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Rational design and evaluation of novel mRNA vaccines against MERS-CoV

Project Number	Former Number	Contact PI/Project Leader	Awardee Organization
7R01AI137472-05	5R01AI137472-04	DU, LANYING	GEORGIA STATE UNIVERSITY

Description

Abstract Text

Abstract Traditional strategies of **vaccine** development suffer from long-term and costly manufacture, and as a result, often fail to respond rapidly to newly emerging and reemerging infectious diseases. By contrast, messenger RNA (**mRNA**) is rising as a new technology platform to develop vaccines “on demand” against viral pathogens, offering attractive advantages such as cell-free production, non-viral delivery, as well as simple, fast and cost- effective manufacture. Further improvement upon mRNA's stability and translation efficiency, understanding of their immune mechanisms, and evaluation of their protective efficacy will facilitate the development of next-generation **mRNA vaccine** technologies against diverse viral pathogens. Middle-East respiratory syndrome (MERS) coronavirus (MERS-CoV) is a highly pathogenic, emerging infectious virus posing a continuous threat to public health worldwide. There are currently no MERS vaccines approved for use in humans. MERS-CoV spike (S) protein, particularly its receptor-binding domain (RBD), is an important **vaccine** target. We have previously shown that MERS-CoV RBD contains a critical neutralizing domain capable of inducing strong cross-neutralizing antibodies and protecting human dipeptidyl peptidase 4-transgenic (hDPP4-Tg) mice against MERS-CoV infection with outstanding efficacy. However, production of subunit vaccines and other traditional vaccines has limitations, such as low expression and complex purification. To address these unmet challenges, we propose to rationally design and evaluate novel **mRNA** vaccines, using MERS-CoV as a model pathogen and MERS-CoV S protein as a target antigen. We hypothesize that with appropriate modification and optimization, MERS-CoV S protein RBD-based **mRNA** vaccines will demonstrate improved stability, increased translation efficiency, and enhanced immunogenicity in both mouse and non-human primates (NHP) models, with protective efficacy on par with the RBD-based subunit **vaccine**. The specific aims are to (1) rationally design MERS-CoV **mRNA** vaccines with improved stability and translation efficiency, (2) carefully optimize **mRNA** formulations and immunization regimens towards in-vivo evaluation of their immunogenicity and mode of action in wild-type mice, and (3) comprehensively evaluate protective efficacy of MERS-CoV **mRNA** vaccines and elucidate their protective mechanisms in hDPP4-Tg mice and NHPs. Of note, we will also examine the utility of new technologies such as microfluidics and next-generation sequencing (NGS) analysis of B-cell response in **mRNA vaccine** development and evaluation. The long-term goal is to develop a safe and effective **mRNA vaccine** that is able to (1) maintain sufficient quantity and quality suitable for industrial- scale production, and (2) meet the WHO Target Product Profiles for rapid onset of immunity in outbreak settings and long-term protection of people at high ongoing risk of MERS-CoV. Together, the proposed project will shed light on protective mechanisms of **mRNA** vaccines, and provide much-needed information and guidelines for developing **mRNA** vaccines against diverse viral pathogens with pandemic potential.

Public Health Relevance Statement

Project Narrative Messenger RNA (mRNA) is emerging as a promising technology platform for developing safe and efficacious vaccines with capability for simple, fast, and cost-effective production. Using MERS-CoV as a model pathogen, the proposed project aims to rationally design and evaluate mRNA vaccine candidates with a focus on stability, translation efficiency, and protective efficacy. The in-depth analysis of newly developed vaccine candidates in vitro and in vivo will elucidate the mode of action and protective mechanisms for mRNA vaccines, and provide a robust platform for developing new vaccines in response to diverse viral pathogens with pandemic potential.

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7R01AI137472-05	5R01AI137472-04	DU, LANYING	GEORGIA STATE UNIVERSITY

Genetic Transcription Goals Guidelines Human Immune Immune response Immunity Immunization Immunize In Vitro Industrialization Influenza Injections Light Lipids Measures

Read More

Details

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Organization Type
ORGANIZED RESEARCH UNITS

State Code
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Congressional District
05

Other Information

FOA
PA-18-590
Study Section
Vaccines Against Microbial Diseases Study Section[VMD]
Fiscal Year
2021
Award Notice Date
15-July-2021

Administering Institutes or Centers
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
DUNS Number
837322494
CFDA Code
855

Project Start Date
01-July-2021
Project End Date
31-January-2023
Budget Start Date
01-July-2021
Budget End Date
31-January-2022

Project Funding Information for 2021

Total Funding	Direct Costs	Indirect Costs
$554,964	$431,729	$123,235

Year	Funding IC	
2021	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$554,964

Sub Projects

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No Publications available for 7R01AI137472-05

Patents

No Patents information available for 7R01AI137472-05

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 7R01AI137472-05

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No Clinical Studies information available for 7R01AI137472-05

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No news release information available for 7R01AI137472-05

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No Historical information available for 7R01AI137472-05

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