



ScienceWatch – How DEET Works

“ as the mosquito is flying towards you, as it encounters a cloud of DEET, it stops being able to smell you. And therefore it doesn’t find you and doesn’t bite.”

It often seems that the best birding spots are the worst for biting insects. Now that the warm weather is upon us we are likely to be in wetlands with swarms of black flies and mosquitoes or woods filled with ticks. However, the wise birder knows to cover exposed skin with *N,N-diethyl-meta-toluamide* otherwise known as DEET. DEET is effective against a wide range of insects (flies and mosquitoes) and arachnids (ticks). It was developed originally for use as a pesticide by the Department of Defense and the Agricultural Research Service. It was first used as an insect repellent for jungle warfare by the army as early as 1946 and by civilians in 1957.

DEET is used in concentrations up to 100%. Tests have shown a direct correlation between DEET concentration and the length of protection it provides against insect bites. DEET at 100% is effective for up to 12 hours. Lower concentrations (20% - 30%) can provide protection for several hours and a concentration of 10% can protect for about an hour. But according to Leslie Vosshall, a professor of neurogenetics at The Rockefeller University, New York, NY, “No one has ever come up with a satisfactory explanation for how it does this, by what’s the mechanism by which DEET works”.

While mosquitoes may use their heat sensing ability to select a target, their attraction to human hosts depends largely on their ability to smell chemicals that we all emanate. Carbon dioxide in our breath, lactic acid in our sweat and 1-octenol-3-ol alcohol (octenol), a volatile substance found both in our sweat and breath, are strong mosquito attractants. To female mosquitoes these odors mean food, blood, which they must have for their developing eggs.



In the March 28, 2008 issue of the journal *Science*, Vosshall and her colleagues have examined DEET’s mode of action. They first checked out the behavior of fruit flies (*Drosophila melanogaster*), the laboratory rat of the fly world, in the presence of DEET. Presented with a choice of entering either of two tubes, both containing food, the flies entered both in equal numbers. If one tube also contained 10% DEET, the flies greatly preferred the DEET-free tube. However, if neither tube contained food, but one still contained DEET, they again entered both in equal numbers. This suggested to the researchers that the flies weren’t being repelled by DEET, but simply couldn’t smell the food when DEET was present.

The team then decided to look at the flies’ odor receptors. As Vosshall put it, we “can turn a frog’s egg into a fly’s nose”. They genetically engineered eggs from the African

clawed frog (*Xenopus laevis*) to produce fly odor receptors. When the receptors are stimulated by a specific odor they set off a flow of positive ions, generating a tiny current that can be measured in the egg. Prior exposure to DEET greatly reduced the current, and it did so in a dose-dependent manner-the more DEET, the greater the reduction. These results show that DEET blocks the ability of the fly to detect food odors by blunting the sensitivity of its odor receptors.

When the experiment was repeated using three different receptors from the malaria-causing mosquito, *Anopheles gambiae*, which were tuned to human body odor, including the one for octenol, similar results were obtained. Thus, rather than repelling mosquitoes, DEET blunts their ability to detect the odors that attract them.

Past attempts to develop improved repellents have been hampered by a lack of understanding of the molecular mechanism by which DEET exerts its effect. Now we not only know the molecular target for DEET, we have an easy *in vitro* assay for testing new compounds that may be more effective and even cheaper. Just think what having a cheaper, better substance that keeps mosquitoes from biting would mean for the one million people who die each year from malaria.