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Biotech In focus

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Fighting Mosquitoes with Mosquitoes: Genetic Engineering for Bio-control

In our last bulletin we described 'gene drive'—genes that are stimulated to break the rules of Mendelian inheritance and spread rapidly through a population— and how they might be used in the future to kill insect pests that transmit diseases. 'Gene drive' includes adding, disrupting or modifying genes and possibly reducing reproductive ability. While 'gene drive' are in the earliest stages of laboratory research and development, other forms of biological pest control based on genetically engineered insects are closer to potentially widespread use.

Genetically modified (GM) mosquitoes have been field-tested in Malaysia, the Cayman Islands, Panama, and Brazil as a form of mosquito control. In March 2016, the Food and Drug Administration responded to a draft environmental assessment submitted by Oxitec Ltd. to support a Florida field trial of Oxitec's GM mosquito. The FDA has released a preliminary finding of no significant impact and is currently taking public comments on the environmental assessment.

Image: www.s.hswstatic.com

GM mosquitoes are a new approach to an old form of insect bio-control: the release of sterile males. In the 1930s scientists with the USDA discovered that X-rays damaged the DNA in the sperm of male flies. When an irradiated fly sperm cell combines with a normal egg cell, the resulting embryo dies because it does not develop properly.

Sterile male release was first used during the 1950s to control the screw-worm fly that lays its eggs in wounds of warm-blooded animals. After the eggs hatch, the maggots feed, tunneling into the flesh and eventually killing the animal in about ten days. The flies once plagued cattle in the southern half of the U.S. mainland.

Screw-worm fly reproduction was the target of earlier research and proved very successful. Large populations of the flies were grown in laboratories. Immature flies were irradiated, raised to adulthood, and released into the environment. The released sterile flies males outnumbered wild fertile males. Most female flies mated with sterile males and failed to produce offspring. The technique completely eradicated screw-worm in the United States and Mexico. More recently in Hawaii, sterile male release was part of an integrated pest management program that helped farmers grow crops that are vulnerable to fruit flies that attack fruit.

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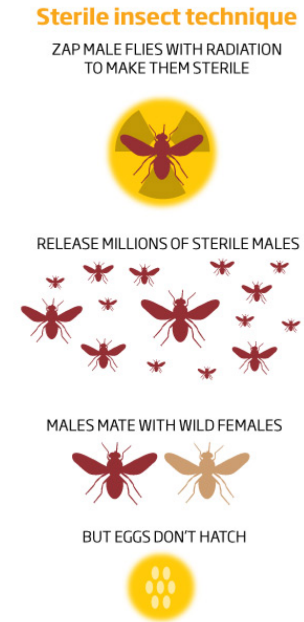
Sterile Insect Technique

In most types of sterile insect technique (SIT), it is preferable to only release males. Like male sperm, the eggs of female insects are vulnerable to radiation, but sterile female flies might harm crops or livestock while laying their eggs. In the screw worm program both male and females were released as there was no way to separate males from females. Later methods were developed with fruit flies that allowed the male to be separated from females and greatly enhancing the effectiveness of the sterile release programs.

Researchers hope to use sterile insects to combat Aedes aegypti, an invasive mosquito that has evolved to preferentially bite humans. Aedes aegypti females transmit viruses such as yellow fever, dengue, chikungunya, and Zika. Populations of Aedes aegypti are established on the Big Island.



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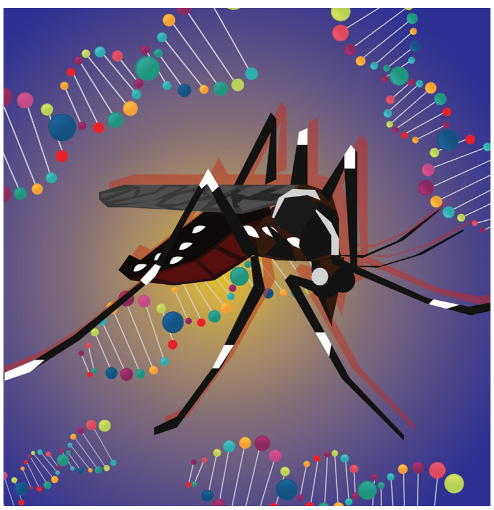
Conditional Gene

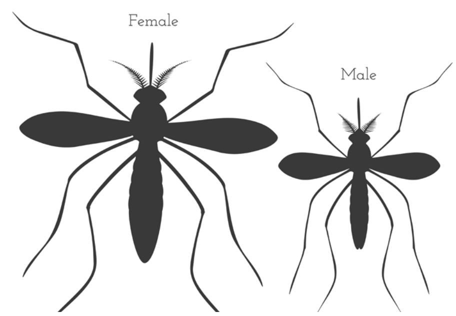


Unfortunately, the radiation required to sterilize male Aedes aegypti mosquitoes also hurts their ability to mate. As an alternative to irradiated sterile males, researchers have used genetic engineering to breed mosquitoes with two copies of a conditional lethal gene, that is, a gene that causes the mosquito to die, but only under certain conditions.

Activating Genes

In the hatchery, the GM mosquitoes are given tetracycline, an antibiotic that prevents the lethal gene from becoming active. When male GM mosquitoes are released into the environment, they lose their source of tetracycline, and the lethal gene is activated. Before they die, the male GM mosquitoes mate with wild females, passing on a copy of the lethal gene to each embryo. In the absence of tetracycline, these offspring die before reaching maturity. The engineered gene is called self-limiting, because it can't be passed from one generation to the next unless tetracycline is available.

Reducing Populations



Male mosquitoes do not bite, so they don't spread diseases. Immature male and female mosquitoes can be separated by size, so releases consist almost entirely of males. Any stray GM female mosquitoes that are released will die without a source of tetracycline.

Previous field trials of the GM mosquito have reduced wild populations of Aedes aegypti by over 90%. We don't yet know whether this level of control can be sufficient to limit the spread of disease in places where wild Aedes aegypti are abundant.

Spraying insecticides and encouraging the public to eliminate mosquito breeding sites—sources of standing water—have not prevented recent outbreaks of mosquito-borne illness. At the same time, many members of the public are wary of genetic engineering. Will fear of emerging diseases trump fear of DNA technology? If the Florida field trials with GM mosquitoes goes forward, what will we learn that will make us safer from insect-borne diseases?

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