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SELECTION OF VACCINE ANTIGENS FOR PROTECTION FROM HEPATITIS C VIRUS INFECTION

Project Number
1R01DK122401-01A1

Contact PI/Project Leader
RAY, RANJIT

Awardee Organization
SAINT LOUIS UNIVERSITY

Description

Abstract Text

Abstract Chronic hepatitis C virus (HCV) infection often causes end stage liver disease. Although current anti-HCV drugs are successful in eliminating viral RNA load, they do not prevent reinfection. In addition, eliminating HCV RNA load does not reduce the risk for progression to end stage liver disease. Therefore, the urgent need for the development of a comprehensive strategy to control HCV infection must include a **vaccine**. HCV envelope glycoproteins are the key components for the initiation of viral infection. Our phase I safety and immunogenicity trial of a recombinant HCV envelope glycoprotein candidate **vaccine** did not induce a strong immune response in most vaccinated volunteers. Subsequent studies indicated that purified HCV E2 has an immunoregulatory role and biases primary macrophage activation toward the M2 phenotype (via E2-CD81 interactions), impairs DC/CD4+T cell functions, and leads to an environment for a muted response to antigen. Nevertheless, HCV E2 still contains strong cross-genotype specific B- and T-cell epitopes vital to an active immunity. We hypothesize that modifying E2 by discrete point mutations to inhibit interaction with CD81 will improve immune functions and induce robust protective responses in combination with other HCV regions as candidate **vaccine**, and will generate stronger protective efficacy. Outstanding abilities of nucleoside modified **mRNA**-lipid nanoparticle (LNP) to elicit potent immune responses against pathogens makes it a viable new cost-effective platform for **vaccine** development. The incorporation of modified nucleosides in the **mRNA** will offer advantages for generation of modified antigens to induce a broad effective immune response. The premise and rigor of the study stems from our own work, and information in the literature. Thus, the use of nanoparticle encapsulated **mRNA** of modified E2 for stronger immunogenicity together with other viral antigens (E1 and non-structural (NS) genomic regions) for prime and boost with proteins/peptides as a candidate **vaccine** for HCV cross protective efficacy will generate robust B- and T- cell responses for protection against HCV. The results from our study will advance **vaccine** development against persistent HCV infection.

Public Health Relevance Statement

Project Narrative Hepatitis C virus (HCV) infection causes silent liver disease and is a major health problem worldwide. A comprehensive strategy to control HCV infection must include an effective vaccine development approach. We will study and select vaccine antigens, use novel vaccine delivery platform, and optimize immunization regimen to induce robust protective immune response against HCV infection.

NIH Spending Category

Biotechnology | Chronic Liver Disease and Cirrhosis | Digestive Diseases | Emerging Infectious Diseases | Genetics | Hepatitis | Hepatitis - C | Immunization | Infectious Diseases | Liver Disease | Prevention | Vaccine Related

Project Terms

Active immunity | Address | Adjuvant | Antigen-Presenting Cells | Antigens | Antiviral Agents | B-Lymphocytes | Binding Sites | CD4 Positive T Lymphocytes | CD81 gene | Cell Culture Techniques | Cell physiology | Cells

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Read More

Details

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Other PIs

Not Applicable

Program Official

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SAINT LOUIS UNIVERSITY

City
SAINT LOUIS

Country
UNITED STATES (US)

Department Type
INTERNAL MEDICINE/MEDICINE

Organization Type
SCHOOLS OF MEDICINE

State Code
MO

Congressional District
01

Other Information

FOA
PA-19-056

Study Section
Vaccines Against Microbial Diseases Study Section[VMD]

Fiscal Year
2020

Award Notice Date
01-July-2020

Administering Institutes or Centers
NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

DUNS Number
050220722

CFDA Code
847

Project Start Date
01-July-2020

Project End Date
30-April-2025

Budget Start Date
01-July-2020

Budget End Date
30-April-2021

Project Funding Information for 2020

Total Funding
$340,875

Direct Costs
$225,000

Indirect Costs
$115,875

Year	Funding IC	
2020	NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES	$340,875

NIH Categorical Spending

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Funding IC	FY Total Cost by IC	NIH Ca

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Ger
Hep
Hep
Imr
Infe
Dis
Live
Pre
Vac
Rel

Sub Projects

No Sub Projects information available for 1R01DK122401-01A1

Publications

No Publications available for 1R01DK122401-01A1

Patents

No Patents information available for 1R01DK122401-01A1

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 1R01DK122401-01A1

Clinical Studies

No Clinical Studies information available for 1R01DK122401-01A1

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No Historical information available for 1R01DK122401-01A1

Similar Projects

No Similar Projects information available for 1R01DK122401-01A1