New molecular target for malaria control identified

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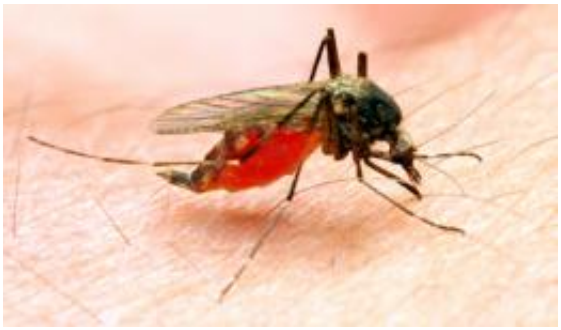

A new study led by Harvard School of Public Health (HSPH) and University of Perugia (UNIPG) researchers has shown that egg development in the mosquito species primarily responsible for spreading malaria depends on a switch in the female that is turned on by a male hormone delivered during sex. Blocking the activation of this switch could impair the ability of the species, *Anopheles gambiae*, to reproduce, and may be a viable future strategy for mosquito and malaria control.

The study appears online October 29, 2013 in *PLoS Biology*.

"These findings represent a significant step forward in our understanding of how these devastating malaria vectors reproduce," said Flaminia Catteruccia, associate professor of immunology and infectious diseases

at HSPH and UNIPG.

Malaria is a leading cause of death in tropical and subtropical regions. According to the U.S. Centers for Disease Control and Prevention, malaria claims nearly 660,000 lives per year, 90% of them in Africa—and most of them children. There were an estimated 216 million malaria cases worldwide in 2010, mostly among pregnant women and children.

The researchers based their investigation on existing knowledge about *Anopheles gambiae*, a highly efficient vector of the malaria parasite because those mosquitoes primarily feed on human blood and have a remarkably high reproductive rate.

The researchers studied the interaction between a steroid hormone called 20-hydroxy-ecdysone, or 20E—which is transferred from the male to the female mosquito during mating—and a female "Mating-Induced Stimulator of Oogenesis," or MISO, protein. (Oogenesis is the creation of an egg cell.)

They used chemical techniques to suppress MISO's functioning in female mosquitoes and found that doing so reduced egg development. They also found that MISO and 20E interact in the female mosquito's reproductive tract. Further, they identified the pathway through which 20E affects MISO. The 20E-MISO interaction boosts the accumulation of lipids in the ovaries, leading to a more rapid and higher production of eggs.

The researchers found that egg development depends on a switch—the MISO protein—in the female that is turned on by a male hormone delivered during sex. Male-transferred 20E essentially acts as a "mating signal" for the female to produce more eggs. "How males contributed to egg development had been previously unknown; with the identification

of the molecular players of this male-female interaction we can now find ways to switch off the signal and prevent females from reproducing," said Catteruccia.

This new finding holds promise for the development of new tools for controlling malaria-transmitting mosquito populations, the researchers said.

"This is the first time, in any insect species, that a male hormone has been shown to directly interact with a female protein and alter the ability of the female to reproduce," said co-author Francesco Baldini, a UNIPG graduate student who performed part of the analyses as a visiting scientist at HSPH.

More information: "The interaction between a sexually transferred steroid hormone and a female protein regulates oogenesis in the malaria mosquito Anopheles gambiae," Francesco Baldini, Paolo Gabrieli, Adam South, Clarissa Valim, Francesca Mancini, Flaminia Catteruccia, *PLoS Biology*, online October 29, 2013. www.plosbiology.org/article/in … journal.pbio.1001695

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