IU BLOOMINGTON

EMERGING AREAS OF RESEARCH

Abstract Template -- Due June 30, 2017

Title of initiative to be proposed:

Accelerating evolution with CRISPR gene drives

Name of lead PI, with title, department/school:

Michael Wade, Distinguished Professor of Biology

Key team member names and departments/schools (up to 10 names):

Andrew Zelhof, Associate Professor of Biology
Gabriel Zentner, Assistant Professor of Biology

Description of area to be proposed. What constitutes this area of research or creative activity as emerging? (Word limit=500)

Genome editing technology based on clustered regularly interspersed palindromic repeats (CRISPR) has revolutionized biological research. In the lab, CRISPR is used to introduce genetic modifications that permit fine-scale dissection of gene function. Beyond the lab, the potential of CRISPR is apparent in many areas, particularly human health and agriculture, where CRISPR might be used to correct genetic defects underlying human diseases and engineer crops that resist pests and drought while producing additional nutrients. An additional potential application of CRISPR that has received increased attention is the idea of 'gene drives,' which could address key issues in public health, conservation, and agriculture.

What is a gene drive? In nature, there are genetic elements that bias their own transmission, ensuring that they are present in a population at a greater than expected frequency. Gene drives are thus considered 'selfish,' in that they cheat to ensure their own propagation. Notably, gene drives persist even though they may cause harm to their host. Drawing inspiration from naturally occurring gene drives, researchers have proposed CRISPR-based gene drives as a means by which to control populations of disease-vectoring insects, particularly mosquitoes, which transmit malaria, dengue, zika, chikungunya, and many other diseases. Diseases transmitted by mosquitoes and other insects account for ~17% infectious diseases and cause over 1 million deaths annually.

A handful of CRISPR drives have been successfully implemented in the lab, demonstrating the promise of this approach. However, there are factors that complicate their use in wild populations. We have found that genetic variation and inbreeding, which commonly occurs in populations of disease-vectoring insects, present substantial obstacles to propagation of a CRISPR gene drive. Such impediments will slow and eventually remove a CRISPR gene drive from a population of interest unless they are taken into account when designing the drive.

We propose to build a research group focused on applied genome editing, with a particular interest in designing and testing CRISPR gene drives. Such a group will capitalize on existing faculty strengths (Zelhof, Zentner, Wade) and focus on three immediate research goals: 1) expand the genome editing toolkit for the red flour beetle, Tribolium castaneum, a model organism in insect development and a major pest of stored food products; 2) design and construct novel approaches to CRISPR gene drives and effective reversal-of-drive mechanisms; 3) address the flaws we have identified in currently implemented CRISPR gene drives by drawing on our understanding of naturally occurring gene drives.

We propose to recruit 1-2 faculty with expertise in novel applications of genome editing technology, particularly in organisms of relevance to gene drive research. Combined with our existing strengths in molecular and population biology, these new faculty will transform IU Bloomington into a leader in CRISPR gene drive research. In the end, we anticipate that the technologies developed and insights gained, especially with respect to gene drives systems for both medical and agricultural insect vectors, will form a foundation for further public-private cooperation.

Please submit to earprogram@indiana.edu