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A 'Selfish' Solution for Eradicating Malaria

Using work done to rapidly introduce a transgenic element in fruit flies, researchers hope to cure mosquitoes—and humans—of malaria.

By Nikhil Swaminathan

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By appropriating a genetic mechanism used by the common flour beetle—a pest that can stowaway in cereal boxes bound for kitchen cabinets and pantries—Caltech researchers helped a transgenic fruit fly take over a population. The work, if replicated in malaria-resistant mosquitoes, could help battle the debilitating parasitic disease that kills between 700,000 and 2.7 million people annually, according to the Centers for Disease Control and Prevention.

Image: © ISTOCKPHOTO/OLEG MITIUKHIN

"SELFISH GENE" AMONG US: Researchers suggest that by using a "selfish gene" mechanism, whole populations of mosquitoes can be replaced with a malaria-resistant variety.

The scientists, led by biologist Bruce Hay, developed a set of "selfish" genes for the *Drosophila* fruit fly. This genetic process was first observed in the flour beetle in 1992, and involves a complicated but elegant system: Females inherit a genetic complex that includes a selfish driver—in the form of a toxin—along with an antidote, called a Medea, which stands for "maternal-effect dominant embryonic arrest."

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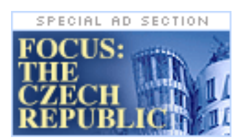

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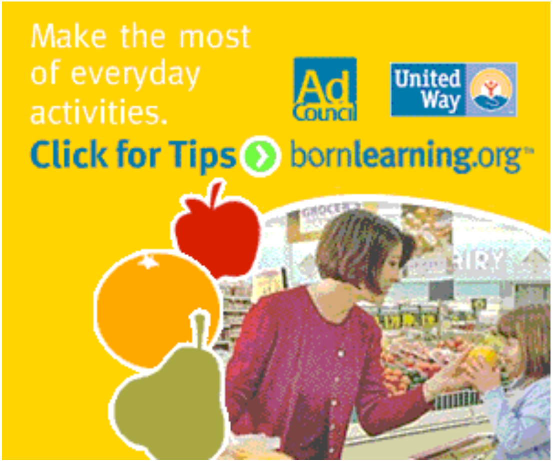

The driver causes the female's eggs to be flooded with a poisonous protein during development, which would kill the embryos unless they also inherit the Medea. The baby flies that receive this element will live because the antidote has been passed to them. If a normal male mates with a female that is heterozygous for the Medea complex--meaning she has a Medea complex on one chromosome, but not on its homologue--50 percent of the couple's offspring will perish. Over time, the Medea element will take over a population, sparing only those that carry it.

Hay and his colleagues report in *Science* that they believe the technique can be used in mosquitoes to enable them to resist picking up malaria, which females spread to humans when they bite them. "*Drosophila* and mosquitoes are very different," Hay admits, "but the way they undergo early development is very similar. … The parts may be different but the kind of machine being built will be the same."

In the *Drosophila* selfish gene model, researchers used a piece of noncoding microRNA as the Medea element instead of a toxin. The piece of RNA blocks the function of the *myd88,* a gene responsible for orienting the embryo in the mother's eggs while they are undergoing early cell division. "Mothers that carry our element give rise to completely screwed up eggs," Hay says, because silencing that particular gene disrupts the "ability of the embryo to know its top from bottom." The antidote, in this case, is a functioning copy of *myd88* that is on during early embryogenesis.

Hay's team then took equal numbers of normal males and males bearing their Medea element and put them in a confined space with unaltered females. Within 10 generations, a period of about six months, the Medea element was present in all of the fruit flies. "That's the point at which, if you had a disease gene there," Hay says, "you would have blocked the ability for the disease to spread."

In the case of mosquitoes, Hay notes, the Medea complex would be made up of the *myd88*-blocking microRNA, a malaria-resistant transgene and then the correct copy of *myd88*. Only embryos

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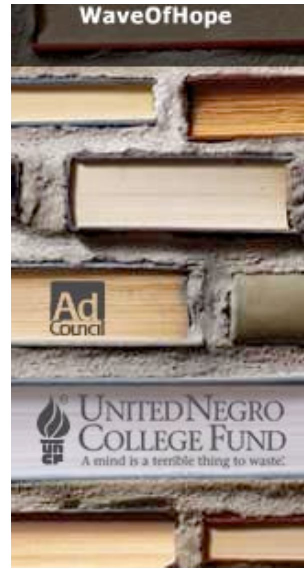

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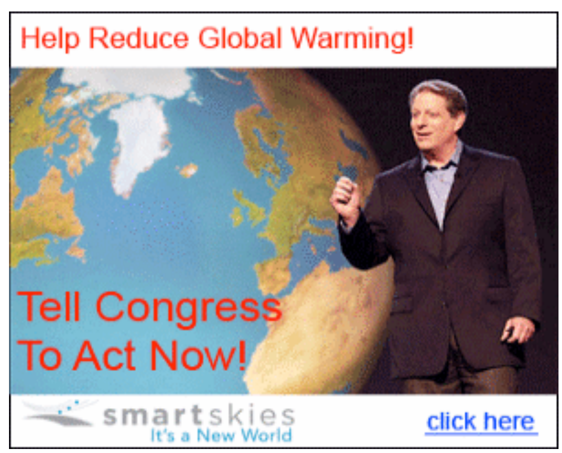

inheriting the complete driver-transgene-antidote set will survive. He estimates that if a sufficient quantity of males with Medea elements is released into a certain population of mosquitoes, it could be completely malaria-resistant within a year.

Hay, whose group typically works with *Drosophila,* says researchers plan to take a stab at inserting a Medea-complex into mosquitoes." We'll try and make it work in the mosquito as well," he says, adding that this innovation is a notable case in which "drosophila engineering can be used to make an impact on a really important set of human diseases."

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