Mutant mosquitoes lose their appetite for humans

June 10 2013

Mosquitoes with a mutation in the orco gene, crucial for detecting odors, aren't repelled by DEET-covered skin like normal mosquitoes. They'll land on an arm (middle image), but are repelled upon contact, and will fly off without biting (right image), showing that DEET works through two pathways: olfactory and tactile.

(Phys.org) —What draws a mosquito to bite its host has long been studied from the perspective of the victim—uncovering which smells and chemicals lure the insect in. But researchers at Rockefeller's Laboratory of Neurogenetics and Behavior, headed by Robin Chemers Neustein Professor Leslie Vosshall, are aiming instead to get inside the perpetrator's mind. Or rather, its genome.

Recent research led by a postdoc in the lab, Matthew DeGennaro, uses a genetically modified mosquito to show that a specific gene called orco gives the insects a strong preference for humans over other mammals, and that the insect repellant DEET uses this pathway to deter mosquitoes

from biting.

DeGennaro and his colleagues created a mutation in the mosquito Aedes aegypti, which spreads the dengue fever virus, using zinc-finger nucleases—enzymes that can make precise breaks in an organism's DNA and have been used in fish, rats, crickets and other creatures. They made a mutation in the mosquito's orco gene, which codes for a co-receptor essential to the insect's ability to use its 131 odorant receptors. The researchers hypothesized that the odorant receptors help the mosquitoes sniff out their human hosts, and wanted to see how altering those receptors would affect the bug's behavior.

DeGennaro and his colleagues devised a potent human odor carrier to test the mosquitoes' behavior—a modified nylon stocking that the lab members wore on their arms for 24 hours sans deodorant, letting the fabric soak up their scent. "The mutant mosquitoes were not drawn to human odors alone," says DeGennaro. "But in the presence of carbon dioxide, the insects were drawn to the sleeve. This shows us that mosquitoes use several mechanisms for sensing human odor, and CO2 plays an important role here."

The A. aegypti mosquitoes normally show a strong preference for humans compared with other animals, but when given the option, the mutant mosquitoes were nearly as attracted a guinea pig as they were a human arm. The odorant receptors proved to be crucial for the insect's attraction to humans.

The researchers then looked at how these mutant mosquitoes behaved in the presence of DEET, the active ingredient in many insect repellants. Without their normal odorant receptors, the insects had no qualms about landing on a DEET-covered arm. But then a peculiar thing happened—they flew off without biting. DeGennaro and his colleagues confirmed this behavior by taking a video of the insects and watching it

in slow-motion.

"This is evidence that DEET works through two pathways," says DeGennaro. "One is the odorant receptors. Without them, the mosquitoes aren't repelled by DEET, at least initially. But then upon contact, DEET works through its other, tactile mechanism."

"It's been hypothesized that DEET works by masking human odors, but we've shown that it likely hijacks the odorant receptor responses instead," says DeGennaro. "We plan on continuing to uncover how these mechanisms work, because designing a better insect repellant can save lives and keep these illnesses at bay."

More information: DeGennaro, M. et al. orco mutant mosquitoes lose strong preference for humans and are not repelled by volatile DEET, *Nature* online: May 29, 2013. www.nature.com/nature/journal/ … abs/nature12206.html

Provided by Rockefeller University