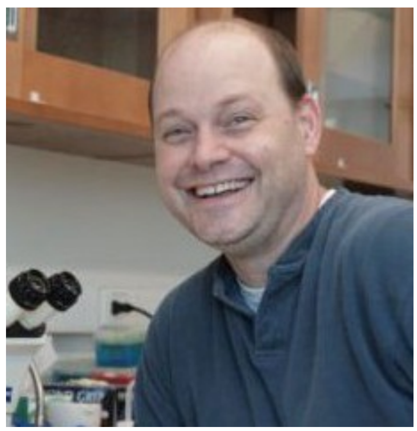
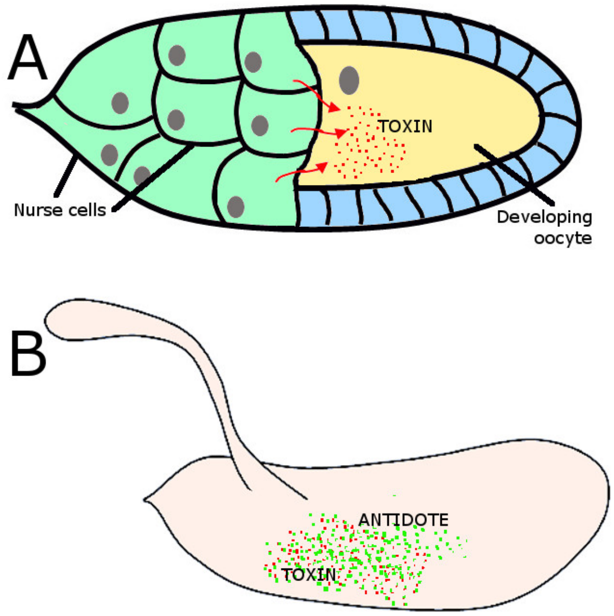
Gene Drive in a Major Agricultural Pest

MAY 21, 2018BY WILLIAM REID



BILL REID, PH.D. POSTDOCTORAL RESEARCHER, UNIVERSITY OF MISSOURI, DEPARTMENT OF VETERINARY PATHOBIOLOGY IN THE LABORATORY OF DR. ALEXANDER FRANZ.

In a recent report in ***PNAS***, Buchman et al. (2018) describe the construction and development of a MEDEA-based gene drive system in the crop pest, *Drosophila suzukii*. Buchman et al revisited the MEDEA-based gene drive approach developed in *D. melanogaster* by Chen at al (2007) and adapted it for *D. suzukii* by identifying the orthologous elements in *D. suzukii* and building them into a similar system. The objective of the work was to develop a gene drive system in *D. suzukii*, that can serve as a platform to drive anti-pest effectors that could reduce *D. suzukii* populations, such as they proposed- a conditional lethal gene activated by diapause.

