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The role of gamma-aminobutyric acid (GABA) in the pathogenesis of Brucella

Project Number
5R21AI125958-02

Contact PI/Project Leader
CASWELL, CLAYTON C

Awardee Organization
VIRGINIA POLYTECHNIC INST AND ST UNIV

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Description

Abstract Text

Project Summary Brucella spp. are bacteria that naturally infect a variety of domesticated and wild animals leading to abortions and sterility, and these bacteria are also capable of causing debilitating human infections, which often result from human exposure to infected animals and animal products. Brucella spp. are considered threats as potential **biological weapons**. Importantly, antibiotic treatment against brucellosis is prone to disease relapse, and there is currently no safe and effective vaccine to protect humans against infection with Brucella. The brucellae are intracellular pathogens that reside within immune cells called macrophages where they replicate in a specialized compartment, and the capacity of Brucella to survive and replicate within macrophages is essential to their ability to cause disease. Over the last few years, our laboratory has characterized a genetic pathway that is critical for the intracellular survival and pathogenesis of Brucella strains, and recently, we have discovered that one arm of this genetic circuitry controls the production of an ABC transport system, called GasABCDE, that is essential for Brucella virulence. Preliminary experiments revealed that GasE is required for the ability of Brucella abortus to colonize experimentally infected mice. Moreover, bioinformatic analyses determined that GasABCDE is homologous to ABC transporters in other closely related bacteria that function in the import of γ-aminobutyric acid (GABA), and experiments in our lab have demonstrated that GasABCDE is a bona fide GABA transporter in B. abortus. We have also demonstrated that GABA uptake by the brucellae results in transcriptional changes, leading to the hypothesis that Brucella strains use GABA as a means of sensing the intracellular environment of the host macrophage. Overall, very little is known about the role of GABA in bacterial pathogenesis, and the current project is designed to define how GABA and the transport of GABA are linked Brucella virulence. In the end, it may be possible to target bacterial GABA transport systems with novel vaccines and/or therapeutic strategies.

Public Health Relevance Statement

Project Narrative Brucella spp. are bacteria that cause a debilitating, flu-like disease in humans, and these bacteria are classified as Select Agents due to their potential use as biological weapons. Currently, no safe and effective vaccine exists to protect against human Brucella infection. The proposed research will define a novel transport system in Brucella biology that may be targeted for vaccine and/or therapeutic development.

NIH Spending Category

Biodefense Biotechnology Emerging Infectious Diseases Genetics Infectious Diseases

Project Terms

ATP-Binding Cassette Transporters ATP-binding cassette transport Animals Antibiotic Therapy Antibiotics Bacillus subtilis Bacteria Binding Bioinformatics Biology Brucella Brucella abortus Brucellosis Carbon Cells Chronic DNA DNA Binding Data Development Disease Domestic Animals Environment Exposure to Future Gene Expression Gene Expression Regulation Genes Genetic Genetic Transcription Goals Human Immune Infection Laboratories Link Mediating Mediator of activation protein Molecular Mus Names Neurotransmitters Pathogenesis Pathway interactions Plants Process Production Promoter Regions Property Proteins Reactive Nitrogen Species Recurrent disease Regimen

Read More

Details

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Awardee Organization
VIRGINIA POLYTECHNIC INST AND ST UNIV

City
BLACKSBURG

Country
UNITED STATES (US)

SCHOOLS OF VETERINARY MEDICINE

09

Other Information

FOA
PA-16-161

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

Fiscal Year
2019

Award Notice Date
17-May-2019

Administering Institutes or Centers
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

DUNS Number
003137015

CFDA Code
855

Project Start Date	01-June-2018
Project End Date	31-May-2021
Budget Start Date	01-June-2019
Budget End Date	31-May-2021

Project Funding Information for 2019

Total Funding
$183,957

Direct Costs
$125,000

Indirect Costs
$58,957

Year	Funding IC	FY Total Cost by IC
2019	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$183,957

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	$183,957	Biodefense; Biotechnology; Emerging Infectious Diseases; Genetics; Infectious Diseases;

Sub Projects

No Sub Projects information available for 5R21AI125958-02

Publications

No Publications available for 5R21AI125958-02

Patents

No Patents information available for 5R21AI125958-02

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 5R21AI125958-02

Clinical Studies

No Clinical Studies information available for 5R21AI125958-02

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No news release information available for 5R21AI125958-02

History

No Historical information available for 5R21AI125958-02

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