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Previous exposure to dengue as a risk factor for Zika during pregnancy

Project Number	Former Number	Contact PI/Project Leader	Awardee Organization
5R01AI132563-03	**1R01AI132563-01A1**	**ALIOTA, MATTHEW T**	**UNIVERSITY OF MINNESOTA**

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▤ Description

Abstract Text

Project Summary Dengue **virus** (DENV) is endemic in many regions of the Americas where Zika **virus** (ZIKV) is emerging. These two viruses are closely related genetically and antigenically, so immunity to DENV may influence the outcome of ZIKV infection. The goal of this project is to understand the impact of pre-existing DENV immunity induced by infection or vaccination on ZIKV infection during pregnancy. This question is important because it has been hypothesized that the unexpectedly high rate of adverse consequences associated with ZIKV infection during pregnancy may be the result of previous infection with one of the four DENV serotypes. Primary infection with one DENV serotype is protective against secondary infection with the same serotype. Secondary infection with a different serotype can lead to enhanced disease because cross-reactive, inadequately neutralizing, an- tibodies can facilitate enhanced viral replication and skewed immune responses. DENV and ZIKV are similar enough in the envelope protein (the major target of these enhancing antibodies) that ZIKV could theoretically function as a "fifth" DENV serotype. This has been explored to some degree, but controversy remains, as some groups have reported cross-protection while others have reported the potential for enhanced disease. Critically, interactions between DENV and ZIKV have not been explored in the setting of pregnancy, even though congenital ZIKV infection is associated with birth defects. Accordingly, through this NIH/ NIAD R01 we will use our nonhuman primate model of ZIKV infection to evaluate whether the severity of ma- ternal and fetal ZIKV infection during pregnancy are enhanced by previous exposure to DENV. There are two Specific Aims: Specific Aim 1. Define the impact of prior DENV infection on the severity of maternal and neonatal ZIKV infection in pregnant macaques. Specific Aim 2. Define the impact of prior DENV vaccination on the severity of maternal and neonatal ZIKV infection in pregnant macaques. In these studies, we will contrast maternal viremia, immune responses, and fetal outcomes with those in DENV-naive individuals infected identically with ZIKV. Our strategy to induce DENV-specific immune re- sponses includes exposure to both wildtype DENV and a leading DENV vaccine candidate, Sanofi Pasteur's Dengvaxia®. These studies are critically important because 1) ZIKV is circulating in many locations where DENV is hyperendemic and 2) Dengvaxia® is currently licensed for use, and licensure of other DENV vaccines is imminent, in areas where ZIKV is circulating. By definition, large-scale vaccination campaigns will increase the prevalence of DENV immunity. Whether immunization with Dengvaxia®—which simultaneously exposes an individual to all four DENV serotypes—can lead to more severe ZIKV disease is unknown. The results from these experiments will provide important answers to an epidemiologically relevant question; is it safe to vacci- nate against dengue where ZIKV also is co-endemic?

Public Health Relevance Statement

Project Narrative Infection with Zika virus (ZIKV) during pregnancy has been implicated as the cause of a number of adverse consequences for the developing neonate, including mirocephaly. It has been speculated that coinfections of ZIKV and closely related dengue virus (DENV) might be interacting to cause the high incidence of particularly severe birth defects in Brazil. No studies have evaluated the potential for pre-existing DENV immunity to en- hance subsequent ZIKV infection during pregnancy; therefore, through this project we will use the nonhuman primate as a tractable, laboratory model to begin to understand whether the severity of maternal and fetal ZIKV increases in pregnant, dengue-immune individuals.

NIH Spending Category

Biodefense   Emerging Infectious Diseases   Immunization   Infectious Diseases   Pediatric

Pregnancy   Prevention   Rare Diseases   Vaccine Related   Vector-Borne Diseases   Women's Health

Project Terms

9 year old   Adult   Americas   Amino Acids   Antibodies   Area   Binding   Brazil   Cells

Complication   Conflict (Psychology)   Congenital Abnormality   Costa Rica   Country   Data

Dengue   Dengue Infection   Dengue Vaccine   Dengue **Virus**   Development   Disease   Dose

El Salvador   Epidemic   Epidemiology   Exposure to   Fc Receptor   Fetal Development   Flavivirus

Goals   Government   Guillain-Barré Syndrome   Immune   Immune response   Immunity

Immunization   Immunize   Immunology   Incidence   Individual   Infection   International

Laboratories   Lead   Licensure   Life   Link   Location   Macaca   Mexico   Microcephaly

Modeling   Mus   Neonatal   Neurologic   Outcome   Paraguay   Pathogenesis   Philippines

Read More

Thank you for your feedback!

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Organization

Name	Department Type	State Code
UNIVERSITY OF MINNESOTA	**VETERINARY SCIENCES**	**MN**
City	Organization Type	Congressional District
MINNEAPOLIS	**SCHOOLS OF VETERINARY MEDICINE**	**05**
Country		
UNITED STATES (US)		

Other Information

FOA
PA-16-160

Study Section
Virology - B Study Section[VIRB]

Fiscal Year
2019

Award Notice Date
19-December-2018

Administering Institutes or Centers
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

DUNS Number
555917996

CFDA Code
855

Project Start Date
01-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	Direct Costs	Indirect Costs
$629,055	**$499,142**	**$129,913**

Year	Funding IC	FY Total Cost by IC
2019	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$629,055

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	$629,055	Biodefense; Emerging Infectious Diseases; Immunization; Infectious Diseases; Pediatric; Pregnancy; Prevention; Rare Diseases; Vaccine Related; Vector-Borne Diseases; Women's Health;

⛭ Sub Projects

No Sub Projects information available for 5R01AI132563-03

📖 Publications

No Publications available for 5R01AI132563-03

💡 Patents

No Patents information available for 5R01AI132563-03

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No Outcomes available for 5R01AI132563-03

⚕ Clinical Studies

No Clinical Studies information available for 5R01AI132563-03

▤ News and More

Related News Releases

No news release information available for 5R01AI132563-03

◷ History

No Historical information available for 5R01AI132563-03

⬡ Similar Projects

No Similar Projects information available for 5R01AI132563-03

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