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Pathogenesis of and host response to chikungunya virus infection of the central nervous system

Project Number
5K01OD026529-02

Contact PI/Project Leader
BAXTER, VICTORIA K

Awardee Organization
UNIV OF NORTH CAROLINA CHAPEL HILL

Description

Abstract Text

Abstract The purpose of this K01 SERCA application is to provide the protected research time and mentorship necessary for Dr. Victoria Baxter, DVM, PhD, DACLAM to make the transition to independent investigator. Dr. Baxter is a veterinarian with a strong background in comparative medicine, viral immunology, and animal models of **infectious disease**, making her uniquely qualified for a career in translational research. Under the guidance of her mentor Dr. Mark Heise and an experienced interdisciplinary advisory committee, the training and aims outlined in this proposal will allow Dr. Baxter to expand her knowledge in viral and host genetics in order to establish a solid foundation for her own independent research program focused on understanding the pathogenesis of **emerging** and re-**emerging** viral diseases. The University of North Carolina at Chapel Hill will provide the interactive and collaborative environment necessary to support her transition to independence. Encephalitic arboviruses represent a re-**emerging** cause of human **disease** and disability, as patients who survive the initial acute **disease** are often left with lifelong neurological deficits. While chikungunya virus (CHIKV), an alphavirus that has recently spread to the Americas and Caribbean, typically causes a systemic **disease** characterized by rash and arthritis, individuals frequently develop neurological complications. Very little has been done to examine CHIKV encephalomyelitis, as no reliable small animal model currently exists. Most of the knowledge regarding the pathogenesis of alphavirus infection of the central nervous system (CNS) comes from the well-characterized mouse model of alphavirus encephalomyelitis using Sindbis virus. Outcome of CNS infection by Sindbis virus is dependent on both viral and mouse strain genetics, and CNS damage is primarily mediated by the immune response. This suggests three independent but interrelated factors drive CHIKV encephalomyelitis: viral genetics, host genetics, and the host immune system. The central hypothesis of the proposed studies is that CHIKV encephalomyelitis develops due to a combination of viral and host genetic factors, resulting in CNS damage that is primarily mediated by the host immune response rather than directly by CHIKV. This hypothesis will be tested with the following specific aims: Specific Aim #1: Determine if CHIKV genetic variation confers neurovirulence in a mouse model of CHIKV encephalomyelitis. Specific Aim #2: Elucidate the contribution of the adaptive immune system to CHIKV encephalomyelitis. Specific Aim #3: Determine if host genetic variation impacts susceptibility to CHIKV encephalomyelitis. These studies will generate valuable data that will provide a foundation for a future R01 application aimed at further elucidating mechanisms of CHIKV neuropathogenesis, and SERCA funding will provide Dr. Baxter with the skills necessary to establish similar models for examining other **emerging** viral diseases in the future.

Public Health Relevance Statement

Project Narrative Encephalitic arboviruses, including alphaviruses and flaviviruses, present a re-emerging public health concern, as surviving patients are often left with lifelong neurological deficits, and treatment is currently limited to supportive care. Examining the neuropathogenesis of chikungunya virus, a naturally arthritogenic alphavirus that frequently induces neurological disease, is severely limited by the lack of a robust small animal model. This proposal aims to establish and characterize a mouse model of chikungunya virus infection of the central nervous system that can then be used to elucidate the mechanisms of chikungunya virus neuropathogenesis and identify viral and host pathways that may be targeted by potential therapeutics.

NIH Spending Category

Brain Disorders | Emerging Infectious Diseases | Genetics | Infectious Diseases | Neurosciences | Rare Diseases | Vector-Borne Diseases

Project Terms

Acute **Disease** | Adaptive Immune System | Advisory Committees | Affect | Age | Alphavirus | Alphavirus Infections | Americas | Animal Model | Arboviruses | Arthritis | Arthritogenic | Autopsy | Award | B-Lymphocytes | C57BL/6 Mouse | Caribbean region | Central Nervous System Infections | Cessation of life | Chikungunya virus | Child | Clinical | Culicidae | Data | Development | **Disease** | **Disease** Outcome | Doctor of Philosophy | Emotional | Encephalitis | Encephalomyelitis | Exanthema | Flavivirus | Foundations | Funding | Future | Genetic | Genetic Variation | Geography | Human | Immune | Immune response | Immune system | Immunology | Individual | Infant | Infection | Inflammatory Response | Knowledge | Left | Maus Elberfeld virus | Mediating

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Awardee Organization
UNIV OF NORTH CAROLINA CHAPEL HILL

RESEARCH ASSISTANT PROFESSOR

Contact
vbaxter1@jhmi.edu

bruce.tuchs@nih.gov

Organization

Name
UNIV OF NORTH CAROLINA CHAPEL HILL

City
CHAPEL HILL

Country
UNITED STATES (US)

Department Type
PATHOLOGY

Organization Type
SCHOOLS OF MEDICINE

State Code
NC

Congressional District
04

Other Information

FOA
PA-16-190

Study Section
Special Emphasis Panel[ZRG1-IMST-D(80)S]

Fiscal Year
2019

Award Notice Date
11-July-2019

Administering Institutes or Centers
OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DUNS Number
608195277

CFDA Code
351

Project Start Date
01-August-2018

Project End Date
31-July-2023

Budget Start Date
01-August-2019

Budget End Date
31-July-2020

Project Funding Information for 2019

Total Funding
$126,222

Direct Costs
$116,872

Indirect Costs
$9,350

Year	Funding IC	FY Total Cost by IC
2019	OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH	$126,222

NIH Categorical Spending

Click here for more information on NIH Categorical Spending

Funding IC	FY Total Cost by IC	NIH Spending Category
OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH	$126,222	Brain Disorders; Emerging Infectious Diseases; Genetics; Infectious Diseases; Neurosciences; Rare Diseases; Vector-Borne Diseases;

Sub Projects

No Sub Projects information available for 5K01OD026529-02

Publications

No Publications available for 5K01OD026529-02

Patents

No Patents information available for 5K01OD026529-02

Outcomes

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Clinical Studies

No Clinical Studies information available for 5K01OD026529-02

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No news release information available for 5K01OD026529-02

History

No Historical information available for 5K01OD026529-02

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