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Project I: Discovery and Evaluation of Antibodies and Cocktails

Parent Project Number	Sub-Project ID	Contact PI/Project Leader	Awardee Organization
5U19AI142777-02	8148	CHANDRAN, KARTIK	ALBERT EINSTEIN COLLEGE OF MEDICINE

Description

Abstract Text

Abstract – Project I The overarching goal of the Prometheus consortium is to develop antibody-based prophylactics and therapeutics against three major groups of Category A priority viruses that pose the highest risk to national security and public health and cause zoonotic disease—ebolaviruses, the nairovirus Crimean-Congo hemorrhagic fever virus (**CCHFV**), the New-World hantaviruses Andes virus (ANDV) and Sin Nombre virus (SNV), and the Old-World hantavirus Puumula virus (PUUV). No approved treatments are available for any of these viruses. Given the safety and efficacy of over 50 mAb-based therapies currently available in market for various diseases, mAbs are a low-risk platform to develop countermeasures for these Category A viruses. The rapid discovery and development of large numbers of pathogen-specific human monoclonal antibodies (mAbs) from convalescent and acutely infected donors is the central strength to our platform. Coming from hosts who have already mounted an effective antibody response, these naturally occurring mAbs are less likely to elicit tissue cross-reactivity and in vivo toxicity in humans and also obviate the need for chimerization or time- consuming humanization. Prometheus will use these mAbs as raw material to produce broadly protective immunotherapeutics that (i) are robust to natural viral genotypic variation; (ii) leverage multi-epitope targeting and an innovative feature we term RAVE (reciprocal antagonism to viral escape) to enhance potency and resist escape of viral neutralization; (iii) exploit tuned Fc effector properties for extended in vivo half-life and more effective elimination of viral particles and infected cells; and (iv) can be directly and rapidly transitioned to advanced pre-clinical development. Project I will work collaboratively with Project II to identify human mAbs and oligoclonal mAb cocktails against **CCHFV** and hantaviruses (SNV, ANDV, and PUUV) with these properties—pan-ebolavirus lead human mAbs have already been identified by Prometheus members. We will hand off lead mAbs and cocktails to Core B as candidates for advanced development of therapeutics, and to Project III for studies aimed at the generation of DNA-encoded mAbs (DMAbs) for prophylactic delivery. In consultation with the SAC, lead molecules will be evaluated by Core C for protective efficacy in NHP models of **CCHFV** and SNV challenge.

Public Health Relevance Statement

Narrative – Project I No FDA-approved treatments exist for medically important and globally prevalent human viruses such as ebolaviruses, Crimean-Congo hemorrhagic fever virus (CCHFV) and hantaviruses. Projects I will work collaboratively with Project II to isolate highly potent antibodies against CCHFV and hantaviruses from human survivors of these deadly virus infections; antibodies against ebolaviruses have already been identified by Prometheus members. We will hand over the best antibodies to Core C to test in animal models and to further develop them for antiviral therapy for delivery as antibodies (Core B) or DNA (Project III).

NIH Spending Category

Biodefense Biotechnology Clinical Research Emerging Infectious Diseases Immunization Immunotherapy Infectious Diseases Orphan Drug Rare Diseases Vector-Borne Diseases

Project Terms

Acute Advanced Development Affinity Andes Virus Animal Model Antibodies Antibody Response Antibody Therapy Antigens Antiviral Agents Antiviral Therapy B-Lymphocytes Biological Assay Biophysics Blood Screening Blood specimen Categories Cells Collaborations Collection Complex Consultations Consumption Crimean-Congo Hemorrhagic Fever Virus DNA Data Development Disease Dose Ebola virus Epitopes European Evaluation FDA approved Generations Genome Genotype Glycoproteins Goals Half-Life Hand Hantavirus Human Immunotherapeutic agent In Vitro Infection Lead Medical Modeling

Read More

Details

Contact PI/ Project Leader

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Organization

Name
ALBERT EINSTEIN COLLEGE OF MEDICINE

City
BRONX

Country
UNITED STATES (US)

Department Type
Unavailable

Organization Type
Domestic Higher Education

State Code
NY

Congressional District
14

Other Information

FOA
RFA-AI-17-042

Study Section
ZAI1-LG-M

Fiscal Year
2020

Award Notice Date
24-January-2020

Administering Institutes or Centers
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

DUNS Number
081266487

CFDA Code

Project Start Date

Project End Date

Budget Start Date
01-February-2020

Budget End Date
31-January-2021

Project Funding Information for 2020

Total Funding
$1,781,360

Direct Costs
$1,377,739

Indirect Costs
$403,621

Year	Funding IC	FY Total Cost by IC
2020	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$1,781,360

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	$1,781,360	Biodefense; Biotechnology; Clinical Research; Emerging Infectious Diseases; Immunization; Immunotherapy; Infectious Diseases; Orphan Drug; Rare Diseases; Vector-Borne Diseases;

Sub Projects

No Sub Projects information available for 5U19AI142777-02 8148

Publications

No Publications available for 5U19AI142777-02 8148

Patents

No Patents information available for 5U19AI142777-02 8148

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.

Thank you for your feedback!

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Clinical Studies

No Clinical Studies information available for 5U19AI142777-02 8148

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Related News Releases

No news release information available for 5U19AI142777-02 8148

History

No Historical information available for 5U19AI142777-02 8148

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