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Study on DNA spread by genetically modified mosquitoes prompts backlash

Company and some scientists dispute suggestion that released strain may have made local mosquitoes fitter

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Genetically modified mosquitoes, such as these being released in Brazil, could combat infectious diseases. PAULO FRIEDMAN

For 10 years, the company Oxitec has been testing whether genetically modified (GM) mosquitoes can suppress populations of their natural brethren, which carry devastating viruses such as Zika and dengue. Its strategy: Deploy (nonbiting) male *Aedes aegypti* mosquitoes bearing a gene that should doom most of their offspring before adulthood.

Now, a team of independent researchers analyzing an early trial of Oxitec's technology is raising alarm—and drawing fire from the firm—with a report that some offspring of the GM mosquitoes survived and produced offspring that also made it to sexual maturity. As a result, local mosquitoes inherited pieces of the genomes of the GM mosquitoes, the team revealed last week in *Scientific Reports*.

There's no evidence that these hybrids endanger humans more than the wild mosquitoes or that they'll render Oxitec's strategy ineffective, both the paper's authors and the company agree. "The important thing is something unanticipated happened," says population geneticist Jeffrey Powell of Yale University, who did the study with Brazilian researchers. "When people develop transgenic lines or anything to release, almost all of their information comes from laboratory studies. … Things don't always work out the way you expect."

But the paper's suggestion that this genetic mixing could have made the mosquito population "more robust"—more resistant to insecticides, for example, or more likely to transmit disease—has triggered anti-GM news reports, a backlash from some scientists, and strong pushback from Oxitec. The company, a subsidiary of U.S. biotech Intrexon, has a lot at stake; it recently submitted a new generation of its GM mosquitoes for U.S. regulatory review and hopes to conduct its first U.S. field test next year.

"We're not surprised by the results, but what we are surprised by are the speculations that the authors have made," says Nathan Rose, head of scientific and regulatory affairs at Oxitec in Oxford, U.K. He says the company has asked Nature Research, which publishes *Scientific Reports*, to "address the range of misleading and speculative statements" in the study. On Tuesday, the journal added an editor's note to the paper saying its conclusions "are subject to criticisms that are being considered by editors."

Even before Oxitec conducted pilot releases of its altered mosquitoes in Brazil, Malaysia, and the Cayman Islands, it knew the inserted gene wasn't inevitably lethal. Lab tests had shown that when the GM males mated with wild females, roughly 3% of their offspring survived. "We've been very clear about that," Rose says.

What wasn't clear was whether those rare offspring, often sickly in the lab, could themselves produce progeny, Powell says. To see whether the survivors fared well enough in the wild to spread their DNA, he contacted Oxitec's collaborators on the eve of a large field trial in the Brazilian city of Jacobina. From 2013 to 2015, Oxitec released roughly 450,000 GM male mosquitoes per week there—which the company reported reduced the overall mosquito population by about 90%. Powell and his collaborators collected mosquitoes from several neighborhoods before, during, and in the 3 months after the trial. Within these populations, they estimate, between 5% and 60% of the insects had some DNA from the Oxitec strain in their genome—as much as 13% of the genome in one case.

Jason Rasgon, an entomologist at Pennsylvania State University in State College who studies insect-borne diseases, says the genetic finding is important. "But I think there are a number of things that are really overhyped and kind of irresponsible about the paper," says Rasgon, who has no financial ties to Oxitec. The authors should have emphasized that they didn't find any mosquitoes carrying Oxitec's transgenes, he says, referring to the two genes, foreign to *A. aegypti*, introduced to kill offspring and to fluorescently label the mosquitoes as GM. The novel DNA that did show up in the Jacobina population was from the Oxitec mosquitoes' genetic "background"—a cross between strains from Cuba and Mexico.

Rasgon, like Oxitec, takes issue with the paper's assertion that the mixing of genomes "likely" made the population stronger by increasing its genetic variation. ("Failed GM mosquito control experiment may have strengthened wild bugs," read one headline last week.) "We don't know that that's the case here, but we do know that this population is a hybrid of three strains," Powell says. His team, however, didn't test whether the hybrid mosquitoes were more resistant to pesticides or more likely to transmit disease. Neither was true of the Oxitec mosquitoes themselves, Rose says.

Rasgon is concerned that the *Scientific Reports* paper has fueled unfounded suspicions about GM organisms. Previous proposed Oxitec releases in Florida have faced opposition from residents. "I don't think [the paper] needs to be retracted. But some sort of clarification or a statement or something should be made," he says.

Oxitec's latest strain of GM mosquitoes is designed to spread the lethal gene more effectively. Instead of killing offspring regardless of sex, it eliminates only the females. Male offspring survive to pass on the lethal gene. In a Brazilian field trial, these second-generation mosquitoes caused local populations to dip by as much as 96%, Oxitec announced in June. Last week,

the U.S. Environmental Protection opened a monthlong window for public comments on the company's proposed releases in Florida and Texas.

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