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Dissecting Bubonic Plague

Project Number
5R01AI119032-05

Contact PI/Project Leader
MILLER, VIRGINIA L

Awardee Organization
UNIV OF NORTH CAROLINA CHAPEL HILL

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Description

Abstract Text

DESCRIPTION (provided by applicant): Yersinia pestis is the causative agent of **disease** in a variety of mammals, and humans can become infected when human and animal ecologies intersect. This has led to several pandemics of plague in human history, and infection with Y. pestis is currently considered by the WHO as a re-**emerging infectious disease** because of the increased incidence in a wide number of countries. Bubonic plague (transmitted via flea bite) is the most common form of **disease** and the untreated mortality rate is estimated at 40-70%. Mice are a natural host for Y. pestis and have long been used to study interactions of Y. pestis with a mammal during its normal cycle. Advantages of this are that we can use fully virulent bacteria and small inocula; furthermore, Y. pestis is genetically tractable allowing detailed analyses. These features are useful for gaining a fuller understanding of Y. pestis-host interactions, and it also make Y. pestis a useful and very sensitive model for understanding the hurdles an arthropod borne pathogen needs to overcome. We recently refined an intradermal infection model (to better mimic inoculation via a flea) and also developed a dissemination assay that allows us to monitor population dynamics at very early time points. Our recent results indicate there is a strong bottleneck between the inoculation site and establishment of infection in the draining lymph node (dLN), that neutrophils are not needed either for trafficking to the dLN or for the bottleneck, and that the bacteria can disseminate as free bacteria in the lymphatics. These observations lead to the hypothesis that specific bacterial determinants are not required for trafficking to the dLN but are required for establishing infection in the dLN and/or dissemination from the dLN to systemic sites. Our long-term goal is to understand the early events ultimately leading to a successful systemic infection and transmission to a new host. Specifically we propose to determine how known virulence factors affect specific steps between the inoculation site and blood, and how key host cells affect the development of pathology and systemic colonization. Together these studies will give us a clearer picture of how host-pathogen interactions and specific virulence determinants affect development of bubonic plague, providing a foundation for development of intervention strategies.

Public Health Relevance Statement

PUBLIC HEALTH RELEVANCE: Yersinia pestis, a highly pathogenic bacterium, is the causative agent of disease in humans with bubonic plague being the most frequent form of the disease; it is considered to be both a bioterrorism threat and a re-emerging pathogen due to the increase in incidence in a wide number of countries. Here we propose to do a 'flea-to-flea' analysis of bubonic plague including an assessment of the role of selected virulence determinants and selected host cells. This type of analysis will provide valuable information regarding potential key check points during infection and thus potential targets for intervention.

NIH Spending Category

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

Project Terms

Affect Appearance Arthropods Bacteria Biological Assay Bioterrorism Bite Blood Bubonic Plague Cells Cessation of life Country Data

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Oligonucleotides Pathogenesis Pathology Phagocytes Phenotype

Read More

Details

Contact PI/ Project Leader

Name
MILLER, VIRGINIA L

Title
PROFESSOR

Contact
VIRGINIA@BORCIM.WUSTL.EDU

Other PIs

Not Applicable

Program Official

Name
MUKHOPADHYAY, SUMAN

Contact
mukhopadhyays@mail.nih.gov

Organization

Name
UNIV OF NORTH CAROLINA CHAPEL HILL

City
CHAPEL HILL

Country
UNITED STATES (US)

Department Type
MICROBIOLOGY/IMMUN/VIROL(

Organization Type
SCHOOLS OF MEDICINE

State Code
NC

Congressional District
04

Other Information

FOA
PA-13-302

Study Section
Bacterial Pathogenesis Study Section[BACP]

Fiscal Year	Award Notice Date
2019	17-April-2019

Administering Institutes or Centers
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

DUNS Number 608195277

CFDA Code 855

Project Start Date 01-May-2015

Project End Date 30-April-2020

Budget Start Date 01-May-2019

Budget End Date 30-April-2020

Project Funding Information for 2019

Total Funding
$376,547

Direct Costs
$250,000

Indirect Costs
$126,547

Year	Funding IC	
2019	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$376,547

NIH Categorical Spending

Click here for more information on NIH Categorical Spending

Funding IC	FY Total Cost by IC	NIH Spending Category

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Diseases; Rare Diseases; Vector-Borne Diseases;

Sub Projects

No Sub Projects information available for 5R01AI119032-05

Publications

No Publications available for 5R01AI119032-05

Patents

No Patents information available for 5R01AI119032-05

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.

No Outcomes available for 5R01AI119032-05

Clinical Studies

No Clinical Studies information available for 5R01AI119032-05

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Related News Releases

No news release information available for 5R01AI119032-05

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No Historical information available for 5R01AI119032-05

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