

Genetically modified mosquitoes and malaria in Africa: Top scientist shares latest advances

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Every year, mosquitoes kill more people than any other animal. According to the <u>World Malaria Report (2023)</u>, the African continent bears the brunt of the most deadly mosquito-borne disease, malaria.



Africa has 94% of the cases and 95% of the deaths.

One tool that's being considered in the fight against <u>malaria</u> is genetic modification.

Several research projects around the world are looking to use genetically modified <u>mosquitoes</u> to stop the spread of malaria in Africa. Abdoulaye Diabaté, a medical entomologist and leading malaria researcher, is at the forefront of some of this work. He shares insights into how the technology operates and the research he's working on.

What drove you to focus your work on malaria?

I was born in N'Dorola, a province in western Burkina Faso, where malaria comes back every rainy season. Malaria is endemic and all the population is at risk of getting infected. I was lucky to survive malaria when I was 3 years old; unfortunately, two of my close cousins did not.

Most families in Africa will have, or know of, a tragic malaria story. The region carries a high share of the global malaria burden. There were <u>half</u> a <u>million deaths</u> in Africa in 2022, with children and pregnant women most at risk of <u>infection</u> and death. <u>A child dies from malaria every</u> <u>minute</u>.

This is a major reason I do the work I do. I lead the Target Malaria team—a research consortium aimed at reducing the population of malaria-transmitting mosquitoes in sub-Saharan Africa. We are based at the Research Institute in Health Sciences (Institut de Recherche en Science de la Santé, or IRSS), in Bobo-Dioulasso.

Our research focuses on the potential of innovative genetic technologies.

Malaria is a preventable disease and yet so many lives are still lost.



Why is genetic technology useful against malaria?

Worldwide there are more than <u>3,500 species of mosquito</u>, with over 800 of them in Africa. Of these, three very closely related species <u>are</u> <u>responsible</u> for most of the malaria cases: Anopheles gambiae, Anopheles coluzzii and Anopheles arabiensis.

The <u>genetic modification</u> of mosquitoes has the potential to be a powerful ally in the fight against malaria. Technologies are being developed that could help reduce the number of mosquitoes that carry malaria—by making them less fertile, for instance. By reducing the population of mosquitoes, we hope to reduce malaria transmission.

In 2019, our team <u>released</u>, in Burkina Faso, male mosquitoes which we had <u>genetically modified to be sterile</u>. It was the first time this ever happened in Africa.

The sterile males can mate with wild females but cannot produce offspring. We did this by introducing a gene that prevented fertilized eggs from hatching.

This small-scale release was not intended as a malaria control measure. It provided an essential learning opportunity for our team to gather information for future projects. The scientific data we collected has played a crucial role in the successful advancement of our next phases.

How does your work aim to reduce malaria?

My work focuses on a strategy called "population suppression." The objective is to reduce the population of malaria mosquitoes sufficiently to stop the transmission of the disease.



We are investigating various approaches using a "gene drive" strategy. "Gene drive" is a genetic engineering technique designed to increase the likelihood that a specific gene, or set of genes, will be passed on to <u>future generations</u> at a higher rate than would normally occur through traditional inheritance.

Our work aims to increase 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%. This means that over the course of several generations, a selected trait could become increasingly common within a specific species.

One of our most promising projects aims to modify mosquitoes with a gene drive that makes females sterile. We can spread this modification through the target population by releasing a small number of gene-drive mosquitoes. These mosquitoes could mate with wild mosquitoes, passing on the modified gene to their offspring. Only when both mosquito parents carry the modified gene will their offspring be sterile.

There are several reasons why using genetically modified mosquitoes is more effective than other malaria control tools: the local population do not need to change their behavior, do not need to buy equipment and do not need to depend on health systems.

Because it is an environmental intervention, the mosquitoes spread on their own, effectively doing the work for us.

Another future project that we're working on is the release of non-genedrive genetically modified male mosquitoes which carry a gene with a "male bias." This means they've been modified to produce almost only male offspring.



In the future, we hope to be able to test our final technology, gene drive mosquitoes, by conducting <u>experimental field trials</u> in Africa. However, gene drive mosquitoes have never been tested in the field before and are currently not in any of our insectaries in Africa.

How far along is your research?

We have a gene drive mosquito in our labs in Europe with a modified gene that affects female fertility, which is currently undergoing efficacy and safety studies. It will take a few more years to complete our studies. We would then seek permission from regulatory authorities to conduct experimental field trials.

The most immediate next phase of our work in Burkina Faso is focused on non-gene-drive genetically modified male bias mosquitoes. We submitted a regulatory dossier to conduct a controlled field release of this strain in the next two years. These mosquitoes will not have an impact on malaria, because they won't carry the <u>gene-drive</u> technology and are fertile, but it is an important learning step. We hope further field evaluations may happen within the next five years.

What about unintended consequences of gene editing?

In the last five years, Target Malaria has partnered with the University of Ghana and the University of Oxford to conduct ecological studies to find out the exact role of <u>Anopheles gambiae</u> in their ecosystems and answer some fundamental questions: are they a keystone species in their ecosystem? Are they a key part of their predators' diet? Are they pollinators?

We have not yet published the result of this work, but the data collected indicates that these mosquitoes play a very marginal role in the



ecosystem. In Africa alone there are over 800 species of mosquitoes. We are planning to target very few: the ones responsible for transmitting malaria to humans.

Our goal is a world free of malaria. We consider risks very seriously and we are looking at all possible outcomes in our <u>risk assessments</u>.

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