Chemical in bug spray works by masking human odors

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Fifty years have passed since the United States Department of Agriculture and the U.S. Army invented DEET to protect soldiers from disease-transmitting insects (and, in the process, made camping trips and barbecues more pleasant for the rest of us civilians). But despite decades of research, scientists still didn't know precisely how it worked.

Now, by pinpointing DEET's molecular target in insects, researchers at Rockefeller University have definitively shown that the widely used bug repellent acts like a chemical cloak, masking human odors that blood-feeding insects find attractive. The research, which will be published in the March 13 issue of *Science Express*, now makes it possible not only to systematically improve upon the repellent properties of DEET but also to make it a safer chemical.

"For all these years, there were a lot of theories but no consensus on how DEET worked," says Leslie Vosshall, head of the Laboratory of Neurogenetics and Behavior. "Does it smell bad to mosquitoes or does it blind them to odors" It was a great unsolved problem."

Mosquitoes are strongly attracted to odors in human breath and sweat, including carbon dioxide, lactic acid and an alcohol-based compound called 1-octen-3-ol. Different receptors within their olfactory system detect these odors, among others, and lead them to their prey. DEET simply interferes with the proper functioning of odorant receptors, making the hunt for a tasty meal all the more difficult.

But this interference is selective.

To see DEET's effect on different odorant receptors, the researchers recorded the electrical activity of cells in the mosquito olfactory system while exposing the insects to the chemical. They found that DEET only shuts down those receptors that work in tandem with a smell coreceptor called Or83b, which is present in all insects. Whereas DEET shuts down the receptor pairs that detect 1-octen-3-ol and two other sweaty odors, it doesn't affect the lone receptor that detects carbon dioxide. That's because this carbon dioxide receptor doesn't require Or83b to function, whereas the sweaty-odor receptors do. "Each receptor complex has different properties," says Vosshall. "And the idea is that DEET is acting on the uniqueness of this complex."

Since mosquitoes that lack this coreceptor have yet to be genetically engineered, Vosshall and her group used fruit fly mutants that do not have the coreceptor. While normal flies avoid a vial treated with DEET, the researchers found that flies without the coreceptor ventured into the vials, suggesting that Or83b is required to detect this potent chemical. Vosshall then proved that DEET specifically affected the receptor/coreceptor as a unit by isolating the RNA of each and injecting both into a frog egg. As expected, DEET inhibited the odorant receptor/coreceptor complex even in this environment, which was isolated from the olfactory system.

By targeting the coreceptor complex rather than the coreceptor alone, DEET doesn't shut down the entire olfactory system, says Vosshall. "Instead, it seems to shut down strategically different parts of it. It just shuts down enough of these receptors to confuse the mosquito or blind it to the odors it finds attractive."

Although DEET is widely used, concerns about its potential health risks have prompted scientists to pursue alternatives, though so far none have

proven to be significantly more effective than DEET. "We now know how DEET works, and this is the first step in making significantly better insect repellents," says Vosshall.

Source: Rockefeller University