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New tool in the fight against mosquito-borne disease: A microbial 'mosquito net'

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Earlier this year, researchers showed that they could cut the lives of disease-carrying mosquitoes in half by infecting them with a bacterium they took from fruit flies. Now, a new report in the December 24th issue of Cell, a Cell Press publication, suggests that their strategy might do one better: The Wolbachia bacteria also makes the mosquitoes more resistant to infection by viruses that are a growing threat to humans, including those responsible for dengue fever and Chikungunya.

Once infected with Wolbachia, *Aedes aegypti* mosquitoes also become less suitable as hosts for a form of malaria parasite that infects birds, said Scott O'Neill of The University of Queensland. (The mosquitoes under study aren't natural carriers of human malaria.)

"This might be very powerful in reducing pathogen transmission by *Aedes aegypti* to humans, particularly for dengue and Chikungunya," O'Neill said. "Together with the previously described life-shortening effects, the results suggest we might be able to have a major impact on disease." That's if it can be shown that the Wolbachia infection can invade natural mosquito populations, he added, a question his team is working on right now.

There is no vaccine or cure for dengue fever, which is a painful and debilitating disease suffered by some 50 million people worldwide every year. Dengue haemorrhagic fever, the more severe form of the disease, kills more than 40,000 people annually. Chikungunya usually isn't fatal, but can cause symptoms similar to dengue. Human epidemics of

Chikungunya have been cited in Africa, Asia and more recently in Europe, according to the CDC.

Wolbachia is already rampant in nature; the bacterium is estimated to infect up to 60 percent of all insect species. They are passed from mother insect to daughter or son through the insect egg and readily spread to high frequency in many species of mosquito. The species that are the major carriers of human disease don't normally carry them, but that's something O'Neill aims to change.

"We are currently conducting a series of experiments in contained outdoor greenhouse settings that are examining the ability of the Wolbachia infection to spread into natural mosquito populations," he said. "If these prove successful, we hope to move to open field testing within the next one to two years."

The idea would be to seed the natural mosquito population with Wolbachia by releasing mosquitoes that had been purposefully infected in the laboratory. Wolbachia bacteria have a good 'trick' to help ensure their spread, O'Neill explained. They are responsible for a developmental defect that makes the would-be offspring of pairings between infected male mosquitoes and uninfected females inviable. Since the bacteria is passed from mothers to their offspring, that means that infected females can actually have a reproductive advantage over uninfected ones, encouraging Wolbachia's spread from one generation to the next.

O'Neill said his team is working on computational models to determine just how many infected mosquitoes would need to be released for the infection to take hold in the wild.

The researchers don't yet know exactly how Wolbachia protects the insects from human disease-causing viruses. They have some evidence to

suggest that the bacterial symbiont primes the insects' immune system. Wolbachia may also outcompete the virus by limiting resources such as fatty acids inside the mosquitoes.

Even if the strategy works in a natural setting, there's a chance the mosquitoes or the viruses could become resistant to Wolbachia's influence over time.

" We can predict from evolutionary theory that selection will push the system in the direction of resistance, but we do not know the speed with which this might occur," O'Neill said. "Even if it was effective for a few decades it might have a major impact on human disease."

Provided by Cell Press

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