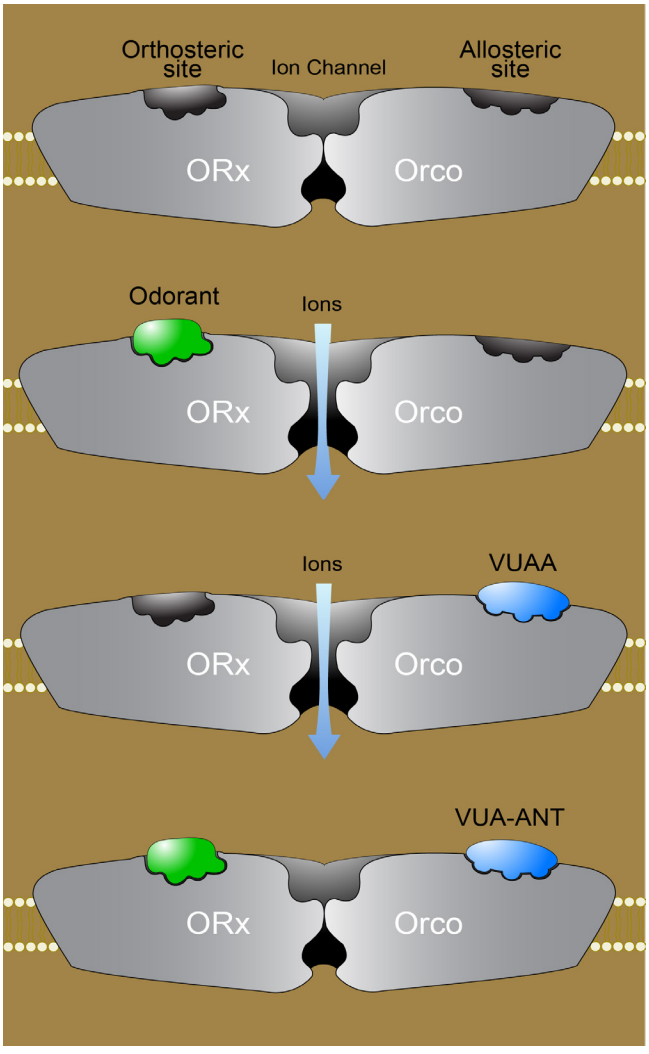
New Insect Repellents Disrupt Olfactory Cues: A Strategy for Pest Protection

VANDERBILT UNIVERSITY
CTTC Center for Technology Transfer & Commercialization

Summary

A multinational research team, led by Dr. L. J. Zwiebel of Vanderbilt University, has identified new compounds with potential as insect repellents. These compounds work by capitalizing on knowledge of how insect odorant receptors detect and respond to scents. Medicinal chemistry efforts have yielded a number of novel compounds that could short-circuit the insect olfactory system, essentially by over-stimulation, to effectively mask attractive odors. These compounds could be used to repel nuisance and disease-carrying insects away from humans and animals, as well as repel agricultural pests from crops or food storage facilities. Vanderbilt University is seeking commercial partners to develop the technology for agricultural uses.

Mechanism of Action



Odorant = Orthosteric Agonist ACTIVATED

"VUAA" Compounds = Allosteric Agonists ACTIVATED

VU-ANT Compounds = Allosteric Antagonists INACTIVATED

For More Information

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VU REFERENCE: VU1113

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Description of Technology

This work was initially conceived as an anti-malaria strategy to "deplete or incapacitate a disease-transmitting insect population" (Grandchallenges.org), but is now recognized to have broader applications for agriculture, animal health, and household use. Insects detect specific scents through a large family of specific odorant receptor (ORx) proteins. These ORx proteins form complexes with highly conserved insect co-receptors (Orco) that act as ion channels. When an odor binds to an ORx, the Orco ion channel is opened, ultimately activating a sensory neuron that detects the odor. The research team has developed a series of compounds (including allosteric agonists and antagonists) that target the highly conserved Orco, and therefore act as broad disruptors of insect odor-sensing. The team has also identified a number of ORx modulators, which could enable insect-specific behavior modification strategies.

