Identification of candidate genes conditioning mosquito immune response to arboviruses

- **Description**
- **Details**
- **Sub-Projects**
- **Publications**
- **Patents**
- **Outcomes**
- **Clinical Studies**
- **News and More**
- **History**
- **Similar Projects**

Project Number	Contact PI/Project Leader	Awardee Organization
5R21AI144095-02	**SEVERSON, DAVID W**	**UNIVERSITY OF NOTRE DAME**

☰ Description

Abstract Text

PROJECT ABSTRACT Dengue virus (DENV) occurs as 4 serotypes that are biologically transmitted between humans principally by Aedes aegypti mosquitoes. This virus causes dengue fever, which is the most widespread and significant arboviral disease in the world. It also is the etiological agent of dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), severe and sometimes fatal forms of the disease. At present, mosquito control remains the only option for preventing transmission to humans of dengue and several other arboviruses. A. aegypti is also a primary vector for Zika and chikungunya virus as well as yellow fever virus in urban areas, throughout the tropics and subtropics, and is a recognized model for innate immunity studies with both protozoan (malaria: Plasmodium gallinaceum) and metazoan (lymphatic filariasis: Brugia malayi) parasite infections. The long-term goals of this research are to identify, isolate, and characterize genetic factors conditioning the A. aegypti innate immune response to arbovirus infection. Our general hypothesis is that a very small number of key genes condition a susceptible or refractory innate immune response to DENV and likely to ZIKV and other pathogens as well. Our rationale for this research is that these genes once identified could provide a foundation to explore development of a next generation of targeted and effective genetic control strategies. Our project builds on extensive preliminary data as well as the existing whole genome assembly for A. aegypti. The project specific aim is designed to employ well-established methods to identify discrete genome regions defined as quantitative trait loci (QTL) containing key genes that condition arbovirus susceptibility and identify all genes within these regions for future targeted functional analysis. The proposed research is significant as we expect it to better inform our basic understanding of the innate immune system in A. aegypti, with an overarching goal to facilitate development of new genetic control paradigms. Our proposed research is innovative because for the first time, it will integrate genetic, genomic, and phenotypic information on the A. aegypti innate immune response to DENV and ZIKV infection as derived from well-characterized susceptible and refractory genetic stocks. We expect that knowledge gained in this R21 proposal will provide critical preliminary data to support future detailed research that has potential to significantly enhance our understanding of the fundamental innate immune responses that promote or prevent successful arbovirus infection in this critical vector species, and could provide a model for conducting similar research in other arthropod/pathogen relationships.

Public Health Relevance Statement

PROJECT NARRATIVE Dengue, Zika and other arboviruses continue as significant global health problems with few options for prevention or treatment, thus the mosquito host often remains the only disease prevention option. This research proposal seeks to characterize the mechanisms responsible for a susceptible or resistant innate immune response of the mosquito to dengue and Zika virus infection. The proposed research is important to human health in that it will enhance fundamental knowledge on the mosquito innate immune system that will inform efforts to develop new mosquito-borne disease prevention strategies.

NIH Spending Category

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

Project Terms

Thank you for your feedback!

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- ☰ **Description**
- ▣ **Details**
- ⛃ **Sub-Projects**
- 📖 **Publications**
- ☀ **Patents**
- ⬈ **Outcomes**
- ⚕ **Clinical Studies**
- 🗞 **News and More**
- ⏱ **History**
- ⤳ **Similar Projects**

Project Number	Contact PI/Project Leader	Awardee Organization
5R21AI144095-02	SEVERSON, DAVID W	UNIVERSITY OF NOTRE DAME

Disease   Disease Vectors   Drosophila melanogaster   Etiology

Experimental Designs   Failure   Filarial Elephantiases   Foundations   Future

Genes   Genetic   Genome   Genomics   Goals   Health   Human

Read More

▣ Details

Contact PI/ Project Leader

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Other PIs

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Program Official

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Country
UNITED STATES (US)

Department Type
BIOLOGY

Organization Type
SCHOOLS OF ARTS AND SCIENCES

State Code
IN

Congressional District
02

Other Information

FOA
PA-18-489

Study Section
Vector Biology Study Section[VB]

Fiscal Year
2020

Award Notice Date
24-January-2020

Administering Institutes or Centers
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

DUNS Number
824910376

CFDA Code
855

Project Start Date
01-February-2019

Project End Date
31-January-2022

Budget Start Date
01-February-2020

Budget End Date
31-January-2022

Project Funding Information for 2020

Total Funding	Direct Costs	Indirect Costs
$193,250	**$138,750**	**$54,500**

Year	Funding IC	
2020	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$193,250

NIH Categorical Spending

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⟨ **Back to Search Results**

- **Description**
- **Details**
- **Sub-Projects**
- **Publications**
- **Patents**
- **Outcomes**
- **Clinical Studies**
- **News and More**
- **History**
- **Similar Projects**

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Diseases; Genetics; Infectious Diseases; Prevention; Rare Diseases; Vector-Borne Diseases;

Sub Projects

No Sub Projects information available for 5R21AI144095-02

Publications

No Publications available for 5R21AI144095-02

Patents

No Patents information available for 5R21AI144095-02

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 5R21AI144095-02

Clinical Studies

No Clinical Studies information available for 5R21AI144095-02

News and More

Related News Releases

No news release information available for 5R21AI144095-02

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〈 **Back to Search Results**

▤ **Description**

▤ **Details**

▱ **Sub-Projects**

▥ **Publications**

▯ **Patents**

▨ **Outcomes**

⚕ **Clinical Studies**

▤ **News and More**

◷ **History**

ᐤ **Similar Projects**

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Contact PI/Project Leader
SEVERSON, DAVID W

Awardee Organization
UNIVERSITY OF NOTRE DAME

ᐤ **Similar Projects**

No Similar Projects information available for 5R21AI144095-02

Thank you for your feedback!