GM moths with autocidal gene tested outdoors in New York state

Open field trials of a genetically modified (GM) diamondback moth began in August, in New York state, adding to what appears to be a growing acceptance of GM insects in multiple countries. Oxitec in Milton Park, UK, developed the moths as a tool to control pest populations that can decimate crops. The US is one of at least four countries that have allowed open-air testing of GM insects.

Oxitec's diamondback moths, called OX4319L, carry an autocidal gene that kills only the females. When lab-reared males carrying the gene are released into the environment, they mate with wild female pests, passing the lethal gene to the next generation, and causing the female progeny to die before reaching the reproductive stage. If the system works, the native pest population in an Oxitec release area will be greatly diminished or eradicated.

Diamondback moths, *Plutella xylostella*, each year cause an estimated $4–5 billion in damage globally to growers of brassica vegetables such as broccoli, cabbage, kale, Brussels sprouts and canola. The insect has evolved resistance to over 90 insecticide ingredients globally, forcing farmers to increase insecticide use and further exacerbate resistance.

Cornell University entomologist Anthony Shelton, who is leading the open-air study, in July received a permit from the US Department of Agriculture (USDA) to release the moths for his test. The Northeast Organic Farming Association of New York criticized USDA for granting the permit, saying the agency had failed to adequately assess the potential impacts of the trials on local farms and residences. The organization called on the New York State Department of Environmental Conservation to require a more extensive environmental review. That agency in July said it had no jurisdiction on the matter, which allowed the trial to proceed.

Oxitec

A diamondback moth for pest control.

Shelton is releasing Oxitec's moths from the center of a circular 7.5-acre cabbage field in Geneva, New York. He and his team are monitoring how far the engineered moths travel from the release point compared with their wild counterparts, and how long the Oxitec moths tend to live. The results will be used to develop a model for implementing the tool. "We are funded by Oxitec but we have complete control over the trial and any of the data," says Shelton.

The study runs in tandem with ongoing experiments conducted in field cages, also run by Shelton, that aim to assess the moths' lifespan, mating competitiveness and ability to suppress a wild pest population (*Nat. Biotechnol.* **33**, 792–793, 2015).

The moths' autocidal, or self-limiting, gene encodes tetracycline repressible transcription activator variant (tTAV), which, at high expression levels, ties up cells' transcriptional machinery, shutting down cell function and eventually killing the insect. Ernst Wimmer, a developmental biologist at Georg-August-University in Göttingen, Germany, who is not affiliated with the Oxitec project, says he would like to see a second killing mechanism added to the Oxitec moth's DNA. "Insects have been so great at developing resistance," says Wimmer. "However, if you have just one killing system in there, you allow for the selection of resistant insects."

Wimmer and his team are engineering other agricultural pests—the Mediterranean fruit fly, or Medfly, and the spotted wing *Drosophila*—with two independent autocidal genes (*BMC Genet.* **15**, S17, 2014). He says he supports Oxitec's program and would like to see it succeed, in part to set the stage for other scientists who are generating GM insects for pest control. If Oxitec's moths develop resistance, that could set back the whole field, he says. "If the technology gets burned, it would be so hard to come back," he says.

Oxitec scientist Neil Morrison, in a statement, responded, "We believe that a single self-limiting mechanism will provide a robust pest management solution," particularly if it is combined with existing pest management tools. "Moreover, in the event that resistance does develop to the approach, we would be able to mitigate that in the insect production process and through application of new genetic technologies" or through breeding approaches, he says.

Oxitec is developing strains of Medfly, the spotted wing *Drosophila* and two species of mosquito—*Aedes aegypti* and *Aedes albopictus*—all engineered with the *tTAV* gene. *A. aegypti* is the primary vector for dengue fever, Zika and other diseases (*Nat. Biotechnol.* **29**, 1034–1037, 2011). Oxitec in September announced it would build, in Oxfordshire, UK, a production facility that can generate one billion mosquito eggs each week—likely the largest GM insect facility in the world. Its parent company, Intrexon Corporation in Germantown, Maryland, said it would invest $9.5 million in the factory. Oxitec will ship the eggs to facilities in other countries to be reared and released.

The company reports it has already released into the environment over 200 million engineered *A. aegypti*, and that the system reduces wild populations by 80% or more (*Nat. Biotechnol.* **30**, 828–830, 2012). Many of those *A. aegypti* have been released in Brazil, where Oxitec has the approval to operate commercially (*Nat. Biotechnol.* **34**, 221–222, 2016).

At least two Brazilian municipalities—Piracicaba and Juiz de Fora—have contracted Oxitec to treat their pest problems. Panama and the Cayman Islands have allowed open-air releases of Oxitec's *A. aegypti,* and the municipality of Santiago de Cali, Colombia, in April announced its intention to deploy the insects as well (*Nat. Biotechnol.* **29**, 9–11, 2011).

Unlike those regions, in the US, members of the public have pushed back on open-air tests of *A. aegypti* in the Florida Keys in a highly publicized public relations battle. A loss there for Oxitec could mean a setback elsewhere for scientists engineering insects. Says Wimmer: "We need the technology working in mosquitoes for a while before it will be allowed in mosquitoes in Europe, and even longer before it will be acceptable in agriculture."

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