Back to Search Results

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

Structure-based Vaccine Design for CCHFV

Project Number
1R01AI152246-01

Contact PI/Project Leader
MCLELLAN, JASON SCOTT Other PIs

Awardee Organization
UNIVERSITY OF TEXAS, AUSTIN

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Description

Abstract Text

Project Summary/Abstract Crimean-Congo hemorrhagic fever virus (**CCHFV**) causes a life-threatening tick-borne disease in humans. The disease presents as a severe form of hemorrhagic fever with a case fatality rate of 10–40%. **CCHFV** outbreaks have spanned a wide geographic area ranging from Western and Central Asia, the Middle East, Africa and Southern Europe. Increasing global temperatures, migratory birds, and the international livestock trade have all potentially contributed toward the spread of Hyalomma ticks—the primary vector for **CCHFV**. Expanding endemic zones, widespread morbidity and significant mortality make **CCHFV** an acute threat to public health and thus is listed as a NIAID Category A priority pathogen. The viral genome encodes a glycoprotein precursor that is processed into two structural glycoproteins—Gn and Gc—and two secreted glycoproteins—a mucin-like domain and GP38. Protective antibodies have been isolated that target Gc or GP38, suggesting that these two proteins should be given priority for vaccine development. Here we propose to engineer Gc- and GP38-based immunogens that focus the immune response onto broadly conserved epitopes that are capable of eliciting protective antibody responses. To accomplish our goal, we will structurally characterize **CCHFV** glycoproteins and their interactions with human-derived antibodies, rationally engineer vaccine antigens based in part on the structural information, and characterize the immune responses elicited by these antigens in animal models. These results will be used to guide further improvements of the immunogens, including display on self-assembling multi-valent nanoparticles, and the most promising candidates will be evaluated in a lethal murine model of **CCHFV** challenge. Given our expertise, unique reagents, and preliminary data, we are confident that we can deliver a state-of-the-art subunit vaccine candidate with the potential to induce cross-reactive protective antibodies, thereby satisfying an unmet need against this NIAID Category A tick-borne pathogen.

Public Health Relevance Statement

Project Narrative Crimean-Congo hemorrhagic fever is the most widespread tick-borne viral disease in humans with case-fatality rates of 10–40%. Here we propose to employ structure-based vaccine design principles to engineer immunogens that induce cross-reactive protective antibodies. Our studies will provide insight into the structures and antigenicity of CCHFV glycoproteins and will deliver a bona fide vaccine candidate against a NIAID Category A pathogen.

NIH Spending Category

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

Project Terms

Acute Africa Animal Model Antibodies Antibody Response Antibody Therapy Antigens Antiviral Agents Case Fatality Rates Categories Category A pathogen Cells Central Asia Chimeric Proteins Complex Coronavirus Crimean Hemorrhagic Fever Crimean-Congo Hemorrhagic Fever Virus Crystallization Data Data Protection Disease Disease Outbreaks Dyes Engineering Epitope Mapping Epitopes Evaluation Family Filovirus Funding Genome Geographic Locations Glycoproteins Goals Human IFNAR1 gene Immune response Immunocompromised Host Immunologics Incidence International Laboratories Laboratory Animal Models Life Livestock Maps

Read More

Details

Contact PI/ Project Leader

Name
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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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Awardee Organization
UNIVERSITY OF TEXAS, AUSTIN

UNIVERSITY OF TEXAS, AUSTIN

City
AUSTIN

Country
UNITED STATES (US)

BIOLOGY

Organization Type
SCHOOLS OF ARTS AND SCIENCES

TX

Congressional District
10

Other Information

FOA
RFA-AI-19-037

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

Fiscal Year
2020

Award Notice Date
25-June-2020

Administering Institutes or Centers
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

DUNS Number
170230239

CFDA Code
855

Project Start Date **25-June-2020**
Project End Date **31-May-2025**
Budget Start Date **25-June-2020**
Budget End Date **31-May-2021**

Project Funding Information for 2020

Total Funding
$441,966

Direct Costs
$351,007

Indirect Costs
$90,959

Year	Funding IC	FY Total Cost by IC
2020	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$441,966

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	$441,966	Biodefense; Bioengineering; Biotechnology; Emerging Infectious Diseases; Immunization; Infectious Diseases; Nanotechnology; Prevention; Vaccine Related; Vector-Borne Diseases;

Sub Projects

No Sub Projects information available for 1R01AI152246-01

Publications

No Publications available for 1R01AI152246-01

Patents

No Patents information available for 1R01AI152246-01

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 1R01AI152246-01

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Back to Search Results

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

Related News Releases

No news release information available for 1R01AI152246-01

History

No Historical information available for 1R01AI152246-01

Similar Projects

No Similar Projects information available for 1R01AI152246-01

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