Most Widely Used Organic Pesticide Requires Help to Kill

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The world's most widely used organic insecticide, a plucky bacterium known as Bacillus thuringiensis or Bt for short, requires the assistance of other microbes to perform its insect-slaying work, a new study has found.

Writing in the Sept. 26 issue of the *Proceedings of the National Academy of Sciences* (PNAS), a team of researchers from the University of Wisconsin-Madison reports that without the help of the native bacteria that colonize the insect gut, Bt is unable to perform its lethal work.

The startling new insight into the workings of one of the most important and environmentally friendly weapons in the human arsenal against insect pests has significant implications not only for the control of insects in agriculture, forestry and human health, but for understanding microbial disease in humans and other animals.

"The take-home message is that we've shown that the mechanism of killing for Bacillus thuringiensis is facilitated by the normal gut community," says Nichole Broderick, a UW-Madison graduate student and the lead author of the PNAS study. "This is a mechanism that was not previously known."

First discovered in 1911, Bacillus thuringiensis was developed as a commercially important insecticide in the 1950s. It is by far the most widely used natural agent to control important insect pests, and the genes that make Bt's toxic proteins have been engineered into numerous crop plants. Transgenic crops using the bacterium's genes are the most prevalent of any engineered plants, and are planted on millions of acres in the United States alone.

Although Bt and the toxic proteins it makes have been studied for decades, how the microbe goes about killing the insects it infects has been assumed to be a simple toxin-mediated disruption of the cells that line the insect gut. The damaged cells, according to the prevailing hypothesis, lead to starvation. An alternative hypothesis holds that the spread of the bacterium in infected insects leads to blood poisoning and death.

"It was one of those assumptions built on assumptions -- a scientific house of cards," explains one of the report's authors, Jo Handelsman, of the long-held view of Bt's mode of killing. "What was proposed as a hypothesis in one paper became cited as proven in another and no one seemed to go back to the original literature until now."

Handelsman is a Howard Hughes Medical Institute Professor in the UW-Madison department of plant pathology.

The new work, conducted in the laboratories of Handelsman and Kenneth F. Raffa, a professor in the UW-Madison department of entomology, demonstrates that Bt requires the presence of other bacteria to exert its lethal influence.

Virtually all animals, including humans, depend on the interplay of numerous species of bacteria that, beginning at birth, routinely colonize the stomach and intestines. The caterpillars of moths and butterflies, for example, have anywhere from seven to twenty species of gut bacteria. Humans have between five hundred and one thousand species of micro flora that take up residence in the intestinal tract.

"In moths and butterflies, the complexity is much lower than in mammals, and even some other insects," Broderick explains.

The Wisconsin study was conducted using antibiotics to clear all of the native bacteria that colonize the gut of gypsy moth caterpillars. Exposed to Bt, the caterpillars whose intestinal tracts had been cleared of their native microbial communities showed none of the agent's toxic effects.

When the insect's microbial gut flora were reestablished, Bt's insecticidal activity was restored.

To further test their results, the Wisconsin team used a strain of live E. coli engineered to carry the Bt toxin to infect caterpillars, a lethal treatment whether or not the insect gut contained its normal complement of microbes. However, if the engineered E. coli was killed before administration, it only killed those caterpillars whose microbial gut flora were intact.

"The significance of the microbial community has been overlooked," Broderick asserts. "Ultimately, this is a toxin-mediated septicemia (blood poisoning) modulated by the gut community."

The exact role played by the microbes to promote the Bt toxin's lethal effects remains unknown.

The upshot of the new work may have immediate application in designing strategies to manage insect pests by enhancing the killing effects of BT using indigenous insect gut microbes or other bacteria known to promote blood poisoning.

"The work also raises the possibility that the genes encoding the (Bt) toxins could be deployed more effectively in transgenic crops by exploiting the role of insect-borne bacteria that enhance insecticidal activity," the Wisconsin team writes in its PNAS report.

What's more, the insight that gut microbes mediate the effects of bacterial toxins could have application in human and animal medicine as the roles of those bacteria become better understood. Bacterial infections in humans may account for as much as 10 percent of mortality in the United States.

"It is thought that the gut is the source of bacteria for a large portion of cases of human septicemia, so if this mechanism is shared by Bt and toxins produced by human pathogens, the implications could be far greater in medicine than in agriculture," Handelsman says.

Source: University of Wisconsin-Madison

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