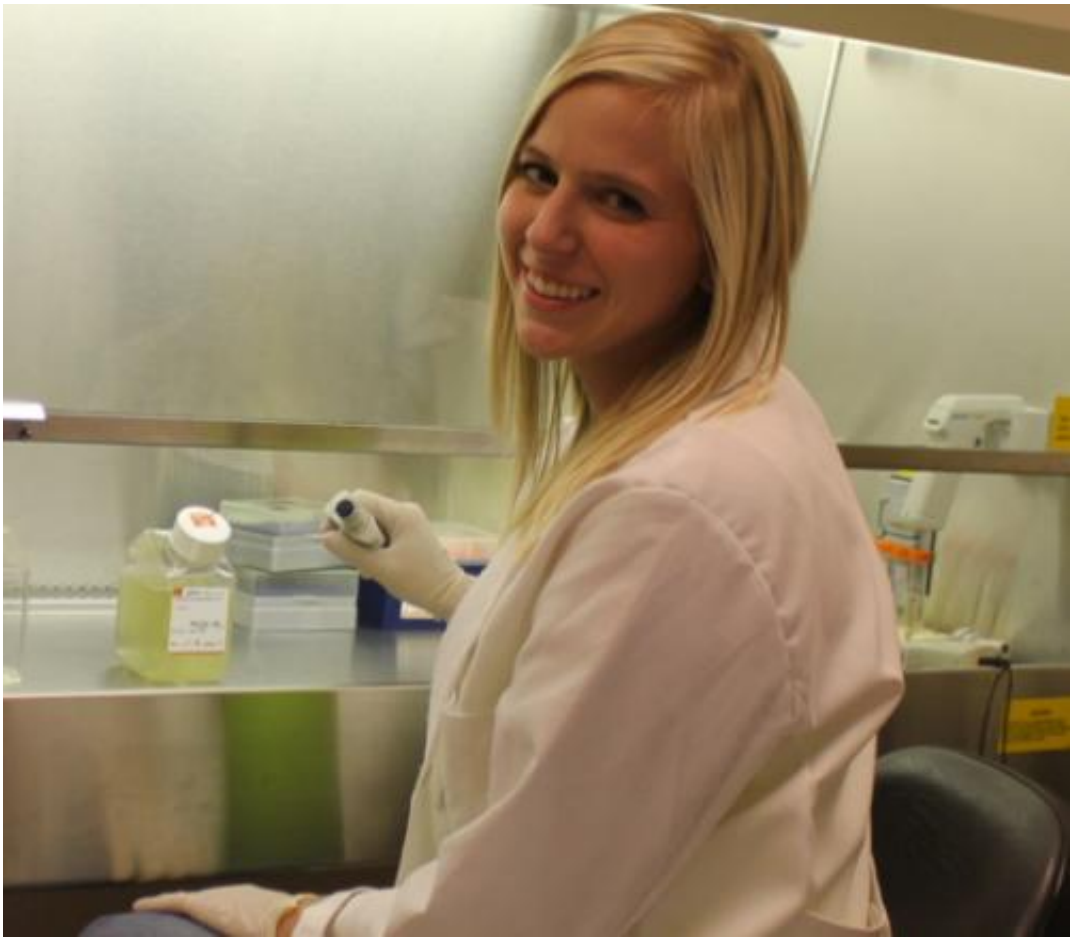
Scientists identify important mechanism involved in production of mosquito eggs

January 20 2015



Keira J. Lucas, a fifth-year Ph.D. graduate student in the Graduate Program in Genetics, Genomics and Bioinformatics at UC Riverside, is the research paper's first author. Credit: Raikhel Lab, UC Riverside.

Diseases transmitted by mosquitoes have contributed to the death and suffering of millions throughout human history, earning the mosquito the title as the world's most dangerous animal. Even today, several devastating mosquito-borne diseases (such as malaria, dengue fever and West Nile virus) continue to rage.

The urgent need to better control mosquito numbers and interfere with disease transmission has guided much mosquito research in laboratories worldwide. Female mosquitoes rely on a blood-meal as a source of nutrients required for reproduction. The thinking is that if the mechanisms that govern mosquitoes' egg production are better understood, novel approaches to controlling the reproduction and population of mosquitoes can be devised.

Now a team of scientists at the University of California, Riverside has made a research breakthrough in understanding, at the molecular level, one such mechanism related to the mosquito reproductive process. This mechanism includes small regulatory RNA molecules known as microRNAs or miRNAs.

The researchers report in this week's issue of the *Proceedings of the National Academy of Sciences* that they have identified microRNA-8 (miR-8) as an essential regulator of mosquito reproductive events. They note that its depletion in the female mosquito results in severe defects related to egg development and deposition.

Using newly established genetic tools in mosquito biology and doing analysis that identifies microRNA targets, they were able to show that miR-8 plays an essential role in the female mosquito "fat body" (fatty tissue analogous to the mammalian liver) by regulating a molecule, called "swim," that miR-8 directly targets. High levels of this molecule are detrimental to egg development.

"To our knowledge, this is the first time a mosquito miRNA has been investigated in this specific manner," said Alexander Raikhel, a distinguished professor of entomology, who has received wide acclaim for his research in the areas of insect reproductive biology. "In the lab, female transgenic mosquitoes with deficiency in miR-8 displayed severely compromised ovary development and reduced egg-laying."

While the researchers focused in this study on only *Aedes aegypti*, the mosquito that spreads dengue and yellow fever, their research results can be applied also to other disease-spreading mosquitoes.

"Our work provides insight into the importance of miRNAs in adult mosquito development and how these small regulatory molecules have potential to serve as novel control approach to regulate mosquito numbers," Raikhel said.

He explained that what his lab had set out to do was introduce birth control in mosquitoes.

"We were looking to find a way to disrupt the host-seeking behavior of mosquitoes by interrupting their egg development," he said. "With egg development halted, the population of mosquitoes would eventually collapse."

At UC Riverside, Raikhel's lab specializes in understanding the molecular basis of events in the mosquito reproduction cycle linked to a blood meal and pathogen transmission. His research focuses, too, on how pathogens of major human diseases, transmitted by mosquitoes, interact with their mosquito hosts. A member of the National Academy of Sciences, he occupies the Mir S. Mulla Chair in Entomology at UCR, as well as the University of California President's Chair.

To date, no effective vaccines for malaria, dengue fever or West Nile

virus exist. This lack of vaccines, along with increasing pesticide resistance in mosquitoes, adds to the urgency of exploring alternative strategies for mosquito control.

Nearly 2.5 billion people are at risk for contracting dengue fever. Each year, there are 100 million cases of dengue in the world. Yellow fever results in 30,000 deaths per year; about 200,000 cases are reported each year. Malaria alone causes over a million deaths annually. Dengue fever is emerging across the globe at an alarming rate; more than three billion people are now at risk of contracting this serious and debilitating viral disease. West Nile virus has invaded and spread throughout North America in just one decade; thousands in the United States are afflicted with this mosquito-borne virus every year.

More information: MicroRNA-8 targets the Wingless signaling pathway in the female mosquito fat body to regulate reproductive processes, *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1424408112

Provided by University of California - Riverside