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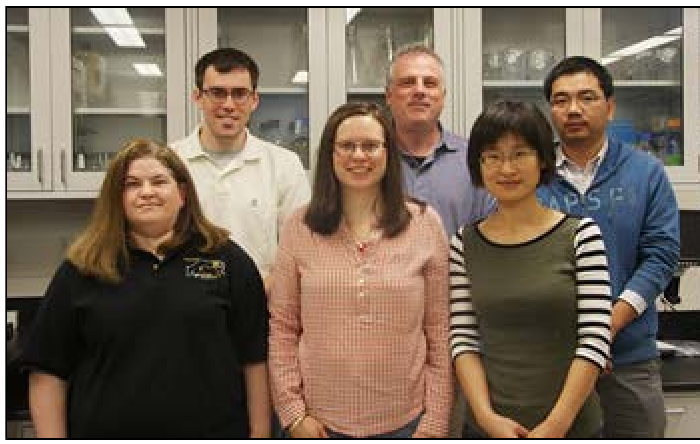
NEWS & EVENTS

Franz Receives Award for Best Paper

Alexander Franz, PhD, assistant professor in the Department of Veterinary Pathobiology at the MU College of Veterinary Medicine, has won the 2014 award for best paper in the journal *Insect Molecular Biology*. Sponsored by the Royal Entomological Society, the award recognizes the best paper over a two-year period.


Members of Dr. Alexander Franz's laboratory study the molecular interactions of arboviruses with the yellow fever mosquito, Aedes aegypti. Pictured are (from left) Michelle Gregory, Asher Kantor, Dr. Nicole Held, Dr. Alexander Franz, Jingyi Lin and Dr. Shengzhang Dong.

The paper, "Transgene-mediated suppression of the RNA interference pathway in Aedes aegypti interferes with gene silencing and enhances Sindbis virus and dengue virus type 2 replication," was published in February 2013. Franz's co-authors were C.C.H. Khoo, J.B. Doty, M.S. Heersink and K.E. Olson, all of Colorado State University. The research was funded by the National Institutes of Health and the National Institute of Allergy and Infectious Diseases.

Franz's research focuses on the molecular interactions of arboviruses with the yellow fever mosquito, Aedes aegypti. Arboviruses cause numerous emerging and resurgent human and veterinary diseases. Dengue virus and chikungunya virus are the two arboviruses the Franz group is currently studying. According to

Aedes aegypti mosquitoes are infected with chikungunya virus in a biosafety level 3 biocontainment laboratory of the MU Laboratory of Infectious Disease Research.

estimations by the Centers for Disease Control and Prevention, dengue virus has become the most wide-spread mosquito-borne virus infecting humans in tropical and subtropical regions of the world. Chikungunya virus, which often causes symptoms similar to dengue, is a newly emerging virus of African origin. It recently found its way to the Caribbean and into South America, causing disease outbreaks among the local human population.

Dengue and chikungunya viruses circulate between humans and mosquitoes. Following uptake of a bloodmeal from an infected human during biting, the viruses need to persistently infect the mosquito vector before being able to be transmitted to another human host. Control of these mosquito-borne viruses is difficult due to the lack of vaccines and therapeutics. Principal control efforts rely on vector control, such as insecticide applications, use of bed nets and removal of potential mosquito breeding containers around human premises.

There is a highly specific genetic interaction between an arbovirus and its mosquito vector, Franz said. Inside the mosquito an arbovirus is confronted with several hurdles such as tissue barriers and the mosquito’s immune responses. Importantly, mosquitoes do not get sick from being infected with dengue virus or chikungunya virus, whereas humans frequently develop severe disease symptoms following infection.

Franz said it is assumed that an infected mosquito does not try to get rid of an arbovirus, as the human host would do. Nevertheless, the mosquito somehow still keeps the replicating virus in check, which allows the virus to survive and be transmitted to a new vertebrate host, fulfilling the transmission cycle.

The aim of Franz’s research is two-fold: to understand the major genetic constituents in the mosquito that render the insect able to acquire and transmit an arbovirus, and to exploit or modulate these genetic factors to interrupt the transmission cycle as an alternative, novel arbovirus control strategy.

“As part of these efforts we previously discovered that the RNA interference pathway is a major antiviral immune pathway in the mosquito, which recognizes and destroys viral RNA genomes in a highly specific manner,” Franz said. “In a previous effort, we were able to manipulate the RNA interference pathway in genetically modified mosquitoes in such a way that they became resistant to dengue 2 virus. In these mosquitoes the virus was completely eliminated.”

In the research described in his award-winning paper, Franz and his co-authors tried the opposite: In genetically modified mosquitoes, they over-expressed a small protein originating from a beetle-killing virus known to disable the RNA interference pathway in invertebrates.

"Thus, we wanted to see what effect a dysfunctional RNA interference pathway would have on dengue virus and Sindbis virus, another human-infecting arbovirus, inside the mosquito," Franz said.

Their major observation was that these viruses reached significantly higher concentrations in the genetically modified mosquitoes in a much shorter period of time than in non-modified control mosquitoes, confirming the gatekeeper role of the RNA interference pathway.

Before coming to MU in January 2013, Franz spent 11 years at Colorado State University. There he worked as a postdoctoral researcher and a research scientist before being named an assistant professor. He received his bachelor's and master's degrees in agricultural sciences, as well as a PhD in plant pathology (plant virus-insect interactions), from the University of Kiel in Germany.

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