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Novel vita-vaccine formula combines safety of dead and efficacy of live vaccines

Project Number	Former Number	Contact PI/Project Leader	Awardee Organization
5R01AI127658-06	1R01AI127658-01	BLANDER, JULIE MAGARIAN	WEILL MEDICAL COLL OF CORNELL UNIV

Description

Abstract Text

PROPOSAL SUMMARY Live attenuated vaccines have proven to be the most efficient human vaccines for many serious infectious diseases. When compared to their dead counterparts, live vaccines induce superior immune protection and lasting memory. But despite the efficacy of live vaccines, concerns over their safety have led to **vaccine** refusal by some and withholding their administration to the very young, the elderly and immunocompromised. Preservation and delivery of live vaccines especially to impoverished areas in developing countries is difficult and expensive. Understanding the molecular basis for the efficacy of live vaccines is significant because it would enable targeting of the relevant immune pathways that induce optimal and long-lasting protective immunity. Importantly, it would set the stage for the development of vaccines that are safe and afford the same protection as live vaccines, alleviating public fears and increasing the segment of the population that is vaccinated. We began our work eight years ago with the hypothesis that innate immune cells sense microbial viability as a distinct set of pathogen associated molecular patterns (PAMPs), and we identified bacterial messenger RNA (**mRNA**) as a vita-PAMP that signifies bacterial viability and mobilizes a tailored immune response not warranted for dead microorganisms. The Toll-like receptor (TLR) signaling adaptor TRIF plays a central role here upstream of inflammatory type I interferon and NLRP3 inflammasome pathways. Adding bacterial **mRNA** to dead bacteria recapitulates these innate responses, and supplementing a dead **vaccine** with bacterial **mRNA** (what we call a vita-**vaccine**) augments its performance in mice. A vita-**vaccine** performed similarly to a live **vaccine** in uniquely eliciting a follicular T helper cell response (that helps B cells), germinal center formation, and B cell isotype class switching, all in a TRIF-dependent manner. These studies provide strong evidence that vita-**vaccine** versions of existing vaccines could represent a significant advance in being able to combine the efficacy of live vaccines with the safety of dead vaccines. The three overlapping areas we will investigate in this project are: 1. We will determine how adaptive immunity elicited by the supplementation of a dead bacterial **vaccine** with the vita-PAMP bacterial **mRNA** compares to that elicited by PAMPs such as bacterial lipopeptides and others. 2. We will investigate how bacterial **mRNA** impacts the performance of subunit vaccines. We will test vita- **vaccine** versions of the licensed anthrax subunit **vaccine** and Influenza A virus monovalent subunit **vaccine**. 3. We will test a vita-**vaccine** version of a trivalent inactivated Influenza virus **vaccine** and compare it to the live attenuated influenza **vaccine**. The completion of these studies should provide sufficient experimental evidence to warrant the use of bacterial mRNAs as superior vita-**adju**vants that restore the signatures of microbial viability to dead vaccines and improve existing inactivated and subunit vaccines for protection against either bacterial or viral diseases.

Public Health Relevance Statement

PROPOSAL NARRATIVE Vaccines comprised of live attenuated microorganisms are superior to their dead counterparts, yet concerns about the safety of live vaccines have dampened their popularity We discovered that bacterial messenger RNA signals microbial viability to the immune system an when used as an **adju**vant augments the performance of dea

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as a new adjuvant, the work we propose here will advance the development of dead vaccines that work as well as live ones, improve the performance of existing vaccines, and salvage vaccines that may have been shelved due to inefficacy, all while achieving superior protection and maintaining desired safety.

NIH Spending Category

Anthrax Biotechnology Emerging Infectious Diseases Genetics HIV/AIDS Immunization Infectious Diseases Influenza Orphan Drug Pneumonia & Influenza Prevention Rare Diseases Vaccine Related Vaccine Related (AIDS)

Project Terms

Adjuvant Advanced Development Agonist Anthrax Vaccines Anthrax disease Antibodies Antibody Response Area Attenuated Live Virus **Vaccine** Attenuated Vaccines B-Lymphocyte Subsets B-Lymphocytes Bacillus anthracis Bacteria Bacterial Infections Bacterial RNA Bacterial Vaccines Biothrax CASP1 gene CD8-Positive T-Lymphocytes Cell Differentiation process Cells Chitosan Communicable Diseases DNA Developing Countries Elderly Escherichia coli Evaluation Formulation Fright Health Helper-Inducer T-Lymphocyte Hematopoietic Human IRF3 gene Imiquimod

Read More

Details

Contact PI/ Project Leader

Name
BLANDER, JULIE MAGARIAN

Title
PROFESSOR

Contact
View Email

Other PIs

Not Applicable

Program Official

Name
LAPHAM, CHERYL K

Contact
View Email

Organization

Name
WEILL MEDICAL COLL OF CORNELL UNIV

City
NEW YORK

Country
UNITED STATES (US)

Department Type
INTERNAL MEDICINE/MEDICINE

Organization Type
SCHOOLS OF MEDICINE

State Code
NY

Congressional District
12

Other Information

FOA
PA-13-302

Study Section
Vaccines Against Microbial Diseases Study Section[VMD]

Administering Institutes or Centers
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Project Start Date
23-September-2016

Thank you for your feedback!

Award Notice Date
Fiscal Year **2020**
06-August-2020

DUNS Number **060217502**
CFDA Code **855**

Budget Start Date **01-September-2020**
Budget End Date **31-August-2021**

Project Funding Information for 2020

Total Funding **$419,267**
Direct Costs **$250,000**
Indirect Costs **$169,267**

Year	Funding IC	
2020	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$419,267

NIH Categorical Spending

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Funding IC	FY Total Cost by IC	NIH Spending Category
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$419,267	Anthrax; Biotechnology; Emerging Infectious Diseases; Genetics; HIV/AIDS; Immunization; Infectious Diseases; Influenza; Orphan Drug; Pneumonia & Influenza; Prevention; Rare Diseases; Vaccine Related; Vaccine Related (AIDS);

Sub Projects

No Sub Projects information available for 5R01AI127658-06

Publications

No Publications available for 5R01AI127658-06

Patents

No Patents information available for 5R01AI127658-06

Outcomes

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No Outcomes available for 5R01AI127658-06

Clinical Studies

No Clinical Studies information available for 5R01AI127658-06

News and More

Related News Releases

No news release information available for 5R01AI127658-06

History

No Historical information available for 5R01AI127658-06

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