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Development of vaccines targeting a tick-borne phlebovirus

Project Number
1R01AI152236-01

Contact PI/Project Leader
BATES, PAUL

Awardee Organization
UNIVERSITY OF PENNSYLVANIA

Description

Abstract Text

Severe Fever with Thrombocytopenia Syndrome virus (SFTSV) is a pathogenic, tick-transmitted bunyavirus that can cause a severe febrile hemorrhagic-like disease with case fatality rates of up to 30%. Discovered during a 2009 outbreak of febrile illness in China, the geographic distribution of SFTSV extends into Korea and Japan with recent reports of infection in Vietnam and Russia. The tick vector for SFTSV is widespread throughout Asia. Numerous domestic and wild animals are naturally infected by SFTSV suggesting a large reservoir with potential spillover to humans. There are currently no vaccines or therapeutics for SFTSV. Because of its epidemic threat the WHO included SFTSV in its 2017 recommendation “A research and development Blueprint for action to prevent epidemics” and identified SFTSV as one of 11 pathogens most likely to cause severe outbreaks in the near future and proposed development of vaccines. Here we will explore two complementary and potentially synergistic strategies for an SFTSV **vaccine**: a recombinant viral vector and nucleoside-modified **mRNA** encoding the SFTSV viral glycoproteins. Vesicular stomatitis virus (VSV) is a cytopathic virus that has been developed as a **vaccine** vector due to its ability to rapidly induce strong, protective antibody and T cell responses to encoded foreign antigens after a single dose. Using a VSV vector expressing the SFTSV viral glycoproteins (similar to the currently employed VSV-Ebola **vaccine**), we demonstrate single dose induction of a neutralizing antibody response and protection from SFTSV challenge in an IFNAR1 knockout mouse model. Separately, we show that vaccination of wt mice with a single dose of nucleoside-modified **mRNA** lipid nanoparticles (**mRNA**-LNP) encoding the SFTSV glycoproteins elicits high levels of SFTSV neutralizing antibodies that are capable of conferring partial SFTSV protection when transferred into the IFNAR1 KO model. Based upon these strong preliminary findings we propose to characterize antibody and T-cell responses in rVSV and **mRNA** vaccinated mice when these vaccines are used alone or in a prime-boost regimen. These studies are significant as there is limited knowledge regarding vaccines for this highly pathogenic virus (a single report) and use of rVSV and **mRNA** in a prime-boost vaccination has not been reported. Finally, current small animal models of SFTSV infection are limited to animals with type I IFN responses knocked out. Because these animals lack an important innate immune response mechanism that supports amplification of cellular and humoral immune responses, we will develop an immune competent mouse vaccination model using transient monoclonal antibody blockade of IFNAR1 during SFTSV challenge.

Public Health Relevance Statement

Severe Fever with Thrombocytopenia virus (SFTSV) is a highly pathogenic, tick- transmitted virus that causes a severe hemorrhagic disease. There are no treatments or prophylactics available for SFTSV. This proposal will develop and analyze immune responses to mRNA and recombinant viral vaccines for use either alone or in combination to prevent infection.

NIH Spending Category

Biodefense Biotechnology Emerging Infectious Diseases Immunization Infectious Diseases Prevention Vaccine Related Vector-Borne Diseases

Project Terms

Affinity Animal Model Animals Antibodies Antibody Response Antigens Antiviral Agents Asia B-Lymphocytes Bunya

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Goals Hemorrhage Human IFNAR1 gene Immune response Immunity Immunize Immunocompetent Infection Infection prevention Influenza

Read More

Details

Contact PI/ Project Leader

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Not Applicable

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Country
UNITED STATES (US)

Department Type
MICROBIOLOGY/IMMUN/VIROL(

Organization Type
SCHOOLS OF MEDICINE

State Code
PA

Congressional District
03

Other Information

FOA
RFA-AI-19-037

Study Section
Special Emphasis Panel[ZAI1 FDS-M (M1)]

Fiscal Year	Award Notice Date
2020	10-July-2020

Administering Institutes or Centers
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

DUNS Number **042250712**
CFDA Code **855**

Project Start Date	**10-July-2020**
Project End Date	**30-June-2025**
Budget Start Date	**10-July-2020**
Budget End Date	**30-June-2021**

Project Funding Information for 2020

Total Funding
$535,986

Direct Costs
$376,169

Indirect Costs
$159,817

Year	Funding IC	
2020	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$535,986

NIH Categorical Spending

Click here for more information on NIH Categorical Spending

Funding IC	FY Total Cost by IC	NIH Spending Category

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UNIVERSITY OF PENNSYLVANIA

Immunization; Infectious Diseases; Prevention; Vaccine Related; Vector-Borne Diseases;

Sub Projects

No Sub Projects information available for 1R01AI152236-01

Publications

No Publications available for 1R01AI152236-01

Patents

No Patents information available for 1R01AI152236-01

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 1R01AI152236-01

Clinical Studies

No Clinical Studies information available for 1R01AI152236-01

News and More

Related News Releases

No news release information available for 1R01AI152236-01

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No Similar Projects information available for 1R01AI152236-01

Thank you for your feedback!