New model reveals pesticide-free method that takes a bite out of mosquito-borne disease

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Scientists have modeled a system that may be used to control mosquitoes and the diseases they transmit, without the use of pesticides. In the proposed system, mosquitoes are engineered to carry two genes. The first gene causes males to transmit a toxin to females through their semen. The second gene, when expressed in females, makes them immune to this toxin. This research, published in the February 2011 issue of *Genetics*, describes a system that can be created using currently available molecular tools and could confine the spread of mosquitoes to isolated populations. It also allows the genes to be recalled if necessary.

"I hope that the results of this theoretical study will inspire molecular biologists to explore new ways of driving transgenes into populations," said John M. Marshall, Ph.D., a researcher involved in the work from the Department of Infectious Disease Epidemiology, School of Public Health at the Imperial College of London in the United Kingdom. "Ultimately, I hope that the application of these ideas will help move transgenic mosquito technology forward, and thereby contribute to the many efforts to reduce the prevalence of malaria and dengue fever in disease-endemic countries."

The gene transfer system was modeled using mathematical equations that describe how genetic alterations in the mosquitos' DNA are inherited from one generation to the next, and predict how these alterations will either spread or be eliminated from the population. The system has two basic components—a toxin expressed in the semen of transgenic males that either kills female recipients or renders them infertile, and an antidote expressed in females that protects them from the effects of the toxin. An all-male release should result in population suppression because wild females that mate with transgenic males produce no offspring. A release that includes transgenic females propagates the desired gene because females carrying the toxin gene are favored at high population frequencies.

The scientists used simple population genetics models to explore the utility of this gene-transfer system, and found that it can work under a wide range of conditions. It requires a high frequency of gene transfer, which is desirable because it means that genetically altered insects released accidentally are unlikely to persist in the wild. Furthermore, it means that those released intentionally can be spatially confined and that the altered genes can be removed from a population through sustained release of wild-type insects. The scientists found few technical barriers to implementing this system, increasing prospects for engineering and testing in the coming years.

"Mosquito bites can mean more than an itchy annoyance," said Mark Johnston, Editor-in-Chief of the journal *Genetics*. "For far too many people, they can lead to life-threatening diseases. But mosquitoes play a role in the greater ecosystem, and completely eradicating them may have unintended consequences that could be worse than the diseases they carry. This study is exciting because it suggests a way to control mosquito populations without pesticides, and in a way that gives us control of the process."

More information: John M. Marshall, Geoffrey W. Pittman, Anna B. Buchman, and Bruce A. Hay, Semele: A Killer-Male, Rescue-Female System for Suppression and Replacement of Insect Disease Vector Populations, *Genetics* 2011 187: 535.
www.genetics.org/cgi/content/abstract/187/2/535

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