Discovery of mosquito survival tactics leaves room for new disease vector control tactics

June 1 2022

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The appendages that protrude from a mosquito's head hold the sensory systems that account for nearly all of its ability to detect and respond to a wide range of chemical signals that are critical for its reproduction and its survival. At the molecular level, these systems rely on genes that make up three families of chemosensory receptors. These genes include

gustatory (taste) receptors, ionotropic receptors and odorant receptors that collectively facilitate a wide range of essential behaviors.

To better understand how these chemosensory pathways help the malaria-carrying mosquito Anopheles coluzzii transmit disease, LJ Zwiebel, Cornelius Vanderbilt Chair and professor of biological sciences and his lab utilized CRISPR gene editing techniques to create mutant mosquitoes in which they could map and functionally characterize the role of a crucially important IR gene known as Ir76b.

"While CRISPR is widely used in other model organisms, it remains technically demanding in Anopheles mosquitoes," said Zi Ye, co-first author and a graduate student in Zwiebel's lab. "We managed to delicately deliver CRISPR components into mosquito eggs with microinjection, whereby genetic elements were precisely inserted into the Ir76b locus to disrupt and localize gene expression."

Because of earlier work at Vanderbilt and other universities, the Zwiebel lab had good reason to believe that Ir76b acts as a crucial co-receptor required to form active IR complexes on the mosquito head appendages. The data they collected supported that belief.

"We show that female mosquitoes need the IR pathways for olfactory and probably gustatory responses to amines, which are a diverse family of chemical compounds that notably includes ammonia, an important component of human body odor that attracts biting mosquitoes," said Zwiebel, who also is a professor of pharmacology. "Even more compelling, we discovered that Anopheline mosquitoes behaviorally require Ir76b for mating and for taking up a blood meal (the actual sucking not the biting)."

The data reveal discrete roles of Ir76b across olfactory and gustatory pathways, shedding light on a potential molecular target for the design of

new disease vector control strategies.

"One exciting discovery we found is the unusually enhanced activities of mosquito antenna neuronal response to several amines, which are components of human sweat," said Alex Liu, co-first author of this study and a postdoctoral scholar in Zwiebel lab.

Mosquito-borne diseases such as malaria have persisted since the dawn of humanity. For much of the developing world, these diseases are an ongoing, existential global health crisis that is responsible for deaths of more than 500,000 people annually. This and other mosquito-centered research open the door to developing another approach to reducing mosquito-borne disease.

"These data point to the complex interactions between the mosquito chemosensory system and its behavior," Zwiebel said. "It also points to a new target for controlling mosquito transmission of malaria and other diseases."

The study appears today in *Proceedings of the National Academy of Sciences*.

More information: Zi Ye et al, Discrete roles of Ir76b ionotropic coreceptor impact olfaction, blood feeding, and mating in the malaria vector mosquito Anopheles coluzzii, *Proceedings of the National Academy of Sciences* (2022). DOI: 10.1073/pnas.2112385119

Provided by Vanderbilt University

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