

## Dengue-resistant mosquito developed

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Researchers have successfully created a genetically engineered mosquito that shows a high level of resistance against the most prevalent type of dengue fever virus, providing a powerful weapon against a disease that infects 50 million people each year.

Anthony James, a University of California Irvine vector biologist, is one of a team of researchers who injected DNA into mosquito embryos, creating the first stable transgenic mosquito resistant to Type 2 dengue fever virus, the most prevalent strain of the disease. The mosquitoes that survived the procedure also remained fertile and were able to reproduce, a key factor for any future strategies that may involve replacing mosquito populations with their genetically modified counterparts.

In the study, the researchers exploited a vulnerability of the dengue virus to make the mosquitoes resistant to infection. This vulnerability occurs when the virus replicates and its single strand of RNA “a chemical cousin of DNA” briefly becomes double-stranded. At this point, the virus is vulnerable because of a naturally occurring protein called dicer-2. This protein initially has no effect on a single strand of RNA, but acts like scissors on the double strand, chopping it up and rendering its genetic material useless. Once this process is started, the single-stranded RNA also becomes vulnerable to dicer-2 and is cut up, thereby preventing further virus replication.

On its own, this process of self-destruction happens only after the virus has already replicated and been transmitted; however, the researchers found a way to control and speed up the process. They accomplished this by cloning a section of

the virus' RNA and injected two inverse copies of it into mosquito embryos. The copies formed a double-stranded RNA, which, as expected, bound with dicer-2 and was chopped up. The virus never had the opportunity to replicate. As a result, they could "inoculate" mosquitoes with a form of the virus that would essentially be benign.

James and his colleagues performed tests on a family of mosquitoes descended from one of the original embryos that survived the procedure. They found that the vast majority of that family was highly resistant to dengue infection. They also were able to detect the engineered RNA in the mosquitoes, a sign that the genetic alteration had been successful and passed down through reproduction. Furthermore, when that genetic modification was reversed, the mosquitoes were as susceptible to the virus as they had been before the procedure.

Dengue fever is endemic in more than 100 countries in Africa, the Americas, the Eastern Mediterranean, Southeast Asia and the Western Pacific. The virus is transmitted to people by mosquitoes of the species *Aedes aegypti*. The WHO estimates 50 million cases of dengue infection each year. Approximately 20,000 people die annually from the disease.

According to James, the next step of this research will be to explore population replacement strategies using the genetically modified mosquitoes. He stressed that no genetically altered mosquitoes will be released at any time during these studies.

*Source: University of California - Irvine*