Here’s what you should know about disease-fighting GMO mosquitoes

Mosquitoes—vampires of the insect world. At best, these small insects act as minor annoyances during our summertime plans. Their whine a telltale giveaway that they’ve marked you as their next meal. Before you know it, a red, itchy bump is the only evidence that you’ve served as dinner. If this was the only consequence of these bloodsucking bugs, we might be able to tolerate them like we do any other insect.

Unfortunately, in many cases, mosquitoes bring far more harm to their victims. They serve as carriers for a multitude of diseases like malaria, yellow fever, Zika virus, and dengue. While many of these diseases may sound rare and exotic, mosquito-borne diseases are becoming more prevalent even in industrialized nations. As an example, this year we’ve seen seven deaths from mosquito-borne Eastern Equine Encephalitis, better known as EEE. In some cases, EEE results in no symptoms at all; in others, it’s a bit like having the flu.

But what makes EEE deadly is that it can cause inflammation of the brain. Just for perspective, between 2009 and 2018 there were 30 total deaths from EEE. In addition to the diseases mosquitoes can carry, they are also invasive. These pesky insects act as unnatural competitors in most places where they spread disease, so they have ecological as well as health impacts.

We’ve all heard the common recommendations to try to combat mosquitoes: remove standing water from our property, wear long-sleeved shirts and pants, use repellent, or simply avoid being outside during the hours when mosquitoes are most active. While suggestions like these do help, they never quite eliminate the threat of mosquito bites.

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A worker sprays anti-mosquito fog to control dengue fever in Indonesia.
Achmad Ibrahim / AP Photo

As a result, some cities resort to deploying ground- or aerial-based pesticides during evening or nighttime to further reduce mosquito populations. But, to minimize adverse impacts on other insect species, the pesticides used tend to break down quickly, necessitating recurrent applications throughout the summer season. They also invite the onset of resistance, which could compromise future efficacy of these chemicals when we need them.

Sterilization > pesticides

To better control mosquito populations, scientists at the biotech firm Oxitec Ltd. set out to use genetic tools to modernize the decades-old strategy of Sterile Insect Technique (SIT). SIT involves the mass sterilization of an insect population, often using radiation, before release into the wild. The idea is that the sterile insects will compete for mates in the natural population but produce no offspring. And while SIT has been used for over 60 years to control insects like tsetse fly and Mediterranean fruit fly, it does not work for all bugs. Too much radiation negatively affects the insects’ health and fitness, while too little results in

a population that isn't completely sterilized. SIT is being studied for use on mosquitoes but has not yet achieved this delicate balance.

But what if modern molecular tools could achieve this goal more precisely? Oxitec Ltd. aimed to effectively sterilize the target population, but instead of using radiation, they generated a transgenic (genetically engineered) Aedes aegypti mosquito strain (OX513A) that carries a dominant lethal gene that can easily be turned off in a laboratory setting. Once released, these mosquitoes become silent carriers of a gene that is lethal in the next generation, reducing the invasive, disease-vectoring population.

This technology has shown to be successful in field studies, reducing population size by 80-90 percent, according to a 2015 report. Another pilot study is being planned in the Florida Keys and has received approval from the Food and Drug Administration (FDA), which concluded that the trial would not result in significant impacts on the environment. The Environmental Protection Agency (EPA), which now has regulatory jurisdiction over Oxitec's mosquito, is holding a public comment period and would benefit from your input.

GE mosquitoes gone wild?

In early September, the journal Scientific Reports published an article that followed up on a trial conducted in Jacobina, Bahia, Brazil. While the study confirmed that the local mosquito population was reduced by 85 percent for 18 months following the release of Oxitec's engineered insects, the finding that media outlets blew out of proportion was that the genetics of the released mosquitoes were found in subsequent generations.

Jurassic Park film still

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Jurassic Park scientists

The report found that 20-60 percent of the tested mosquitoes showed introgression of the transgenic background. In other words, the OX513A mosquitoes had produced some offspring possessing a mix of the native genome and the transgenic one. Media outlets began reporting that the experiment had backfired, breeding hybrid mosquitoes, strengthening wild populations, and surprising researchers. An example of this can be seen in the recent New York Post headline "Plan to kill off mosquitoes backfires, spawning mutant hybrid insects":

> In what sounds like the plot to a Syfy channel original movie, a plan to curb a mosquito population has backfired spectacularly …. Now, the region has been left with a huge population of hybrids (combinations of the Brazilian native mosquitoes and the Cuban and Mexican breeds that were genetically altered in the lab) — an outcome that could make the entire population more resistant to the original mosquito control measures.

Such coverage leaves readers thinking that Oxitec committed a Jurassic Park-level catastrophe. But is the situation as bad as the media reported? Not quite. To begin, this finding did not come as a surprise. The researchers at Oxitec knew that 3-4 percent of OX513A matings would result in progeny that could survive the lethal gene. This would be bad if the strain of mosquito the researchers chose to carry the lethal gene had resistance to pesticides the native population didn't, or if the transgenic mosquito strain served as a better vector for disease.

However, neither of these concerns have any merit. The OX513A strain tested positive for susceptibility to commonly used pesticides like temephos, permethrin, eltamethrin, and malathion. Furthermore, the Scientific Reports article tested infectivity of dengue and Zika viruses in both the transgenic and native populations, finding both to be equivalent.

So, unlike the mythical insect described in media reports, the hybrid mosquitoes aren't some sort of uber-bug that is stronger than the local population. This is precisely what was observed in the mating behaviors: evidence of genetic mixing between local and introduced mosquitoes that decreased as time went on. If the hybrid mosquitoes carried some sort of selective advantage, we would expect the number of hybrid mosquitoes to increase.

The problem with the Scientific Reports article is that its language made the findings seem like a bigger blow to the experiment than what the data actually showed, which fuels unsubstantiated claims and sensational headlines that ultimately slow the implementation of a potentially life-saving technology. Now, six authors have asked that the article be retracted. According to co-author Dr. Margareth Capurro, the article that was published in Scientific Reports was different from the version all the authors had agreed upon. Unfortunately, even with a retraction, most of the media headlines about the report will remain, while the good news about the experiment receives far less attention.

The strategy that Oxitec Ltd. is using to try to combat disease-carrying mosquitoes remains sound. Their next- generation insects carry a lethal gene that only prevents the biting females from surviving. This aims to account for the rebound in population after 18 months, which the Scientific Reports article hypothesizes might be due to discrimination against sterile males. With these further improvements, hopefully summers filled with disease-carrying mosquitoes will one day be a thing of the past.

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