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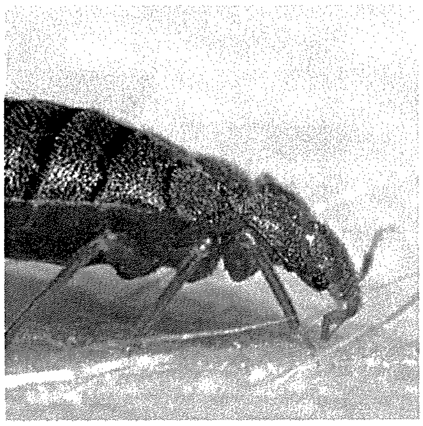
Massive Resistance: Bed Bugs' Genetic Armor Shields Them from Pesticides

The nocturnal pests are equipped with a large array of genes that thwart chemical sprays, but scientists are probing for weaknesses

By Marissa Fessenden | March 14, 2013 | 0



By Piotr Naskrecki from CDC Public Health Image Library (Public Domain)

One of humankind's most intimate blood-sucking roommates, the bed bug, is notoriously resistant to the pesticides used against it. Now researchers have pinpointed the genes responsible for this resistance. The finding highlights how ineffective our current chemical arsenal has become, and could help researchers design pesticides better able to destroy the pests.

In the past 15 years bed bug infestations have spiked in the U.S., perhaps due to increased travel. Once the insect hitchhikers enter a new area, they spread readily: A single fertilized female can infest an entire apartment building. Getting rid of bed bugs can be expensive, time-consuming and tricky. Their paper-thin bodies let the bugs squeeze into cracks in furniture and walls, which are difficult to spray effectively.

To find clues that uncover how bed bugs are able to survive pesticides, a team of researchers from the University of Kentucky first sequenced the genes that were active in 21 pesticide-resistant bed bug populations obtained from infestations. By comparing the active genes in the field bed bugs with a susceptible lab-bred population's active genes, they identified 14 genes in the collected DNA having variants associated with pesticide resistance. Different populations carried different combinations of the gene variants. The team reported on March 14 in *Scientific Reports* they found as well that each of the bed bug populations tested carried at least two resistance variants. (*Scientific American* and *Scientific Reports* are both part of Nature Publishing Group.)

All of the genes identified were active (gave rise to specific proteins) primarily in the outer epidermis—an insect's tough, fingernail-like cuticle—rather than the digestive tract, which is where most insects develop mechanisms of pesticide resistance, says Subba Reddy Palli, a professor of entomology and one of the researchers involved in the new study. That finding made sense, given that bed bugs, which eat only blood, are exposed to pesticides solely by contact with their exoskeleton, which now appears to be chock full of protective genes.

Next, the team demonstrated that the genes they had identified caused resistance. They hobbled the genes by injecting young bugs with special RNA fragments designed to specifically silence the resistance genes. When the treated bugs were exposed the pesticides, they were susceptible. (The technique does not alter germ line genes, however, so the next generation would still be pesticide-resistant.) "A few other papers found similar genes," Palli says. "But no one had done the functional study yet—the gene silencing."

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The high number of resistance genes in all populations examined by Palli and his colleagues is "horrifying," says Rajeev Vaidyanathan, an associate director of vector biology in the Center for Immunology and Infectious Disease at SRI International, who was not involved in the study. That the bugs have multiple ways of undermining the effects of pesticides is "devastating," he adds.

The Kentucky researchers' bed bug genomic studies and those of a few other groups are "absolutely critical" for understanding the molecular basis for pesticide resistance, Vaidyanathan says. "This is step one. Step two is identifying novel targets for pesticides."

Two of the mechanisms suggested by the genetic findings were already flagged as contributors to bed bugs' pesticide resistance, Vaidyanathan says. One involves the metabolic enzyme cytochrome p450, which helps to break down toxins. (Humans have the same molecule.) A gene variant that confers resistance enables the bed bug to produce large quantities of the enzyme. The other mechanism relies on a protein found on the surface of nerve cells—an ion channel that tells the cell when to fire. Commonly used insecticides target that ion channel and cause nerves to fire continuously, paralyzing and quickly killing the insect. The resistant bed bugs often carry a mutation in the ion channel that prevents the pesticide from binding.

The roles of the other resistance genes identified by the Kentucky team remain to be fully explained, although the researchers found that most of them code for proteins that participate in metabolism, comprise the exoskeleton or transport chemicals into cell interiors. The researchers suspect the bed bug proteins slow pesticide penetration via the cuticle and detoxify chemicals before they can reach nerve cells, for example. But the very existence of multiple resistance mechanisms means that hitting the pests with our current chemical arsenal is potentially "a waste of time, money and has unnecessary possible toxic side effects," Vaidyanathan says. New ideas are needed; the most recent kind of pesticides approved for bed bugs, neonicotindoids, were first introduced to market in the early 1990s.

Improved understanding of how bed bugs tolerate insecticides could help researchers design toxins that aim at those defenses. The next generation of bed bug sprays may be a cocktail of chemicals that includes inhibitors to cripple the insect's detox mechanisms. "Work is already underway to look for inhibitors," Palli says.