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Engineering sustainable squalene analogues for novel vaccine adjuvant emulsions

Project Number
5R01AI135673-02

Contact PI/Project Leader
FOX, CHRISTOPHER B

Awardee Organization
INFECTIOUS DISEASE RESEARCH INSTITUTE

Description

Abstract Text

Project Summary Global **pandemic** influenza vaccine production capacity is insufficient to meet the expected demand in the event of a highly lethal influenza **pandemic**. Current H5N1 vaccines require high antigen doses (e.g. 90 µg) or are combined with squalene-based oil-in-water emulsion adjuvants for enhanced and broadened immunogenicity as well as antigen dose sparing. Squalene is a naturally occurring oligoisoprene (i.e. a very low molecular weight polymer of isoprene) derived from shark liver, a source with sustainability concerns. Moreover, the biological mechanisms of action of squalene are still not well understood and no systematic comparison of the adjuvant activity of squalene emulsions compared to emulsions based on analog oligoisoprenes has been reported in the literature. This proposal defines a program to develop the sustainable production of various oligoisoprene analogues of squalene using bioengineered organisms and synthetic polymer chemistry. Selected structures will then be formulated in oil-in-water emulsions and evaluated for physicochemical stability. Importantly, we propose to identify structure-activity relationships (SAR) by employing squalene and oligoisoprene analogues in in vitro human and in vivo mouse models in combination with an H5N1 influenza antigen. Moreover, the ability to further enhance adjuvant activity by chemical modification to improve physicochemical properties of selected oligoisoprene structures will be evaluated. The technology generated could be applicable to many other vaccines that have need of emulsion-based adjuvants for antigen dose sparing or enhanced immune responses.

Public Health Relevance Statement

Project Narrative The successful completion of the objectives in this project will result in the discovery and evaluation of novel molecules produced by bioengineering and chemical engineering approaches for vaccine adjuvant applications. These biosynthetic molecules could serve as sustainable replacements for pharmaceutical squalene which is currently derived from sharks. Furthermore, the structure-activity relationship of squalene-like molecules will be elucidated for the first time. Development of this technology could enable formulations with enhanced vaccine dose sparing capability in the event of an influenza pandemic.

NIH Spending Category

Biodefense Bioengineering Biotechnology Clinical Research Emerging Infectious Diseases Immunization Infectious Diseases Influenza Pneumonia & Influenza Prevention Vaccine Related

Project Terms

Adjuvant Antigens Biological Biomedical Engineering Brazil California Characteristics Chemical Engineering Chemicals Data Development Dose Emulsions Engineering Environmental Engineering technology Evaluation Event Formulation Government-Sponsored Programs Human Immune response In Vitro Industrialization Infectious Diseases Research Influenza Influenza A Virus, H5N1 Subtype Isoprene Literature Liver Modification Molecular Weight North Carolina Oils Organism Pathway interactions Pharmacologic Substance Plant Extracts Plant Sources Polymer Chemistry Polymers Preclinical Testing Production Program Sustainability Property Reagent Recombinants

Read More

Details

Contact PI/ Project Leader

Name
FOX, CHRISTOPHER B

Title
DIRECTOR OF FORMULATIONS

Contact

Other PIs

Not Applicable

Program Official

Name
GORDON, JENNIFER L

Contact
jennifer.gordon2@nih.gov

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Project Number
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Contact PI/Project Leader
FOX, CHRISTOPHER B

Awardee Organization
INFECTIOUS DISEASE RESEARCH INSTITUTE

INSTITUTE

City
SEATTLE

Country
UNITED STATES (US)

Organization Type
Research Institutes

Congressional District
07

Other Information

FOA
PAR-16-242

Study Section
Vaccines Against Microbial Diseases Study Section[VMD]

Fiscal Year
2019

Award Notice Date
03-December-2018

Administering Institutes or Centers
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

DUNS Number
809846819

CFDA Code
855

Project Start Date
16-January-2018

Project End Date
31-December-2022

Budget Start Date
01-January-2019

Budget End Date
31-December-2019

Project Funding Information for 2019

Total Funding
$856,636

Direct Costs
$701,831

Indirect Costs
$154,805

Year	Funding IC	FY Total Cost by IC
2019	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$856,636

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	$856,636	Biodefense; Bioengineering; Biotechnology; Clinical Research; Emerging Infectious Diseases; Immunization; Infectious Diseases; Influenza; Pneumonia & Influenza; Prevention; Vaccine Related;

Sub Projects

No Sub Projects information available for 5R01AI135673-02

Publications

No Publications available for 5R01AI135673-02

Patents

No Patents information available for 5R01AI135673-02

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 5R01AI135673-02

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Contact PI/Project Leader
FOX, CHRISTOPHER B

Awardee Organization
INFECTIOUS DISEASE RESEARCH INSTITUTE

News and More

Related News Releases

No news release information available for 5R01AI135673-02

History

No Historical information available for 5R01AI135673-02

Similar Projects

No Similar Projects information available for 5R01AI135673-02