New research predicts stability of mosquito-borne disease prevention

26 August 2019

The team discovered a gene within A. aegypti that is likely involved in Wolbachia's ability to interfere with viral replication, shedding light on a possible mechanism for the blocking trait. Credit: Dan Lesher, Penn State

To reduce transmission of dengue to humans, scientists have introduced Wolbachia bacteria to *A. aegypti* mosquitoes. Now a team of international researchers has found that Wolbachia's ability to block virus transmission may be maintained by natural selection, alleviating concern that this benefit could diminish over time.

"The results of our study have significant implications for the continued use of Wolbachia as a biocontrol agent for this disease," said Elizabeth McGraw, professor and Huck Scholar in Entomology at Penn State, and formerly a professor at Monash University.

The team also discovered a gene within *A. aegypti* that is likely involved in Wolbachia's ability to interfere with viral replication, shedding light on a possible mechanism for the blocking trait.

According to McGraw, Wolbachia bacteria occur in many insects, including some mosquitoes, but they do not naturally occur in *A. aegypti*, the mosquito species that transmits dengue virus. The bacteria were introduced to *A. aegypti* in 2011 and since have been released in trials in several countries, including Australia, Brazil, Colombia, Vietnam and Indonesia, to assess the ability of the bacterium to control the spread of disease.

To investigate the stability of Wolbachia as a virus blocker within *A. aegypti*, McGraw and her colleagues used artificial selection in the laboratory to select for high and low dengue blocking abilities in *A. aegypti*. Next, they sequenced the genomes of these two groups, identified areas that differed and measured the insects' fitness—or ability to survive and reproduce. The team's results appear today (Aug. 26) in *Nature Microbiology*.

"There has been concern that dengue virus could evolve an ability to sneak past Wolbachia or that the insects themselves could evolve resistance to Wolbachia," said McGraw. "We found that mosquitoes exhibiting better blocking had increased fitness, at least under idealized conditions in the laboratory, suggesting the potential for natural selection to maintain blocking."

By comparing the genomes of high and low dengue blockers, the team identified a specific gene—AAEL023845, a cadherin protein—that likely is involved in virus blocking.

Researchers have found that Wolbachia bacteria's ability to block transmission of dengue virus may be maintained by natural selection, alleviating concern that this benefit could diminish over time. Credit: Dan Lesher, Penn State

"We found that much of the genetic variation determining Wolbachia's anti-viral effect was within a mosquito gene controlling cell-to-cell adhesion," said Suzanne Ford, postdoctoral researcher at the University of Oxford and former postdoctoral scholar in entomology at Penn State. "Increased expression of this gene was associated with increased Wolbachia-mediated protection against viruses."

According to McGraw, a previous theory suggested that Wolbachia, as a foreign substance within mosquitoes, could be triggering the insects' immune systems, which in turn, could suppress virus activity. Another theory suggested that Wolbachia could be competing with viruses for nutrients or physical space within mosquitoes.

"Our data do not support either of these theories," said McGraw. "Instead, our results suggest that the cadherin gene may affect cell-to-cell signaling or movement of viruses within cells, altering the virus's ability to enter cells, replicate within them and then exit."

McGraw noted that researchers in the field have long struggled with the concept of Wolbachia-mediated blocking—what it is and how it works.

"Our findings give us a new direction to study with respect to the basis of Wolbachia's blocking of dengue virus," she said.

Ford added that the research is important to understanding the long-term stability of Wolbachia as a biocontrol agent against mosquito-borne viruses.

"By defining this mechanism and understanding how selection might act upon it," said Ford, "we will be better able to predict how effective Wolbachia will be as a biocontrol agent."

More information: Selection on Aedes aegypti alters Wolbachia-mediated dengue virus blocking and fitness, *Nature Microbiology* (2019). DOI: 10.1038/s41564-019-0533-3, https://nature.com/articles/s41564-019-0533-3

Provided by Pennsylvania State University