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Sickly mosquitoes stymie malaria's spread

Researchers harness bacteria to cripple insects that transmit disease.

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Scientists have engineered mosquitoes to carry a bacterium that confers resistance to the malaria parasite — a long-sought advance that could eventually curb malaria cases in humans.

CDC

The mosquito *Anopheles stephensi* is a conduit for malaria infection in humans in the Middle East and South Asia.

A team led by Zhiyong Xi, a medical entomologist at Michigan State University in East Lansing, infected *Anopheles stephensi* mosquitoes with *Wolbachia* bacteria to produce insects that could pass the infection on to their offspring. Female mosquitoes that carried *Wolbachia* also bred with uninfected mates, the researchers report today in *Science,* swiftly spreading the malaria-blocking bacterium to entire insect populations within eight generations[1].

"This is the first paper reporting that it is indeed possible to use *Wolbachia* to control malaria," says geneticist Steven Sinkins of the University of Oxford, UK. But he cautions that field trials will be the real test of this advance.

Wolbachia has already been used to block mosquitoes' ability to transmit other human pathogens. For instance, scientists have created heritable infections in *Aedes aegypti* mosquitoes that stop the insects from transmitting dengue virus[2]. But manipulating those mosquitoes that carry the malaria parasite exclusively — from the genus *Anopheles* — has proved trickier.

Sensitive types

Anopheline mosquitoes are highly sensitive to their environment and prefer conditions that can be difficult to reproduce in a laboratory setting. Moreover, scientists have had a hard time identifying which strains of *Wolbachia* would produce a stable infection in those mosquito species.

"Researchers had been left wondering if anopheline mosquitoes were physiologically able to support *Wolbachia*," says Scott O'Neill, dean of science at Monash University in Melbourne, Australia, who directed the team that found *Wolbachia* could help to stem the transmission of dengue fever.

The successful combination found by Xi and his colleagues pairs the anopheline species that does best in lab conditions — *A. stephensi*, a carrier of malaria in the Middle East and south Asia — with a *Wolbachia* strain known to infect an *Aedes* mosquito. The researchers injected bacteria into hundreds of mosquito embryos before identifying one female that survived to pass on her infection to future generations bred in Xi's lab.

Her descendants overtook populations that were not infected with *Wolbachia* when researchers introduced a few infected females and a large number of infected males to uninfected mosquito populations. Female mosquitoes laid infected eggs, while male mosquitoes infected with *Wolbachia* could breed successfully only with infected females. (If males mate with uninfected females, the resulting offspring will die before they can hatch.)

Those mosquitoes can also fend off *Plasmodium falciparum*, the parasite that causes malaria, researchers found. *Wolbachia*-infected mosquitoes that were fed mouse blood that contained *P. falciparum* later carried up to 3.4 times lower levels of the parasite in their salivary glands, compared with uninfected mosquitoes that were fed the same diet.

Together, these findings suggest that in the wild, Wolbachia-infected mosquitoes that are resistant to malaria infection could potentially replace natural populations of mosquitoes that carry the parasite. Eventually, this might even reduce the transmission of malaria to humans.

Researchers are not sure how *Wolbachia* manages to boot out other pathogens, but they suspect that the bacteria create toxic environments within the mosquito, possibly by activating the insect's immune response. Indeed, Xi and his team found that the tissues of their infected mosquitoes contained more reactive oxygen species — which inhibit pathogens such as *P. falciparum* — than insects that were uninfected with *Wolbachia.*

Now, with the hope that the stably infected line of mosquitoes could stem malaria spread, Xi and his colleagues are working to test them in places ravaged by malaria. The best part of this control strategy, Xi says, is that "once it is deployed in an area, everyone will benefit — no matter if you're rich or poor".

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References

1. Bian, G. *et al*. *Science* **340**, 748–751 (2013).
2. Hoffmann, A. A. *et al*. *Nature* **476**, 454–457 (2013).