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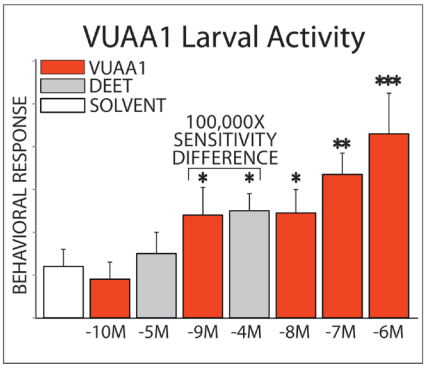
Competitive Advantages

Repels insects more effectively than DEET. In observations of mosquito larval behavior to move away from the source of an insect repellent, Vanderbilt compounds were found to be 100,000-fold more potent than DEET.

Effect of VUAA1 on larval mosquito behavior; the concentration of VUAA1 required to elicit the same response as DEET is 100,000 times less.



Targeting of the highly conserved Orco protein makes it unlikely that insects will develop resistance. Since Orco dictates insect mating and feeding behavior, it is unlikely that resistance mechanisms could develop in insect populations.

As repellents, rather than insecticides, the impact on beneficial insects/pollinators is expected to be minimal. Ongoing studies of the characteristics of Orco and ORx proteins could lead to new classes of insect-selective repellents or attractants.

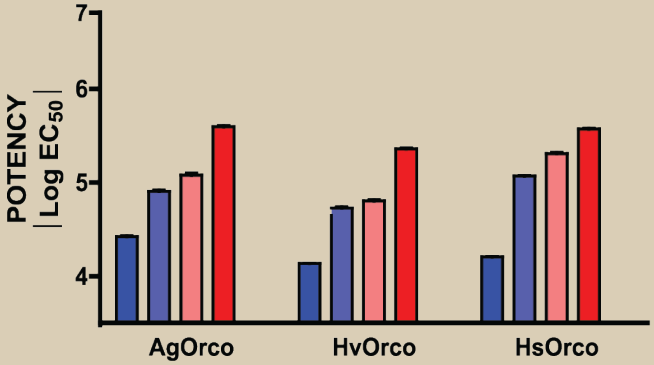
Compounds that target Orco repel broad classes of insects. As such, these compounds may have utility in protecting stored grain, produce, and crops. Further, these compounds could be useful for animal health indications to prevent insect-borne diseases. Orco compounds have been found to be efficacious in disrupting odor sensation in different insect taxa, including Diptera, Lepidoptera, and Hymenoptera (pictured below):

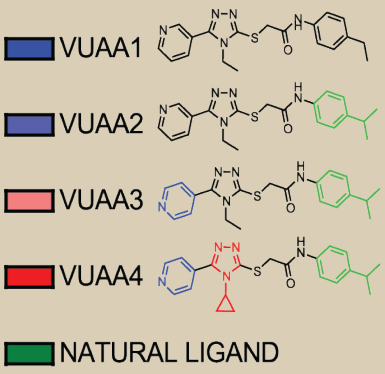
Figure below. VUAA compounds agonize a diversity of insect odorant receptors. VUAA analogues are able to agonize Orco proteins derived from Anopheles gambiae (AgOrco), Heliothis virescens (HvOrco), and Harpegnathos saltator (HsOrco). EC50 values (expressed as the absolute value of Log molarity) of each effective VUAA compound are relatively stable across evolutionary time. Error bars = SEM.

Anopheles gambiae, AgOrco (mosquito)

Heliothis virescens, HvOrco (moth)

Harpegnathos saltator, HsOrco (ant)





Intellectual Property Status: Patent applications have been filed.

References: http://www.ncbi.nlm.nih.gov/pubmed/22924767