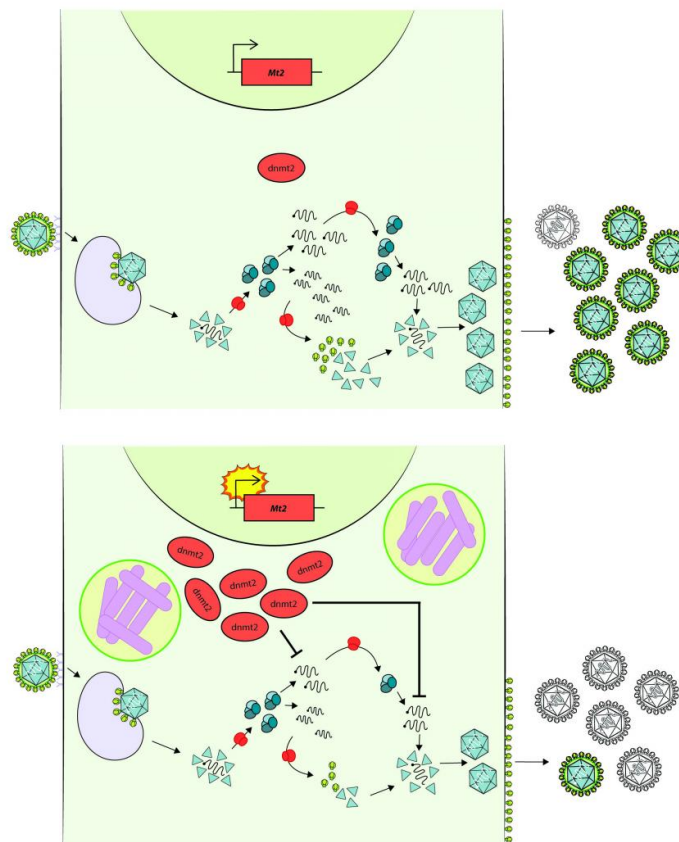


Scientists reveal mechanism behind mosquito-borne-disease 'blocker' used to fight viruses

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This study found the introduction of *Wolbachia* bacteria (in purple) into insect cells, shown in the lower image, increased production of the gene *Mt2*, which reduced the ability of viruses (in blue) to reproduce. The new viruses produced were also less able to cause infection (shown as colorless viruses). Credit: Tamanash Bhattacharya

A new study from Indiana University may explain how a bacterium called *Wolbachia* prevents mosquitoes from transmitting deadly diseases such as dengue fever, West Nile virus and Zika.

Published today in the journal *PLOS Pathogens*, the study is one of the first to identify a specific biological mechanism that prevents mosquitoes infected with this bacterium from transmitting diseases to humans. It could also potentially open a path toward methods to block disease transmission without *Wolbachia*, an organism whose long-term effect on the environment is unknown.

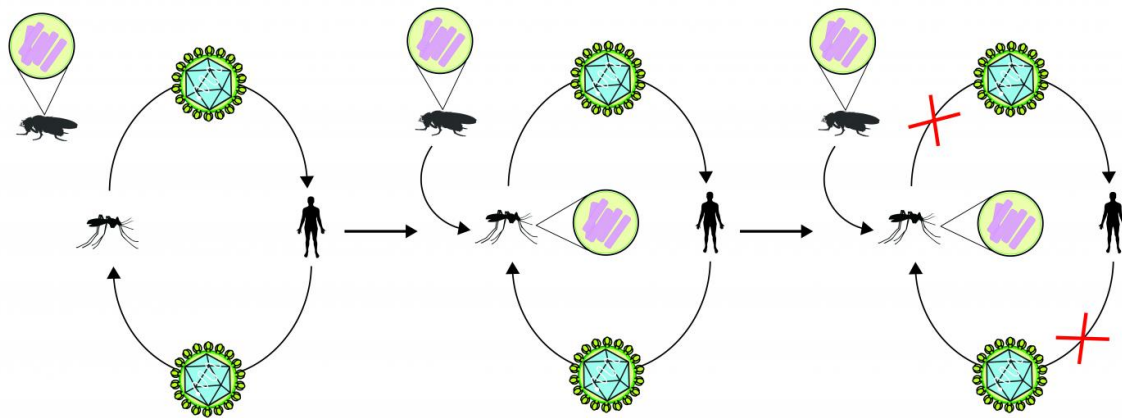
"There's a real argument that some parts of the world are so strongly affected by these diseases that we need to try everything we can right away," said Irene Garcia Newton, assistant professor in the IU Bloomington College of Arts and Sciences' Department of Biology, who led the study. "But you've also got to remember that we're releasing insects into the wild that could potentially spread all over the planet very quickly, so it's important to move cautiously."

