# Let High-Tech Genetically Modified Insects Counter Dengue

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# Let High-tech Genetically Modified Insects Counter Dengue

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**We must be living in the year** of the genetically modified (GM) insect. Last fall, the government of the Cayman Islands experimentally released male GM *Aedes aegypti* mosquitoes (also known as yellow fever or dengue mosquitoes) (Enserink 2010). A similar but smaller release has now been conducted in Malaysia. The modification was an inserted gene (RIDL®, Release of Insects with Dominant Lethal [genes]) developed by the Oxitec Company of the United Kingdom. Male RIDL mosquitoes pass along one copy of this gene with their sperm when they mate with wild females of the same species.

RIDL is a modern adaptation of the much older sterile insect technique (SIT), in which multiple lethal genes are induced by radiation. SIT insects are mass reared and released daily in areas of infestation to block reproduction. This is expensive, because the numbers of insects needed add up to millions daily. A mass-rearing facility is basically an insect factory, with seasonal shifts of workers employed in the preparation of diets, insect rearing, packaging and shipping insects to target areas for release, and monitoring of field populations.

That is worth a moment's reflection. Dozens of countries around the globe, including the Unites States, are releasing insects with multiple lethal genes and have been doing so for decades. It has become a routine part of protecting the fruit trade by preventing invasions of pests from trading partners. Do any of these insects escape? Yes, they do. Can you readily tell a factory insect from a wild type? In many cases, mitochondrial DNA can help one distinguish between them, but that involves the use of a molecular biology lab, which is not usually a part of SIT programs.

Occasionally, a grower will blame a local pest infestation on the released SIT insect and expect the government to do something about it. The organization doing the SIT then has to prove beyond a doubt that the insect in question is not one of those from the mass-produced group; otherwise, they might have to pay damages.

Now along comes the GM mosquito. There has not yet been a successful SIT program aimed at mosquitoes. The RIDL mosquito would be the first. It has one dominant lethal gene. This particular one allows larval development but, in almost all cases, blocks molting to the adult stage.

Colleagues have reported that the RIDL mosquito competes equally with the wild type in cage studies (Gary Clark, US Department of Agriculture Agricultural Research Service, Gainesville, FL, personal communication, 26 May 2011). The Cayman Island releases reportedly caused an 80-percent suppression of the wild *Ae. aegypti* population in the test area. I was told by Oxitec that the company suspected that the 20 percent of normal numbers of wild *Ae. aegypti* that were caught in monitoring vessels came from outside of the test area.

Dengue vector mosquitoes are found in many places, including much of the southeastern United States, although the dengue virus is not present there. There is a global increase in dengue epidemics, possibly tied to climate change. This increases the chance of an infected traveler returning with the virus, which was reported to be the cause of the recent epidemic of serotype 1 in Key West, Florida. Yet, according to Emily C. Zielinski-Gutierrez and Harold Margolis of the federal Centers for Disease Control and Prevention, "Even in Florida—with some of the best mosquito control programs in the United States—we do not presently possess the combination of resources and technology needed to control *Ae. aegypti* mosquitoes to the degree necessary to eliminate dengue transmission" (Zielinski-Gutierrez and Margolis 2010).

Humankind has never completely eradicated any pest insect, even though we have locally eliminated some. California is invaded by a new pest or disease every 60 days (invasive species are a problem everywhere), and we are short of tools to deal with them. For an immediate threat, insecticides are often the only choice. Together with the spread of dengue, these facts suggest that we are witnessing a train wreck in slow motion.

The government of Paraguay recently (April 2011) declared a state of emergency when deaths attributed to dengue reached 22 and the hospitals in several areas became swamped with dengue cases. A particularly severe epidemic season of dengue was reported across Latin America starting in early 2011.

The RIDL mosquito developed by Oxitec is a rare thing, a new technology, something requiring technological breakthrough. I deal mostly with crop pests, but vector-borne pathogens, such as dengue, threaten people's lives. It is disappointing when others do not exercise urgency in addressing this issue. New technologies that involve genetic modification are often blocked before field trials by the so-called "precautionary principle." One of the foundations of science is testing. The foundation of development is trial and error. GM mosquitoes must advance to field trials, if only as a tribute to the people who have already died from dengue and those who are going to die in the future.

Insecticide control is most effective at high population densities, but the efficiency decreases rapidly as a population declines, which is why insecticide-only methods rarely eliminate local populations completely. In contrast, the SIT becomes more efficient as the population decreases, because the sterile insects actively seek out areas inaccessible to insecticides. Multiple dominant lethal mutations are produced by radiation-based SIT, making it virtually impossible to select a target population for resistance to this form of induced sterility. Although RIDL and other strategies based on a single dominant lethal gene show the same efficiency profile as the SIT, use of a single effector might pose some risk of resistance development in a target population, more comparable to the risks incurred with single-insecticide applications (Robinson and Hendrichs 2005).

RIDL as used in the SIT strategy is a sophisticated new technology that can eliminate local populations of vector mosquitoes much more efficiently than insecticides and without side effects or pollution. In doing so, it uses male mosquitoes that do not take blood meals and do not transmit the dengue virus. It is the most sustainable and environmentally friendly technology ever created for insect control, superior to classical biological control, which can threaten indigenous species.

*Aedes aegypti* has been displaced in most of Florida by *Aedes albopictus*, the Asian tiger mosquito. Both mosquitoes are vectors of the dengue virus. Will it be possible to develop a RIDL *Ae. albopictus*? I believe Oxitec could. Florida Keys Mosquito Control district and state officials are eager to try this new method in Key West, but others are blocking permission. Why? It boils down to an objection to human intervention and a vague sense that "we shouldn't be doing that" (the explanation given by the California Fish and Game commission for disallowing sale of GloFish®, a tropical fish with fluorescent protein genes inserted as a novelty).

This view would separate human beings from nature. It holds that people should not swap genes, even though plants, animals, and bacteria do so naturally. It is nonsense. We take responsibility for nature under the banners of "endangered species" and "biodiversity." We can also take responsibility for humans threatened by a painful and sometimes fatal disease.

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