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DNA repair pathway choice and significance in targeted genome editing of Aedes aegypti

Project Number
5R01AI137112-02

Contact PI/Project Leader
ADELMAN, ZACH N.

Awardee Organization
TEXAS A&M AGRILIFE RESEARCH

Description

Abstract Text

Aedes aegypti is the main vector of dengue, Zika, yellow fever and chikungunya viruses, and is a model system for studies of other mosquitoes that vector arboviruses. Current strategies based on suppressing mosquito populations can be effective, but are expensive and require a robust public health infrastructure. The ability to introgress pathogen-resistance genes into mosquito populations has long been sought as a potential alternative for disrupting dengue or malaria transmission where funds and infrastructure are the limiting factors in effective mosquito control. The recent development of effective site-specific nucleases such as homing endonucleases and CRISPR/Cas9 advanced technical solutions to achieving such super-Mendelian introgression, however there are still problems associated with the dominance of end-joining processes preventing the integration and spread of transgenic sequences. In this project, we aim to better understand DNA repair choice in mosquitoes and develop strategies to increase rates of homology-based repair following double-stranded DNA break induction. In Aim1 we will confirm the role of various potential end-joining factors in DNA repair and successful female development, while in Aim 2 we perform temporally-controlled rescue experiments to determine the most critical times during development for end-joining factors. Finally in Aim 3 we will assess the impact of loss of end-joining factors on various forms of homology-dependent repair. The knowledge gained from these experiments will further inform the development of gene drive strategies for vector control as well as provide insight into processes critical for mosquito development and evolution.

Public Health Relevance Statement

Aedes aegypti is the main vector of dengue, Zika, yellow fever and chikungunya viruses, and is a model system for studies of other mosquitoes that vector arboviruses. Gene drive strategies to introduce pathogen resistance genes into wild mosquito populations represent a powerful new control strategy, but the inability to control DNA repair choice limits the utility of many gene drive approaches. Our proposal seeks to examine DNA repair factors in this disease vector and develop strategies to influence repair pathway choice to promote recombination-based repair (gene drive).

NIH Spending Category

Biodefense Biotechnology Emerging Infectious Diseases Genetics Infectious Diseases Rare Diseases Vector-Borne Diseases

Project Terms

Adult Aedes Alleles Arboviruses Behavior Biological Biological Assay Biological Models Biology Bombyx CRISPR/Cas technology Chemicals Chikungunya **virus** Chromosomes Clustered Regularly Interspaced Short Palindromic Repeats Code Culicidae DNA DNA Damage DNA Double Strand Break DNA Repair DNA Repair Pathway DNA-PKcs Data Defect Dengue Development Disease Vectors Double-Stranded RNA Embryo Evolution Female Fertility Funding G22P1 gene Generations Genes Genetic Genetic Recombination Genetic Research Genome Heat-Shock Response Homing Human Immunity Individual Infrastructure Interspersed Repetitive Sequences Knock-in Knowledge

Read More

Details

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TEXAS A&M AGRILIFE RESEARCH

Country
UNITED STATES (US)

Other Information

FOA
PA-16-160

Study Section
Vector Biology Study Section[VB]

Fiscal Year
2019

Award Notice Date
11-December-2018

Administering Institutes or Centers
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

DUNS Number
847205713

CFDA Code
855

Project Start Date
03-January-2018

Project End Date
31-December-2022

Budget Start Date
01-January-2019

Budget End Date
31-December-2019

Project Funding Information for 2019

Total Funding
$425,420

Direct Costs
$289,488

Indirect Costs
$135,932

Year	Funding IC	FY Total Cost by IC
2019	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$425,420

NIH Categorical Spending

Click here for more information on NIH Categorical Spending

Funding IC	FY Total Cost by IC	NIH Spending Category
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$425,420	Biodefense; Biotechnology; Emerging Infectious Diseases; Genetics; Infectious Diseases; Rare Diseases; Vector-Borne Diseases;

Sub Projects

No Sub Projects information available for 5R01AI137112-02

Publications

No Publications available for 5R01AI137112-02

Patents

No Patents information available for 5R01AI137112-02

Outcomes

The Project Outcomes shown here are displayed verbatim as submitted by the Principal Investigator (PI) for this award. Any opinions, findings, and conclusions or recommendations expressed are those of the PI and do not necessarily reflect the views of the National Institutes of Health. NIH has not endorsed the content below.

No Outcomes available for 5R01AI137112-02

Clinical Studies

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5R01AI137112-02	ADELMAN, ZACH N.	TEXAS A&M AGRILIFE RESEARCH

Related News Releases

No news release information available for 5R01AI137112-02

History

No Historical information available for 5R01AI137112-02

Similar Projects

No Similar Projects information available for 5R01AI137112-02

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