Common fungus helps dengue virus thrive in mosquitoes

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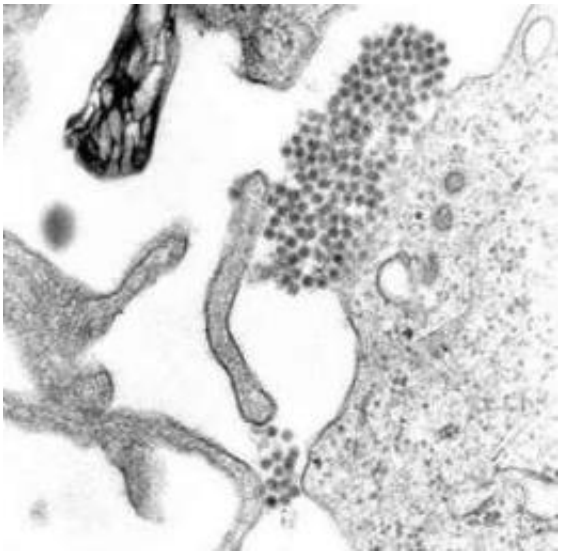

A TEM micrograph showing Dengue virus virions (the cluster of dark dots near the center). Image: CDC

A species of fungus that lives in the gut of some *Aedes aegypti* mosquitoes increases the ability of dengue virus to survive in the insects, according to a study from researchers at Johns Hopkins Bloomberg School of Public Health. The fungus exerts this effect by reducing the production and activity of digestive enzymes in the mosquitoes.

The discovery, reported this week in *eLife*, illuminates a biological mechanism that could turn out to be a general indicator and modifier of

dengue transmission risk in the wild.

"If this common fungus proves to have a significant impact on mosquitoes' ability to transmit dengue virus to people in endemic areas, then we can start to think about ways to translate this knowledge into specific anti-dengue strategies," says George Dimopoulos, PhD, professor in the Bloomberg School's Department of Molecular Microbiology and Immunology.

Scientists have estimated that hundreds of millions of people suffer dengue virus infections—known as "dengue fever"—in tropical regions each year. Dengue infections can involve severe joint and muscle pain and have also been termed "breakbone fever." Although most cases are mild enough that they are never clinically reported, some take a severe hemorrhagic form that require hospitalization and are often fatal.

Dimopoulos and colleagues have discovered certain bacterial species that can live in mosquitoes and affect the insects' ability to transmit dengue and other diseases. In a recent field project in Puerto Rico, as they reported last year, they also discovered a fungus that lives in the gut of *Anopheles* mosquitoes and affects the insects' susceptibility to malaria parasites. In the new study, which stemmed from the same field project, Dimopoulos's team isolated a different type of fungus, from a species called *Talaromyces*, from the gut of dengue-carrying *Aedes aegypti* mosquitoes.

The scientists fed spores of the fungus to *Aedes* mosquitoes via a sugar solution prior to a blood meal laced with dengue virus, and found that mosquitoes harboring the fungus were more likely to become infected by the virus. The dengue-infected mosquitoes that harbored the fungus also tended to have more dengue virus particles in their gut—meaning that the virus could survive and make copies of itself more easily when the fungus was present.

The researchers then showed that this dengue-enabling effect was due to molecules that are secreted by fungal cells and reduce the activity of mosquitoes' digestive enzymes. The process blocks the activity of genes that encode these enzymes, and also directly inhibits the protein-breaking biochemical activity of some of the enzymes.

"This finding tells us that the protein-digesting activity of the mosquito gut can influence the success of dengue virus in establishing infection in the mosquito," Dimopoulos says. "The virus has a protective envelope called a capsid that is protein-based, so it is possible that this capsid is susceptible to some of these mosquito-gut enzymes."

He notes that although many mosquito species feed on human blood, most are not infected by or don't transmit dengue virus—for reasons that researchers have never fully understood. "It is possible that some of these incompatibilities between mosquitoes and dengue virus relate to this enzyme activity in the mosquito gut that can be modulated by fungi and other microbes," Dimopoulos says.

Talaromyces fungi are common, he adds, and are likely to be found in *Aedes* mosquitoes not just in Puerto Rico but globally, although further field studies are needed to demonstrate their influence over dengue transmission to human populations.

If the fungus does have a significant real-world impact, then in principle the presence or absence of the fungus in mosquitoes could be used as a simple marker of local transmission risk. "One also can imagine, for example, anti-fungal solutions being added to the breeding water or to artificial feeding stations to reduce local dengue transmissibility," Dimopoulos says.

"An *Aedes aegypti* -associated fungus increases susceptibility to dengue virus by modulating gut trypsin activity" was written by Yesseinia

Angleró-Rodríguez, Octavio Talyuli, Benjamin Blumberg, Seokyoung Kang, Celia Demby, Alicia Shields, Jenny Carlson, Natapong Jupatanakul, and George Dimopoulos.

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