Potential Public Health Use of Gene Drive Approaches to Reduce Vector-Borne Disease

Gene Drives and Engineered Ecology
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FNIH
Foundation for the National Institutes of Health

Michael Santos, PhD
Associate Vice President, Science

Foundation for the National Institutes of Health

New tools are needed to stop vector-borne diseases

Vector-borne diseases kill 700,000 people per year

Over 200 million malaria cases per year, >90% in Africa

Existing tools are important but control is expensive

>$3B per year is spent on malaria control; still not enough

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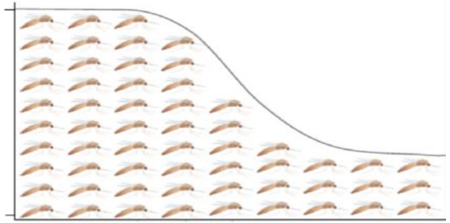
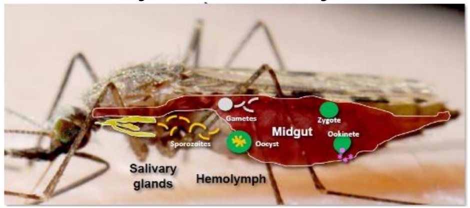
Gene drive approaches may help prevent disease

Less transmission of disease

Fewer vectors over time…

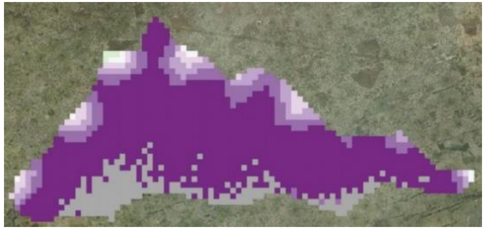


… or they can't carry disease



Spread through mating lowers costs

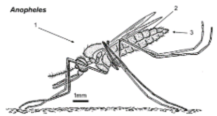
Simulated gene drive spread (purple)



~100 km

Gene drive is specific to vectors

Only 5 main species transmit malaria in Africa



3500 other mosquito species, millions of insect species

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Progress has been impressive; challenges remain

Progress	Challenges
Gene drive demonstrated in malaria vectors in the lab	Translation of lab results to a wide range of environments
Lab mosquito populations suppressed or altered to prevent disease transmission	Potential persistence and/or spread of field studies
Burkina Faso approved genetically sterile male mosquitoes for study	Adapting legal and policy frameworks developed for crops to vectors

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Risks are being systematically identified and assessed

Goal and risk identification

Systematic risk assessment

TABLE 2

Some considerations for possible effects of *Anopheles gambiae* containing gene drive constructs, extrapolated from consideration of biocontrol agents on nontarget species

Potential effect	Concern	Relevance for *An. gambiae*	Trigger for concern
First-order genetic	Construct might spread to a second species through interspecific mating.	May be anticipated and a deliberate part of the implementation strategy—for example, a gene introduced into *An. gambiae* s.s. is expected to spread into closely related vector species such as *Anopheles coluzzii* or *Anopheles arabiensis*. This would be useful for preventing malaria transmission by a second malaria vector, but the possibility of more distant gene transfer through interspecific mating also must be considered in risk assessment	Genetic evidence for low-frequency intraspecific mating outside the *An. gambiae* complex
Second-order genetic	Construct might spread through some other, non-mating, process to a second species	For example, the construct might move into a mobile genetic element that could be transferred through a microbial vector	Genomic evidence for the transfer of genetic material between mosquitoes and distantly related species
First order ecological	Removal of a species from a community might harm species that directly feed on it or which rely on the species for pollination.	The extent to which a predator or plant relies on *An. gambiae*. The harm done to *Plasmodium* through the removal of its vector is an example of a deliberate, anticipated, and beneficial first order ecological effect, but the possibility of detrimental effect on other, more valued, species also should be considered	Evidence that *An. gambiae* s.l. makes up a considerable fraction of the diets of specific predators in the same ecosystem, or that particular plants are largely pollinated by these species
Second order ecological	An indirect ecological effect resulting from removal of a species allows an increase in the density of another species (or resource) on which it fed (first order effect), which in turn allows a competitor species to increase in density by utilizing the unused resource	Removal of *An. gambiae* might result in increased abundance of another species, with detrimental effects	Presence in the same larval habitats as *An. gambiae* of other species of mosquito that share the same food source and pose a worse threat to human health; evidence of indirect ecological effects, including adaptation of the malaria parasite that have arisen after other successful interventions that have reduced *An. gambiae* density (such as bed nets)
Higher order ecological	An ecological perturbation causes further effects that ripple through the ecological community, and which are amplified rather than being damped	Addition or removal of a keystone species have major effects in ecological communities	A plausible mechanism based on comparative ecological studies showing how *An. gambiae* could act as a keystone species

Our goal is to provide new <u>options</u> for disease control

Inputs	Informed decisions	Results
Scientific and technical understanding (lab, field, modeling, strategy)	Regulatory and policy decisions at the national, regional and local levels	Improved disease control and elimination with fewer resources