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Countering Insect Resistance with Designer Bt Toxins

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Toxins from the bacterium *Bacillus thuringiensis* (Bt) provide environmentally friendly control of insect crop pests and mosquitoes. Widespread exposure to Bt toxins, however, increases the chances that pests will adapt and evolve resistance – just as pests have evolved resistance to conventional insecticides. >>

With funding from USDA Cooperative State Research, Education, and Extension Service (CSREES) program, researchers in Arizona and Mexico have collaborated to design, create, and test modified Bt toxins that kill insects that had developed resistance to standard Bt toxins.

Bt toxins kill some key agricultural pests, but cause little or no harm to people, wildlife, and even most other insects including the natural enemies of pests. For decades, Bt toxins have been used successfully in organic and mainstream agriculture. Since 1996, cotton and corn crops have been genetically engineered to produce Bt toxins. These crops have grown on more than 490 million acres worldwide, with most of the acreage in the United States

The Bt toxins most commonly used in sprays and transgenic crops are insecticidal crystal proteins in the Cry1A family. Cry1A toxins are effective against some of the most damaging crop-munching caterpillars. After Cry1A toxins are ingested by caterpillars, they are activated by enzymes in the alkaline caterpillar gut. The activated Cry1A toxins bind to specific receptors on the insects' midgut membrane. This creates holes in the membrane, leading to death.

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Right: In Arizona, transgenic cotton that produces a protein from the bacterium *Bacillus thuringiensis* (Bt) has provided protection from damage by the pink bollworm (*Pectinophora gossypiella*) for more than a decade.

Credit: Timothy Dennehy

Above: A pink bollworm caterpillar emerges after munching on a cotton boll.

Credit: Alex Yelich

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The Cry1A toxin binds to a caterpillar's midgut receptor like a lock and key. There are several types of Bt toxin and each one fits certain receptors, which are like locks. Insect resistance to Bt toxins involves changes in the receptors. In effect, the lock is altered so the key won't fit. This allows resistant insects to survive exposure to the Bt toxin.

Bruce Tabashnik and colleagues at the University of Arizona selected a specific type of resistance to Cry1A toxins in pink bollworm (*Pectinophora gossypiella*), which is a major cotton pest in the southwestern United States. The selected resistance is tightly linked with specific genetic mutations, which occur in a gene that carries instructions for making a receptor protein, called cadherin. The protein binds to the Cry1A toxins. The researchers determined that resistance to Bt toxin occurs when mutations inhibit the cadherin gene from properly binding with Cry1A.

Meanwhile, Mario Soberón, Alejandra Bravo, and their colleagues at the Universidad Nacional Autónoma de Mexico, hypothesized that this type of resistance to Cry1A toxins could be overcome by modified toxins that do not require binding to cadherin to kill caterpillars.

Using knowledge from the study, the scientists designed and created modified toxins called Cry1AMod toxins. Subsequent tests at the University of Arizona showed that Cry1A-resistant pink bollworm caterpillars were killed by the Cry1AMod toxins. The results with pink bollworm suggest that the modified toxins may be useful for countering or delaying resistance to standard Bt toxins in caterpillar pests.

The impact of Bt toxin for pest control and the threat of resistance also mounting, the modified toxins could help to protect the nation's food supply and promote sustainable, environmentally friendly agriculture.

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