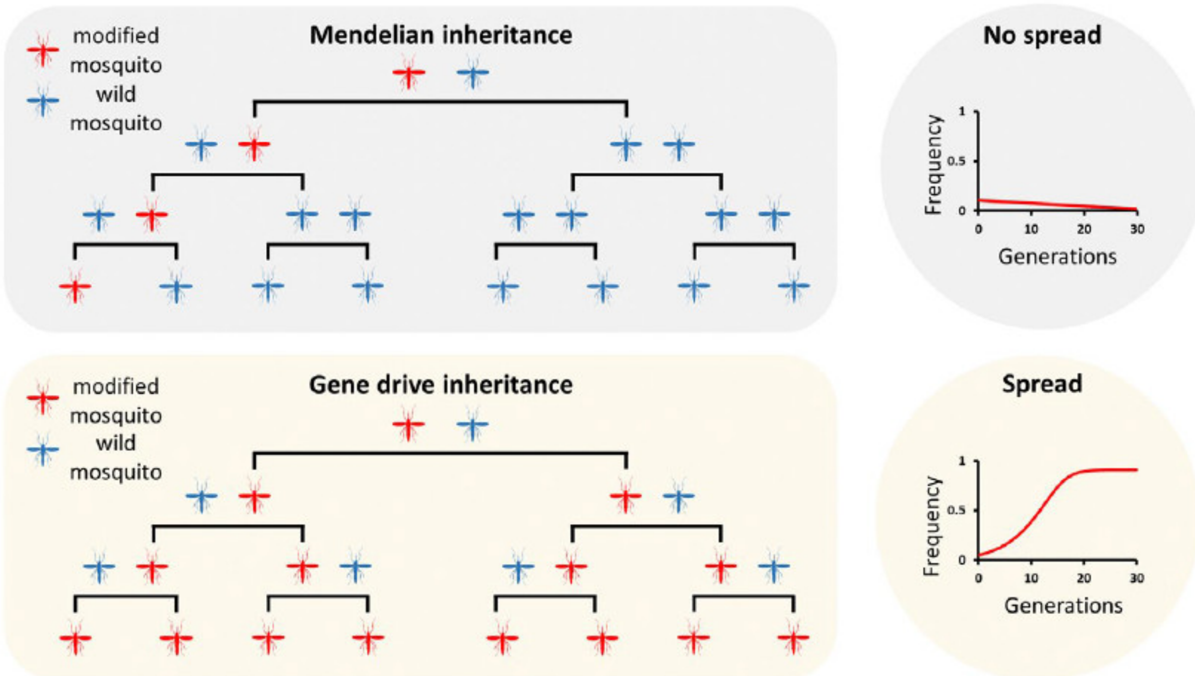


IN MEDEA, A LETHAL 'TOXIN' IS EXPRESSED MATERNALLY IN THE NURSE CELLS AND IS PROVISIONED INTO THE DEVELOPING OOCYTE (A). SINCE THE NURSE CELLS ARE 2N, ALL MEDEA-POSITIVE FEMALES WILL PROVISION THE OOCYTE WITH THE TOXIN, REGARDLESS OF THEIR ZYGOSITY FOR THE MEDEA SYSTEM. THE LETHAL EFFECT OF THE TOXIN WILL OCCUR ONLY DURING EMBRYOGENESIS, AND A RESULT, IF A ZYGOTICALLY EXPRESSED RESCUE/ANTIDOTE IS PRESENT (B), THE EMBRYO WILL SURVIVE, THUS ALL PROGENY WILL BE MEDEA-POSITIVE, PUSHING THE MEDEA ALLELES TO FIXATION IN THE POPULATION.

MEDEA, or "Maternal Effect Dominant Embryonic Arrest" (also a backronym for Medea from ancient Greek tragedy who killed her own offspring), was first identified as naturally-occurring in the red flour beetle *Tribolium castaneum*, and later developed as a synthetic system in *D. melanogaster*. MEDEA relies on the maternal provisioning of a 'toxin' to the oocyte, and a zygotically-expressed rescue 'antidote'.

In such a system, females carrying a single allele of the toxin will provision the toxin to all of her offspring, thus only progeny expressing the antidote will survive. The result of the toxin-antidote interaction is a super-Mendelian inheritance of both components of the MEDEA system, which can then be linked to an anti-pest effector allele to allow for genetic pest management.

The synthetic MEDEA gene drive system developed for *D. suzukii* relies on the maternal expression of miRNAs designed to target the 5'UTR of the native zygotic essential myd88 gene, and a rescue 'antidote' myd88 copy that is refractory (and linked) to the miRNAs. The result was a system that functioned with perfect efficiency for the first four generations, with all MEDEA-positive females yielding MEDEA-positive offspring. As with all gene drive systems, there is potential for both breakdown of the system and for the development of resistance, which the authors hypothesized was due to SNPs present within the target regions of the geographically-diverse populations, although the presence of some SNPs did not impact the efficiency of the MEDEA drive.



COMPARISON OF NORMAL MENDELIAN INHERITANCE TO SUPER-MENDELIAN INHERITANCE AS OBSERVED IN A GENE DRIVE SYSTEM. IN THE UPPER PANELS, OFFSPRING INHERIT THE ALLELE (RED MOSQUITOES) AT AN EXPECTED 50% FREQUENCY. IN THE LOWER PANELS, ALL OFFSPRING INHERIT THE ALLELE, THUS PUSHING THE ALLELE THROUGH THE POPULATION. FIGURE FROM ANDREW M. HAMMOND & ROBERTO GALIZI (2017) GENE DRIVES TO FIGHT MALARIA: CURRENT STATE AND FUTURE DIRECTIONS, PATHOGENS AND GLOBAL HEALTH, 111:8, 412-423, DOI:10.1080/20477724.2018.1438880

To address the development of resistance, the MEDEA system was tested against eight other geographically-diverse *D. suzukii* populations from the Eastern/Western US, and Japan, and remarkably the drive functioned perfectly in some populations, and with near-100% efficiency in others. While complete drive was absent in some populations, the development and establishment of a gene drive system intended to be used under natural conditions in a target insect species is certainly no trivial matter, and multiple approaches may need to be integrated to accomplish successful insect pest population suppression. The work by Buchman et al is a leap forward towards the use of gene drive in genetic pest management.

ADULT MALE SPOTTED WING DROSOPHILA, DROSOPHILIA SUZUKII (MATSUMURA). PHOTOGRAPH BY MARTIN HAUSER, CALIFORNIA DEPARTMENT OF FOOD AND AGRICULTURE.

Anna Buchman, John M. Marshall, Dennis Ostrovski, Ting Yang, Omar S. Akbari (2018) Synthetically engineered Medea gene drive system in the worldwide crop pest Drosophila suzukii. Proceedings of the National Academy of Sciences; 201713139. DOI: 10.1073/pnas.1713139115.

Chun-Hong Chen, Haixia Huang, Catherine M. Ward, Jessica T.Su, Lorian V. Schaeffer, Ming Guo, Bruce A. Hay. 2007. A Synthetic Maternal-Effect Selfish Genetic Element Drives Population Replacement in Drosophila. Science. vol 316, Issue 5824, pp. 597-600. DOI: 10.1126/science. 1138595.

Andrew M. Hammond & Roberto Galizi (2017) Gene drives to fight malaria: current state and future directions, Pathogens and Global Health, 111:8, 412-423, DOI:10.1080/20477724.2018.1438880.