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Correlates of Vaccine-Induced, Tunable-Protection in an Outbred Tularemia Model

Contact PI/Project Leader
HAZLETT, KARSTEN R.O. Other PIs

Awardee Organization
ALBANY MEDICAL COLLEGE

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Project Number

5R01AI123129-05

Abstract Text

DESCRIPTION (provided by applicant): Francisella tularensis is the causitive agent of tularemia, a severe zoonotic disease in humans with fatality rates exceeding 30% in untreated subjects. Infection following inhalation causes the most severe form of disease and combind with its high virulence and history of weaponization makes this pathogen a concern for use as a biological weapon. Development of a vaccine that protects against aerosol infection is a priority. We have engineered a series of live attenuated vaccine candidates based on the highly virulent Schu S4 strain that exhibit a range of protective capacities in the mouse and rabbit models of respiratory challenge. Our studies have confirmed that rabbits are an excellent model of human pneumonic tularemia and a highly relevant model for evaluating tularemia vaccines as they display similar resistance to attenuated strains and susceptibility to virulent strains as humans. We hypothesize that the outbred humanrelevant, rabbit model will allow us to identify correlates of protection using the collection of vaccine strains that confer a range (0% to 83%) of protective efficacies against lethal aerosol challenge. This grant seeks to understand the mechanism(s) underlying this protection. Our hypothesis is that effective vaccination in the rabbit model is a product of i) induction of particular, Ag-specific responses and/or ii) the immunogen's persistence and immuno-stimulatory properties. The first aim will identify the bacterial Ag(s) recognized specifically by protective immune responses. The second aim will explore the humoral and cellular immune response as well as the role of persistence and immune stimulation by F. tularensis derivatives in protection against challenge. The third aim will evaluate the efficacy of a subunit vaccine and an optimized live attenuated vaccine against inhalation of F. tularensis. The information gained under this proposal will expand our understanding of the humoral and cellular immune response to tularemia vaccines, the importance of these responses in protection against tularemia in the rabbit and the relevance to protection in humans.

Public Health Relevance Statement

PUBLIC HEALTH RELEVANCE: Inhalation of Francisella tularensis causes significant morbidity and mortality in humans - an outbred population. The studies proposed in this application will greatly improve our knowledge of the immunological responses elicited by tularemia vaccines and responses important for protection in an outbred model against pneumonic tularemia. This information will be useful in the design and evaluation of vaccines that protect outbred species against inhalation of F. tularensis.

NIH Spending Category

Biodefense Biotechnology Emerging Infectious Diseases Immunization Infectious Diseases

Lung Orphan Drug Prevention Rare Diseases Vaccine Related Vector-Borne Diseases

Project Terms

Adjuvant Aerosols Animal Model Antigens Animals **Attenuated Attenuated Live Virus Vaccine Attenuated Vaccines Biological Response Modifiers** Cells **Characteristics Collaborations** Collection Columbidae Disease **Engineering Enzymes** Francisella tularensis **Exhibits Fatality rate Gram-Negative Bacteria Fever** Genes Goals Human Immunization Immune response Inhalation Literature **Inbred Mouse** Inbreeding Infection Knowledge Lead Metabolic Morbidity - disease rate Modeling Mutation **Oryctolagus cuniculus** Mus **Population Predisposition Positioning Attribute** Prevention **Property Proteome** Pulmonary tularemia

Read More



Contact PI/ Project Leader

Name

HAZLETT, KARSTEN R.O.

Title **PROFESSOR**

Other Pls

Name

BARRY, EILEEN M.

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Thank you for your feedback!

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Project Number Contact PI/Project Leader 5R01AI123129-05 **HAZLETT, KARSTEN R.O.** Other Pls

ALBANY MEDICAL COLLEGE MICROBIOLOGY/IMMUN/VIROLOGY NY

City Organization Type **Congressional District ALBANY SCHOOLS OF MEDICINE** 20

Country **UNITED STATES (US)**

Other Information

2020

FOA Administering Institutes or Centers **Project Start NATIONAL INSTITUTE OF ALLERGY** PA-13-302 Date AND INFECTIOUS DISEASES Study Section

Vaccines Against Microbial Diseases **DUNS Number** CFDA Code

Study Section[VMD] 190592162 855

16-January-2020

Award Notice Date Fiscal Year

15-February-2016

Awardee Organization

ALBANY MEDICAL COLLEGE

Project End Date 31-January-2022

Budget Start 01-February-

Date 2020

Budget End Date 31-January-

2022

Project Funding Information for 2020

Total Funding Direct Costs Indirect Costs \$707,956 \$642,691 \$65,265

Year	Funding IC	FY Total Cost by IC
2020	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	\$707,956

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	\$707,956	Biodefense; Biotechnology; Emerging Infectious Diseases; Immunization; Infectious Diseases; Lung; Orphan Drug; Prevention; Rare Diseases; Vaccine Related; Vector-Borne Diseases:

品 Sub Projects

No Sub Projects information available for 5R01Al123129-05

Publications

No Publications available for 5R01AI123129-05

Patents

No Patents information available for 5R01AI123129-05

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.

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Description

Project Number 5R01AI123129-05 **Awardee Organization ALBANY MEDICAL COLLEGE**

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Related News Releases

No news release information available for 5R01Al123129-05

History

No Historical information available for 5R01Al123129-05

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No Similar Projects information available for 5R01Al123129-05