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Unique pheromone detection system uncovered

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Researchers at UT Southwestern Medical Center have overturned the current theory of how a pheromone works at the molecular level to trigger behavior in fruit flies.

The finding, if it proves true in other species, might lead to new ways to manipulate the actions of harmful insects, the researchers said.

They found that the pheromone, which affects mate recognition and sexual behavior, does not directly attach to nerve cells, as was previously thought. Rather, the pheromone first docks onto a free-floating protein in the insect's antennae called LUSH.

This docking action causes LUSH to change shape. The reshaped protein, not the pheromone itself, is what activates the nerve cells, the researchers found. Their findings show that the pheromone only indirectly controls the animal's behavior.

"If we can inhibit this molecular interaction, we might be better able to control pests that harm crops, carry malaria and so forth," said Dr. Dean Smith, associate professor of pharmacology and neuroscience at UT Southwestern and senior author of the study, which appears online today and in Friday's issue of the journal *Cell.*

Pheromones are molecules that an organism releases to trigger a specific behavior in other members of its species. Insects make wide use of pheromones to attract mates, signal the location of food, warn of attackers and provide other signals. Detection of pheromones is so sensitive that, in some cases, a single molecule is enough to trigger a response.

In agriculture, pheromones for some pest species are already used to protect crops by disrupting reproduction.

The current study used the fruit fly Drosophila melanogaster and focused on a pheromone called cVA (11-cis vaccenyl acetate). Only male flies produce cVA, but both males and females react to it. It is involved in clustering, mate recognition and sexual behavior.

The researchers examined the interaction of cVA with a type of nerve cell called T1 in the antennae of Drosophila. Holes in the antenna allow cVA to enter a fluid-filled chamber that surrounds these nerve cells. When the pheromone enters the antenna, the nerve cells fire.

The fluid surrounding the nerve cells also contains the LUSH protein, which was already known to bind to cVA. The prevailing theory is that LUSH proteins act as a carrier, picking up any cVA molecules that enter the antenna, transporting them to the nerve cells and releasing the pheromone molecules to bind directly to the nerve cells, Dr. Smith said.

In their experiments, Dr. Smith's group examined the nerve cells' firing patterns in genetically altered flies. The researchers also created variations of LUSH with varying abilities to change shape. One variant of LUSH, designed to mimic the shape it takes when bound to cVA, was capable of stimulating the nerve in the complete absence of the pheromone.

"LUSH is clearly important for activating the nerve," Dr. Smith said. "The nerve cell's receptor is designed to work only when cVA and LUSH are bound together. It's a very unusual pathway that allows even single pheromone molecules to activate the nerves."

The researchers are further examining the interaction between the pheromone and the nerve cell receptors.

Dr. Smith said if pheromone systems work this way in other insect species, researchers might be able to design compounds that block the action of pheromones, allowing them to manipulate and control pest behavior, including controlling mating and reproduction.

Source: UT Southwestern Medical Center

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