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Project 2 - Vanderbilt University

Parent Project Number	Sub-Project ID	Contact PI/Project Leader	Awardee Organization
1U19AI142764-01	8020	CROWE, JAMES E	HENRY M. JACKSON FDN FOR THE ADV MIL/MED

Description

Abstract Text

Project Summary The Henipavirus genus of RNA viruses in the family Paramyxoviridae contains five established species. Henipaviruses are found naturally in **bats** in Australia and Asia and more recently have been found in Africa, and they have a wide host range. These zoonotic pathogens can cause severe illness and death in domestic animals and humans. The prophylactic and therapeutic options for Hendra and Nipah virus infections in man are limited. Anti-Hendra/Nipah human mAbs are expected to be valuable antiviral therapeutics as countermeasures to Hendra and Nipah virus disease in humans. Here, we will isolate panels of naturally occurring human monoclonal antibodies (mAbs) that bind cross-reactively to both Hendra and Nipah virus F or G proteins and neutralize both viruses. In preliminary experiments, we have isolated some mAbs that exhibit very high potency in neutralization assays, suggesting they have high potential as prophylactic and therapeutic molecules for humans. We propose here a series of aims that will contribute significantly to the development and characterization of such human mAbs reactive to the F and G glycoproteins of Hendra and Nipah virus in preparation for clinical studies. The work will identify and fully characterize a panel of highly promising antibodies with the goal of identifying and selecting lead compounds and advancing their preclinical development. The work is organized in two major Specific Aims: Aim 1) Isolation of human mAbs from patients previously infected with henipavirus or exposed to henipavirus vaccine antigens. In this Aim, human mAbs will be identified that recognize epitopes that are conserved across henipaviruses and neutralize those viruses at low concentration. Blood cells from a subject exposed to Hendra virus equine vaccine will be screened for virus specific antibodies. These cells will be converted to stable human hybridoma cell lines and subjected to high- throughput screening to identify Abs that bind to Hendra and Nipah G proteins and functionally inhibit virus replication. Aim 2: Develop Abs for the treatment of henipavirus infections. Antibodies identified in Aim 1 will be tested for their broad recognition of conserved epitopes across all henipaviruses and for their ability to neutralize in culture. Prioritized antibodies then will be tested for therapeutic efficacy in multiple animal models of infection including nonhuman primates. The leads will be selected, and CHO cell lines will be made by Mapp Biopharmaceutical for Ab production, in preparation for cGMP manufacture and IND planning. The work promises to yield a best-in-class antibody preparation for broad and potent activity against henipaviruses that can be used to treat or prevent human henipavirus infections.

Public Health Relevance Statement

Project Narrative N/A

NIH Spending Category

Biodefense Biotechnology Emerging Infectious Diseases Immunization Immunotherapy Infectious Diseases Prevention Vaccine Related

Project Terms

Affinity Africa Animal Model Antibodies Antibody Formation Antigens Antiviral Agents Asia Australia Binding Biological Assay Biological Products Biological Response Modifier Therapy Biological Testing Blood Cells Cell Line Cells Cessation of life Chinese Hamster Ovary Cell Chiroptera Clinic Clinical Research Cyclic GMP Development Domestic Animals Epitopes Equus caballus Exhibits Exposure to Family GTP-Binding Proteins Goals Hand Hendra Virus Henipavirus Henipavirus Infections Human Hybridomas Immune

Read More

Details

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Department Type
Unavailable

Organization Type
Research Institutes

State Code
MD

Congressional District
08

Other Information

FOA
RFA-AI-17-042

Study Section
Special Emphasis Panel[ZAI1 LG-M (J1)]

Fiscal Year
2019

Award Notice Date
20-March-2019

Administering Institutes or Centers
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

DUNS Number
144676566

CFDA Code

Project Start Date

Project End Date

Budget Start Date
20-March-2019

Budget End Date
29-February-2020

Project Funding Information for 2019

Total Funding
$862,247

Direct Costs
$862,247

Indirect Costs
$0

Year	Funding IC	
2019	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$862,247

Thank you for your feedback!

NIH Categorical Spending

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Funding IC	FY Total Cost by IC	NIH Spending Category
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$862,247	Biodefense; Biotechnology; Emerging Infectious Diseases; Immunization; Immunotherapy; Infectious Diseases; Prevention; Vaccine Related;

Sub Projects

No Sub Projects information available for 1U19AI142764-01 8020

Publications

No Publications available for 1U19AI142764-01 8020

Patents

No Patents information available for 1U19AI142764-01 8020

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 1U19AI142764-01 8020

Clinical Studies

No Clinical Studies information available for 1U19AI142764-01 8020

News and More

Related News Releases

No news release information available for 1U19AI142764-01 8020

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History

No Historical information available for 1U19AI142764-01 8020

Similar Projects

No Similar Projects information available for 1U19AI142764-01 8020

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