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Regulation of Francisella virulence by sRNAs

Project Number
5R21AI140001-02

Contact PI/Project Leader
GUNN, JOHN S

Awardee Organization
RESEARCH INST NATIONWIDE CHILDREN'S HOSP

Description

Abstract Text

PROJECT SUMMARY Francisella tularensis (Ft) is a potential agent of bioterror, facultative intracellular pathogen and the causative agent of **tularemia**. Based on several of its attributes, Ft has been named by the CDC as a Tier 1 agent. While several advances have been made in the last ~15 years regarding the cell biology of this pathogen, its method of virulence gene regulation remains incompletely understood. To survive and thrive in often hostile environments, a bacterium has to monitor its surroundings and adjust its gene expression and physiology accordingly. This is especially important for pathogenic bacteria that continuously interact with the host during an infection. Gene regulation is traditionally mediated by protein regulatory factors, but Ft contains few protein regulatory factors and is devoid of classically arranged two-component regulatory systems, yet mediates complex host-pathogen processes such as suppression of the immune response early after host contact and escape from the Francisella-containing vacuole into the cytosol. A limited number of orphan two-component members exist including the response regulator PmrA. PmrA is a key factor in Francisella pathogenesis, as it has been demonstrated to regulate Ft biofilm formation, intramacrophage survival and animal virulence. Small RNAs (sRNAs) are also increasingly associated with the regulation of virulence in pathogens, and we have identified 661 Ft sRNAs, including the subset regulated by PmrA (n=81). The overall goal of this research is to understand the transcriptional/post-transcriptional control of virulence in this important pathogen. The overall objective is to identify virulence-associated sRNAs (PmrA-regulated as well as those differentially expressed in macrophages). The central hypothesis is that Ft sRNAs are influenced by PmrA and the macrophage environment to regulate virulence. The achievement of our goals will uncover new targets for Ft vaccines or for therapeutics to counteract this dangerous pathogen.

Public Health Relevance Statement

PUBLIC HEALTH RELEVANCE STATEMENT Francisella tularensis is a potential agent of bioterror and a facultative intracellular pathogen. Francisella can survive and replicate in many different hosts and environments, but is limited in protein regulators. We have identified 661 expressed Francisella small RNAs (sRNAs) and will determine those that play a significant role in regulating virulence of this pathogen.

NIH Spending Category

Biodefense Emerging Infectious Diseases Genetics Infectious Diseases Rare Diseases Vector-Borne Diseases

Project Terms

Achievement Aerosols Affect Animals Arthropods Bacteria Biological Assay Bioterrorism Cells Cellular biology Centers for Disease Control and Prevention (U.S.) Complex Computer Models Cytosol Dangerousness Disease Dose Environment Francisella Francisella tularensis Gene Expression Gene Expression Regulation Genetic Transcription Genome Genomics Goals Immune response Immunosuppression In Vitro Infection Insecta Life Cycle Stages Mediating Methods Microbial Biofilms Monitor Morbidity - disease rate Names Organism Orphan Outcome Pathogenesis Physiology Play Post-Transcriptional Regulation Process Production Proteins Protozoa Regulation

Read More

Details

Contact PI/ Project Leader

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Not Applicable

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RESEARCH INST NATIONWIDE CHILDREN'S HOSP

City
COLUMBUS

Country
UNITED STATES (US)

Research Institutes
03

Other Information

FOA
PA-18-489

Study Section
Special Emphasis Panel[ZRG1-IDM-B(80)S]

Fiscal Year
2020

Award Notice Date
30-January-2020

Administering Institutes or Centers
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

DUNS Number
147212963

CFDA Code
855

Project Start Date
15-March-2019

Project End Date
28-February-2022

Budget Start Date
01-March-2020

Budget End Date
28-February-2022

Project Funding Information for 2020

Total Funding
$228,000

Direct Costs
$150,000

Indirect Costs
$78,000

Year	Funding IC	FY Total Cost by IC
2020	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$228,000

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	$228,000	Biodefense; Emerging Infectious Diseases; Genetics; Infectious Diseases; Rare Diseases; Vector-Borne Diseases;

Sub Projects

No Sub Projects information available for 5R21AI140001-02

Publications

Export

Journal (Link to PubMed abstract)	Authors	Publication Year	Similar Publications	CitedBy	iCit
The Sensor Kinase QseC Regulates the Unlinked PmrA Response Regulator and Downstream Gene Expression in Francisella.					
Journal of bacteriology 2020 10 08; 202 (21)	Hoang, Ky Van; Fitch, James; White, Peter; Mohapatra, Nrusingh P; Gunn, John S	2020			0.28
Two-Component Systems in Francisella Species.					
Frontiers in cellular and infection microbiology 2019; 9 198	van Hoek, Monique L; Hoang, Ky V; Gunn, John S	2019			0.96
Transduction of primitive human marrow and cord blood-derived hematopoietic progenitor cells with adeno-associated virus vectors.					
Blood 1999 Mar 15; 93 (6) 1882-94	Chatterjee, S; Li, W; Wong, C A; Fisher-Adams, G; Lu, D; Guha, M; Macer, J A; Forman, S J; Wong Jr, K K	1999			1.15

Patents

Thank you for your feedback!

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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 5R21AI140001-02

Clinical Studies

No Clinical Studies information available for 5R21AI140001-02

News and More

Related News Releases

No news release information available for 5R21AI140001-02

History

No Historical information available for 5R21AI140001-02

Similar Projects

No Similar Projects information available for 5R21AI140001-02