Description

Details
Sub-Projects
Publications
Patents
Outcomes
Clinical Studies
News and More
History
Similar Projects

Development of Novel Adjuvants LTA and LTA1

Project Number
3R01AI114697-05S1

Contact PI/Project Leader
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Awardee Organization
TULANE UNIVERSITY OF LOUISIANA

Description

Abstract Text

DESCRIPTION (provided by applicant): Vaccines are the established and proven method to prevent diseases. As a technological platform they are also expanding into nontraditional applications such as cancer and Alzheimer's therapy, but continue to be relevant in infectious diseases research, including strategies for controlling **pandemic** Influenza virus. Proper selection and use of adjuvant formulations can overcome barriers to vaccine efficacy by promoting long-lasting protective immunity, overcoming poor immunity in high-risk populations (i.e., young, elderly, immunocompromised), and/or simply augmenting the existing antigen supply to reach a greater number of people (dose-sparing). The objective of this proposal is to develop next generation adjuvants based on the A-subunit of the heat-labile enterotoxin from Escherichia coli (LT), including LTA and LTA1. The enterotoxin family of adjuvants are powerful mucosal adjuvants, but have been hindered by major safety concerns in past clinical trials, particularly for intranasal delivery. Our preliminary studies indicate LTA and LTA1 proteins are safe and effective mucosal adjuvants because they can achieve broad mucosal and systemic immunity without the potential safety risks of the parent proteins and high levels of immunogenicity (i.e., anti-LT antibodies). In this proposal, we will critically evaluate LTA and LTA1 as adjuvants in combination with inactivated, **pandemic** influenza antigen. In our studies, we will determine how these adjuvants (1) improve correlates of protective immunity and responses to viral challenge by intranasal or intradermal influenza vaccination, (2) provide a new, safe and stable alternative to their parent protein or related B-subunit containing derivatives, (3) improve vaccination efficacy through cAMP-mediated dendritic cell activation and Th17 induction. Upon completion of this investigation, we expect to generate clear safety and efficacy data using a candidate influenza antigen for intranasal and intradermal immunization, specifically valuable for future human use in a **pandemic** disease setting or for use in high-risk populations. Based on the nature of the information generated by this proposal, we will also provide clear rational for novel LTA and LTA1 adjuvant inclusion in other unique vaccine formulations targeting bacterial and viral pathogens or degenerative disease like cancer.

Public Health Relevance Statement

PUBLIC HEALTH RELEVANCE: Vaccines are the most cost-effective way to prevent diseases. Adjuvant formulations can improve vaccination by helping to reach high-risk populations and stretching the use existing vaccine stockpiles, and as such, may be a key element during pandemic Influenza. Here, we will explore LTA and LTA1 as novel, next generation adjuvants capable of promoting protective immunity to pandemic Influenza virus, without the potential safety risks of parent proteins.

NIH Spending Category

Biotechnology Emerging Infectious Diseases Immunization Infectious Diseases Influenza Neurosciences Pneumonia & Influenza Prevention Vaccine Related

Project Terms

Adjuvant Adjuvanticity Alzheimer's Disease Animals Antibodies Antigens Bell Palsy Binding Brain Cell Maturation Cell surface Cholera Cholera Toxin Clinical Clinical Trials Communicable Diseases Cyclic AMP Data Degenerative Disorder Dendritic Cells Dendritic cell activation Development Disease Dose Effectiveness Elderly Elements Enterotoxins Erythema Escherichia coli Excipients Facial paralysis Family Fluzone Formulation Future Gangliosides Human Immune response Immunity Immunization Immunocompromised Host In Vitro Induration Infectious Diseases Research Inflammatory Response Influenza Influenza vaccination Injections Investigation Laboratories

Read More

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Details

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Department Type
MICROBIOLOGY/IMMUN/VIROLOGY

Organization Type
SCHOOLS OF MEDICINE

State Code
LA

Congressional District
01

Other Information

FOA
PA-13-302

Study Section
Vaccines Against Microbial Diseases Study Section[VMD]

Fiscal Year
2019

Award Notice Date
01-March-2019

Administering Institutes or Centers
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

DUNS Number
053785812

CFDA Code
855

Project Start Date
01-August-2015

Project End Date
31-January-2021

Budget Start Date
01-March-2019

Budget End Date
31-January-2021

Project Funding Information for 2019

Total Funding
$370,189

Direct Costs
$285,624

Indirect Costs
$84,565

Year	Funding IC	FY Total Cost by IC
2019	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$370,189

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	$370,189	Biotechnology; Emerging Infectious Diseases; Immunization; Infectious Diseases; Influenza; Neurosciences; Pneumonia & Influenza; Prevention; Vaccine Related;

Sub Projects

No Sub Projects information available for 3R01AI114697-05S1

Publications

No Publications available for 3R01AI114697-05S1

Patents

No Patents information available for 3R01AI114697-05S1

Outcomes

Thank you for your feedback!

No Outcomes available for 3R01AI114697-05S1

Clinical Studies

No Clinical Studies information available for 3R01AI114697-05S1

News and More

Related News Releases

No news release information available for 3R01AI114697-05S1

History

No Historical information available for 3R01AI114697-05S1

Similar Projects

No Similar Projects information available for 3R01AI114697-05S1