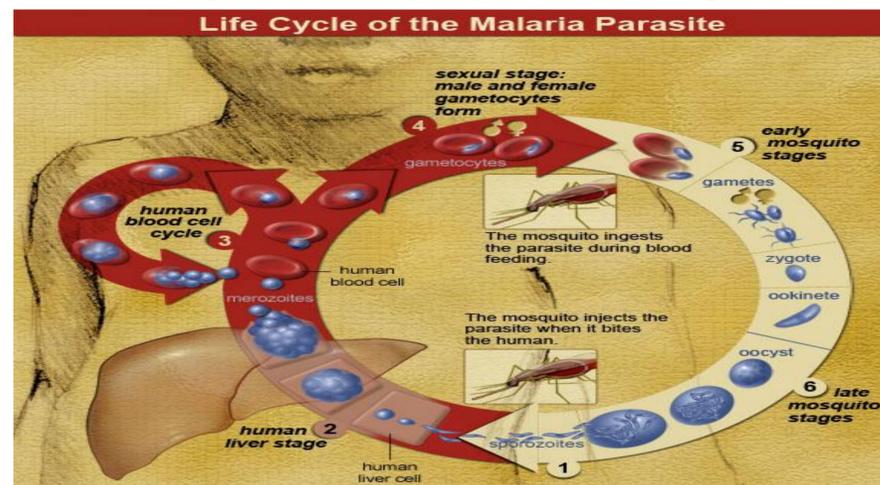


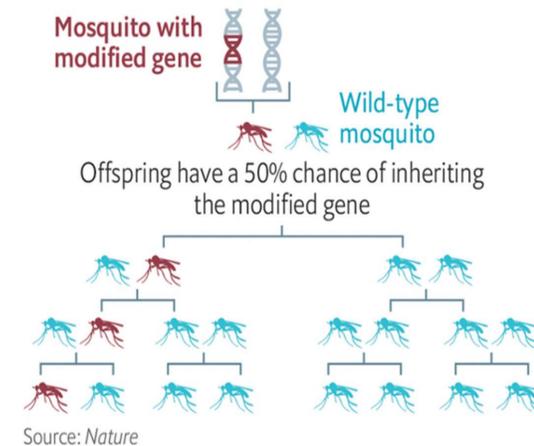
FIGURE 1. (from national Institute of Allergy and Infectious Diseases) Shows how Anopheles (female mosquito) transmits malaria to humans. Male mosquitoes don't bite and don't transmit the protozoan parasite that causes malaria.

Drive-by killing

How gene drives can quickly change whole populations

Normal genetic modification

A gene added to only one chromosome gets into half of offspring



Source: Nature

The Economist

Gene drive

A gene drive inserted into one chromosome copies itself into the other

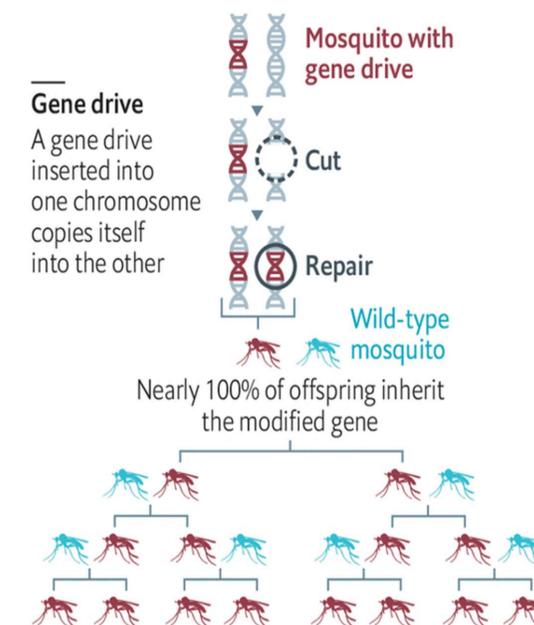


FIGURE 3.(from the Economist) Shows the difference between normal genetic modification and gene drive.

When gene drive is introduced, there is a 100 % chance that the offspring inherit the modified gene and will pass it more and more.

It has been demonstrated that the engineered mechanism of a gene drive by CRISPR/Cas9 worked successfully in mosquitoes and in many other insects/animals. Therefore, CAS9- mediated gene drive might be the best way to eradicate malaria worldwide.

CRISPR/Cas9 Gene drive

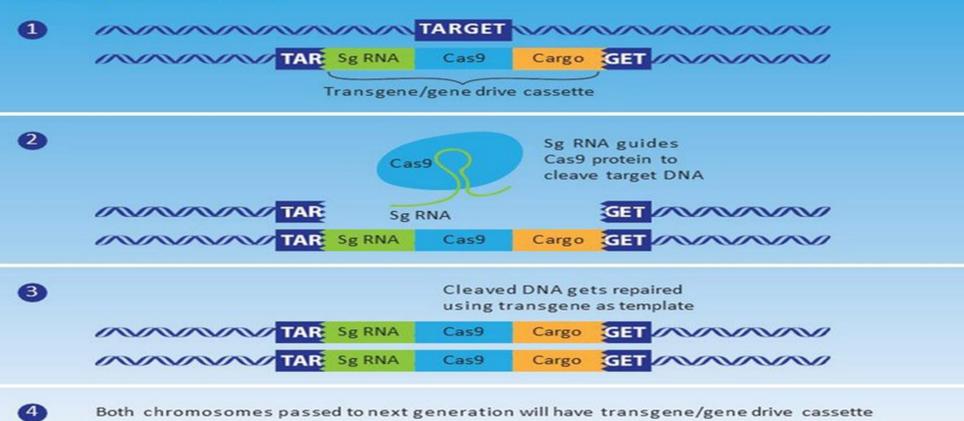


FIGURE 2. (from Australian Academy of Science) Shows how gene drive uses a targeted guide RNA to introduce a gene that encodes resistance to the malaria parasite in mosquitos. Cas9 is an endonuclease which cuts the DNA and cargo is the desired genetic material added. When all three elements are present in a gene drive cassette this ensures that each chromosome will have the desired cargo and will be inherited by the next generation thereby spreading the gene drive.

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