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Mosquito virus could lead to new vaccines and drugs

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A mosquito sample collected three decades ago in Israel's Negev Desert has yielded an unexpected discovery: a previously unknown virus that's closely related to some of the world's most dangerous mosquito-borne pathogens but, curiously, incapable of infecting non-insect hosts.

Researchers believe this attribute could make the Eilat virus a uniquely useful tool for studying other alphaviruses, a genus of largely mosquito-borne pathogens that includes the viruses responsible for chikungunya, Venezuelan equine encephalitis, western equine encephalitis and eastern equine encephalitis. In addition, the researchers say, Eilat could also aid in the development of new alphavirus vaccines, therapies and diagnostic techniques.

"This virus is unique—it's related to all of these mosquito-borne viruses that cause disease and cycle between mosquitoes and animals, and yet it is incapable of infecting vertebrate cells," said University of Texas Medical Branch at Galveston graduate student Farooq Nasar, lead author of a paper on the virus now online in the Proceedings of the National Academy of Sciences. "It's a gift, really, because we can compare it to other alphaviruses and figure out the basis of their ability to infect a variety of animals, including humans."

Eilat was discovered in a virus sample that Joseph Peleg of Hebrew University sent to UTMB's Dr. Robert Tesh, an author of the *PNAS* paper and director of the World Reference Center for Emerging Viruses and Arboviruses. The collection holds over 5,000 identified viruses and

dozens of unidentified samples like the one contributed by Peleg.

All the researchers knew about Peleg's specimen was that it killed insect cells while leaving animal cells untouched, a very unusual behavior. So they sent it to a lab at Columbia University that specializes in doing highly intensive searches for the genetic material of viruses, a process called "deep sequencing." As it turned out, there were two new viruses in the sample. One virus killed insect cells, and the other—Eilat virus—infected them without doing any harm.

"We were extraordinarily lucky to have that other virus in our sample, because without the cell death it caused, we never would have done the work that led us to Eilat," Nasar said. "Essentially, we found it by accident."

Eilat's inability to grow in animal cells—even its genetic material cannot replicate in them—makes it unique among alphaviruses, and it also makes it likely that the virus could be uniquely valuable to researchers who study alphaviruses and work to protect humans and domestic animals from them. For example, the UTMB researchers say, Eilat could be transformed into a vaccine against one of its dangerous relatives by making changes to the genes that produce its envelope proteins, which are exposed on virus particle surfaces and stimulate the critical parts of the immune response.

"We have taken the genes for the envelope proteins of very dangerous viruses like eastern equine encephalitis and used them to replace the genes for Eilat's structural proteins," Nasar said. "That gives us viruses that we can grow in insect cells that can't do anything in vertebrate cells at all, but still produce immunity against eastern equine encephalitis —they can be used to vaccinate animals, and hopefully someday people."

A variety of Eilat-based "chimeric viruses"—viruses made by combining genetic material from other viruses—could be used to study the interactions between host cells and dangerous alphaviruses, leading to the development of antiviral drugs. The viruses could also serve as the basis for new diagnostic tools that could be deployed in an alphavirus outbreak. Because these chimeras, like Eilat, would not be able to infect vertebrates, such research could be done without the elaborate and often cumbersome containment precautions needed for working with pathogens like chikungunya, Venezuelan equine encephalitis, or eastern and western equine encephalitis.

Provided by University of Texas Medical Branch at Galveston