Insect pests of agriculture and human health cause enormous health burdens and economic damage at the individual, community, and global scale. To tackle these insect pest problems, the use of multi-faceted approaches is needed. Conventional control methods such as insecticide spraying, larvicidal treatments, and habitat removal are not enough. Insecticide resistance is increasing each year and habitat removal requires ongoing maintenance and labor, which can be costly and burdensome for homeowners, farmers, and others who need to manage these pests. There is a dire need for alternate approaches and genetic pest management (GPM) offers a multitude of tools and opportunities to control these pests. One use of genetic engineering involves gene drive systems that are designed to spread cargo (desirable) genes through a wild population of pests and alter their disease vectoring abilities, behavior, life cycle, or otherwise to eliminate or reduce their pest behaviors.

Presented here is a novel Killer-Rescue (K-R) gene drive system that has been designed, and constructed in *Drosophila melanogaster* and the mosquito *Aedes aegypti*. This system was built to drive desirable genes through a wild population for the end goal of population replacement or suppression. This system has the potential to drive at low release thresholds, possibly even less than 1:1 (engineered: wild type). This release ratio improves upon the techniques for population suppression without a drive that are currently used, which require continuous releases of 10:1 or higher to achieve and maintain population suppression. Population suppression without a drive can be costly, labor intensive, and fail in large-scale release areas.

The Killer-Rescue system is also considered a self-limiting gene drive. The rescue increases each generation through the lethal effects of the killer component (i.e. all insects that inherit only the killer die), as opposed to gene drives in which every offspring inherits the new engineered traits, such as CRISPR-Cas9 endonuclease-based drives. With K-R, only the insects that survive end up passing on the desirable cargo genes, and other insects that do not inherit the rescue and linked cargo gene die before they are adults.

A self-limiting gene drive system such as K-R has potential benefits compared to limitless drives (CRISPR-Cas9): (1) regulators and communities could be more accepting of field tests and applications, (2) it should require fewer regulations than a limitless drive and could pass more efficiently through federal regulations, and (3) it can be simpler to build.

A complete K-R gene drive system was designed, constructed, and tested in *Drosophila melanogaster*. In cage trials this system was successful in eliminating wild-type flies from the population and increasing the rescue genotype in the population over nine generations. These results suggest that this system has the potential to drive the rescue (and cargo gene) through a wild population for population replacement of an insect pest. In *Aedes aegypti* the system will be further tested to analyze its ability to drive the rescue genotype in cage experiments. Thus far, our results suggest the system has the potential to function as we saw in *Drosophila melanogaster*.