The use of *Wolbachia*-infected mosquitoes to curtail the spread of human diseases—a method called "pathogen blocking"—has already been implemented in some parts of the world. This includes the recent release of these mosquitoes in Florida to block the spread of Zika.

The spread of other insect-borne diseases is also expected to rise significantly in North America over the next several decades due to environmental change, according to the Centers for Disease Control and Prevention. Other viruses whose transmission is blocked in *Wolbachia*-infected mosquitoes include chikungunya, yellow fever and West Nile.

To explore the biological mechanisms behind pathogen blocking, Newton and colleagues designed a model system consisting of *Wolbachia*-infected [fruit flies](#) and the Sindbis virus, which is easier—and safer—to manipulate in the lab than infectious agents such as the Zika or West Nile viruses.

"We've got a lot of genetic tools for Sindbis virus and fruit flies," said Richard Hardy, professor in the IU Bloomington Department of Biology, who is a co-author on the study. "This means we're able to label different parts of the virus genome and track replication of its RNA inside the host insect."



This illustration shows how the transmission of *Wolbachia* bacteria (in purple) from fruit flies to mosquitoes appears to block the transmission of viruses (in blue) to humans. Credit: Tamanash Bhattacharya

Based upon a comparison of *Wolbachia*-infected versus uninfected fruit flies, the scientists found that flies with the bacterium produced significantly higher levels of Mt2, a gene that encodes a type of enzyme known as a methyltransferase.

They then used genetic tools to create two types of fruit flies: one that lacked this enzyme and another that produced unusually high levels of it.

The flies without the enzyme lost their ability to "block" the transmission of the Sindbis virus after infection with *Wolbachia*. The flies that produced high levels of the enzyme were resistant to the Sindbis virus—even if they weren't infected with *Wolbachia*.

"The fact that flies with high expression levels of this enzyme were protected against virus infection despite the absence of *Wolbachia* is very significant," said Tamanash Bhattacharya, an IU Ph.D. student who is first author on the study. "These results suggest that the methyltransferase Mt2 alone is sufficient to create a virus protection effect."

Moreover, this protective effect likely applies to the transmission of other deadlier viruses, not only the Sindbis [virus](#). The lack of genetic similarities between viruses blocked by *Wolbachia* suggests that the bacterium blocks viruses through effects on the host.

There are a number of reasons scientists are interested in pursuing methods of pathogen-blocking without *Wolbachia*, Newton added. The widespread release of *Wolbachia*-infected mosquitoes could potentially trigger the rise of viruses resistant to the bacteria, for example.

There is also a lack of large-scale epidemiological studies to scientifically determine whether pathogen-blocking actually prevents outbreaks.

"Right now, we know only that mosquitoes infected by *Wolbachia* don't transmit diseases—but we don't really know how," Newton said. "If we don't understand the biological mechanisms behind pathogen blocking, we can't really know what will happen over the long term when we release these [mosquitoes](#)."

More information: *PLOS Pathogens* (2017). [DOI: 10.1371/journal.ppat.1006427](#)

Provided by Indiana University

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