Generation game: Gene-edited mosquitos to fight malaria

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Population-level changes in the genetic make-up of one of the world's deadliest animals could provide a key in the fight against malaria, proponents of a radical new technology argue.

So-called gene drive technology, where genetic changes are passed down through generations, could rein in mosquito populations, or prevent them from passing on malaria.

"Through genetic engineering, researchers have modified mosquitoes to favor the inheritance of genes that either will reduce the size of the population of those mosquitoes or stop them from transmitting the malaria parasite," Michael Santos, senior vice-president and chief population health sciences officer at the US-based charity the Foundation for the National Institutes of Health (FNIH), tells SciDev.Net.

"In other words, [it is about] using mosquitoes to control mosquitoes."

Malaria is one of the world's "big three" deadly diseases, killing over half a million people in 2021, the vast majority in Africa.

Santos tells SciDev.Net in an interview that gene drive technology could complement other tools used for controlling malaria such as seasonal malaria drugs, vaccines and rapid diagnostic tools.

"The concept of using gene drive [technology] to prevent the spread of mosquito-borne diseases is over 80 years old, and recent advances in genetic engineering technologies, especially CRISPR-Cas9 [a technology used in editing the complete set of DNA] approaches, made it easier for researchers," Santos explains.

Santos, who is also the director of the GeneConvene Global Collaborative, an initiative of the FNIH that supports informed decision-making about genetic biocontrol approaches for public health, says that mosquito control is one of the most effective ways to reduce the burden of malaria and other mosquito-borne diseases.

Stalled

"For many years, the burden of malaria was declining, but in the last few years, progress has stalled," he says.

"Part of the challenge to continued progress is that malaria mosquitoes are increasingly resistant to the insecticides that are used to control them."

Another part of the challenge is sustaining the financial resources, he adds. The WHO estimates that over US$7 billion per year is required to achieve the global goals for reducing malaria. However, in 2021 just half the amount was spent in fighting malaria, Santos tells SciDev.Net.

He says that working with stakeholders to identify the main questions in the field and bringing people together to help address them is key to aiding gene drive advocacy.

"We worked with the WHO Special Programme for Research and Training in Tropical Diseases to provide an updated second edition of the gene drive guidance framework in 2021 to reflect advances in the field," he explains.

"The framework helps inform researchers and stakeholders on a range of important questions for the development of genetically modified mosquitoes, including evaluating safety and efficacy and ethical and regulatory considerations."

Genetic approaches are species-specific because they work through mating. A handful of mosquito species (out of more than 3,000) are responsible for most malaria transmission, and one of the advantages of gene drive technology and other genetic approaches is the potential to target those few mosquito species directly, Santos says.

Another advantage is cost. For example, in laboratory cage experiments, a small number of modified mosquitoes can spread genes through the entire cage population.

"If gene drives perform like this in the wild, the cost of releasing a small number of gene drive–modified mosquitoes may be small compared to the impact after those genes spread through the wild population," Santos explains, adding that gene drives could be used to reverse insecticide resistance.

Biosafety

Santos says that assessing risks and benefits is an important part of the evaluation of new technologies, and gene drive approaches for malaria would generally be evaluated by both biosafety regulators for their safety as GMOs, and by health authorities for their safety and efficacy as public health tools.

He adds: "Many countries also require broader impact assessments that include potential economic and social risks and benefits.

"Risk assessment is a rigorous process that identifies valued goals (such as biodiversity, human health and, animal health), maps potential pathways to adverse impacts on those valued goals, and assesses likelihood for each path."

Santos further explains that risk assessment is done on a case-by-case basis because it is specific to the technology and location. National regulatory authorities decide whether risks are acceptable and specify the risk management activities that are required.

"The potential risks depend on the gene drive approach and the context it would be used in. No gene drive project has advanced to intended

release yet, so we don't know what risk will be identified by that process."

He adds that GeneConvene supports risk assessment through awareness-raising, capacity-strengthening, and funding third-party risk assessments.

Burkina Faso

The African Union, as part of its malaria strategy, has endorsed the evaluation of gene drive approaches for malaria and instructed the African Union Development Agency-NEPAD (AUDA-NEPAD) to support member states to build capacity to rigorously evaluate these technologies.

"With the support of AUDA-NEPAD, the West African region assembled a steering committee to foster collaboration and build capacity," Santos says.

According to Santos, Burkina Faso approved the pilot study using male mosquitoes which had been genetically modified to make them sterile.

The study was published as a report in October 2022 by Target Malaria, a not-for-profit research consortium which aims to create new, cost-effective and sustainable genetic technologies to control malaria transmission.

"When these non-gene drive sterile male mosquitoes mate with females, the eggs laid by the females do not hatch," the study says.

Santos says that despite the potential benefits of using gene drives for malaria control, the acceptance of the technology is a challenge.

"To have an impact, gene drive development needs to be scientifically

successful—the engineered mosquitoes need to perform as expected in the wild—and countries need to decide to use gene drive approaches. country's decisions may also be motivated by policy recommendations by organizations such as WHO and the Africa Union and on financial support from organizations such as Global Fund," Santos adds.

But the WHO and many others support the rigorous evaluation of all potential new tools to fight malaria, he adds.

"With sufficient innovation, advocacy and commitment, malaria eradication should be possible," Santos says.

Provided by SciDev.Net

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