Researchers alter mosquito genome in step toward controlling disease

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Virginia Tech researchers successfully used a gene disruption technique to change the eye color of a mosquito -- a critical step toward new genetic strategies aimed at disrupting the transmission of diseases such as dengue fever. The varied colors of the eyes of these mosquitoes, modified using TALEN technology, is because of cell-to-cell variability in the degree of gene editing. Credit: Virginia Tech

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as dengue fever.

Zach Adelman and Kevin Myles, both associate professors of entomology in the College of Agriculture and Life Sciences and affiliated researchers with the Fralin Life Science Institute, study the transmission of vector-borne diseases and develop novel methods of control, based on genetics.

In a groundbreaking study recently published in the journal *PLOS ONE*, the scientists used a pair of engineered proteins to cut DNA in a site-specific manner to disrupt a targeted gene in the mosquito genome. *Science* magazine heralded these transcription activator-like effector nuclease proteins, known as TALENS, as a major scientific breakthrough in 2012, nicknaming them "genomic cruise missiles" for their ability to allow researchers to target specific locations with great efficiency.

While TALENS have been previously used to edit the genomes of animal and human cell cultures, applying them to the mosquito genome is a new approach, according to Adelman.

"Unlike model organisms with large collections of mutant strains to draw upon, the lack of reverse genetic tools in the mosquito has made it is very difficult to assign functions to genes in a definitive manner," Adelman said. "With the development of this technology, our understanding of the genetic basis of many critical behaviors such as blood-feeding, host-seeking and pathogen transmission should be greatly accelerated."

To test the capability of TALENs to specifically edit the mosquito genome, the scientists designed a pair of TALENS to target a gene whose protein product is essential to the production of eye pigmentation in *Aedes aegypti*, a mosquito species known for its transmission of the

viruses that cause dengue fever.

Using the TALEN pair to edit the gene in the mosquito's germ cells early in development, they were able to change the eye color of a large percentage of the mosquitoes arising in the next generation from black to white.

"To date, efforts to control dengue transmission through genetics have focused entirely on adding material to the mosquito genome. Ensuring that this added material is expressed properly and consistently has been a challenge," Adelman said. "This technology allows us to pursue the same goals, namely, the generation of pathogen-resistant mosquitoes, through subtraction. For example, removing or altering a gene that is critical for pathogen replication."

"*Aedes* mosquitoes have become increasingly important as vectors of disease from a public health perspective," said George Dimopoulos, a professor of molecular microbiology and immunology at John Hopkins University who was not involved in the study. "The lack of vaccines and drugs for dengue has left the mosquitoes that carry the virus as one of the most promising targets for controlling the disease. A better understanding of how the virus infects the mosquito and other biological properties of the insect will be required to develop intervention strategies that can block virus transmission by the mosquito. The ability to genetically engineer mosquitoes is essential for the study of such biological functions. The TALEN-based system in mosquitoes that that was developed by Dr. Adelman provides this important capacity."

Provided by Virginia Tech