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Description

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Development of Universal Influenza Virus Vaccines Using Nucleoside-Modified Messenger RNA

Project Number

5R01AI146101-02

Contact PI/Project Leader

PARDI, NORBERT

Awardee Organization

UNIVERSITY OF PENNSYLVANIA

Description

Abstract Text

ABSTRACT Influenza virus is one of the most important human infectious diseases. The influenza mortality is estimated to be approximately 650,000 per year worldwide, in addition, occasional global pandemics can infect up to 20- 40% of the world's population. Licensed influenza virus vaccines require annual reformulation and readministration due to poor IgG longevity and lack of neutralization of related viruses. We have developed a new **vaccine** approach against influenza virus that uses antigen-encoding nucleoside-modified **mRNA** encapsulated in lipid nanoparticles (LNPs). This **vaccine** format composed entirely of physiologic components that is simple and cost effective to produce and should induce no adverse events after administration. Additionally, **mRNA vaccine** production is sequence-independent and does not require eggs, cell culture or protein purification. We demonstrated that monovalent **mRNA**-LNP vaccines encoding full-length hemagglutinin (HA) induced potent immune responses against the immunosubdominant HA stalk region, one of the targets of universal influenza virus vaccines, which was associated with protection against homologous, heterologous and heterosubtypic influenza viruses in mice. Furthermore, we showed that a single immunization with nucleoside-modified **mRNA**-LNP vaccines induced durable protective HA stalk-specific antibody responses. Finally, we demonstrated that nucleoside-modified **mRNA**-LNP immunization induced high levels of antigen-specific T follicular helper (Tfh) cells that are critical for the generation of germinal centers, immunoglobulin class switch, and long-term memory, which are vital elements in the development of an effective influenza **vaccine**. In this grant, we aim to develop and evaluate new generation, broadly protective influenza virus vaccines in mice and ferrets using nucleoside-modified **mRNA**-LNPs encoding hemagglutinin, neuraminidase, nucleoprotein and the ectodomain of M2. Additionally, we aim to investigate the mechanisms of action of **mRNA**-LNP influenza virus vaccines. We will have 3 specific aims: 1) Design and production of **mRNA** immunogens for conserved regions of influenza virus. 2) Immunogenicity and protective efficacy of nucleoside-modified **mRNA**-LNP influenza virus vaccines in mice and ferrets. 3) Investigation of the mechanisms of action of nucleoside-modified **mRNA**-LNP influenza vaccines. This proposal will develop safe, new generation influenza virus vaccines that are easy to manufacture and administer and can protect against antigenically distant influenza viruses. The data generated will be capable of moving this **vaccine** approach to clinical trial development.

Public Health Relevance Statement

PROJECT NARRATIVE The development of an easy-to-produce and safe influenza virus vaccine that also has much broader protection than current designs will both increase the elicited protection and the vaccine coverage. Nucleoside- modified mRNA-LNP vaccines achieve all of these attributes and have the potential to change the field of infectious disease vaccines.

NIH Spending Category

Biodefense

Bioengineering

Biotechnology

Emerging Infectious Diseases

Genetics

Immunization

Infectious Diseases

Thank you for your feedback!

Project Terms

Adverse event Affinity Animals Antibodies Antibody Affinity
 Antibody Response Antigens B-Lymphocytes Birds Cell Culture Techniques
 Cellular Assay Cellular Immunity Cessation of life Clinical Trials
 Combined Vaccines Communicable Diseases Data Dendritic Cells
 Development Disease Outbreaks Distant Elements Encapsulated
 Ferrets Ferritin Generations Gold Grant Head
 Helper-Inducer T-Lymphocyte Hemagglutinin Human Humoral Immunities
 Immune Immune response Immunity Immunization Immunize

[Read More](#)**≡ Details****Contact PI/ Project****Leader**

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[PARDI, NORBERT](#)

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Not Applicable

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jennifer.gordon2@nih.gov**Organization**

Name

**UNIVERSITY OF
PENNSYLVANIA**

City

PHILADELPHIA

Country

UNITED STATES (US)

Department Type

**INTERNAL
MEDICINE/MEDICINE**

State Code

PACongressional District
03

Organization Type

SCHOOLS OF MEDICINE**Other Information**

FOA

[PA-18-859](#)

Study Section

[Vaccines Against Microbial
Diseases Study
Section\[VMD\]](#)Administering Institutes or
Centers**NATIONAL INSTITUTE OF
ALLERGY AND INFECTIOUS
DISEASES**Project Start
Date**21-June-
2019**Project End
Date**31-May-
2024**DUNS Number CFDA Code
042250712 855Budget Start
Date**01-June-
2020**

Fiscal Year

2020

Award Notice

22-May-2020Budget End
Date**31-May-
2021****Project Funding Information for 2020**Total Funding
\$609,757Direct Costs
\$481,987Indirect Costs
\$127,770

Year	Funding IC
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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	\$609,757	Biodefense; Bioengineering; Biotechnology; Emerging Infectious Diseases; Genetics; Immunization; Infectious Diseases; Influenza; Nanotechnology Pneumonia & Influenza; Prevention; Vaccine Related

Sub Projects

No Sub Projects information available for 5R01AI146101-02

Publications

No Publications available for 5R01AI146101-02

Patents

No Patents information available for 5R01AI146101-02

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 5R01AI146101-02

Clinical Studies

No Clinical Studies information available for 5R01AI146101-02

News and More

Related News Releases

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No news release information available for 5R01AI146101-02

History

No Historical information available for 5R01AI146101-02

Similar Projects

No Similar Projects information available for 5R01AI146101-02

Thank you for your feedback!