Back to Search Results

Description

Details

Sub-Projects

Publications

Patents

Outcomes

Clinical Studies

News and More

History

Similar Projects

Deciphering the pathogenic potential of Lloviu virus, a novel filovirus

Project Number
5R21AI137793-02

Contact PI/Project Leader
MUHLBERGER, ELKE C

Awardee Organization
BOSTON UNIVERSITY MEDICAL CAMPUS

Description

Abstract Text

Recent advances in sequencing technologies have led to the discovery of a multitude of novel zoonotic viruses, some of which are closely related to known human pathogens. In most cases, only partial viral genome sequences were identified, and no infectious viruses were isolated, hampering research aimed at assessing the pathogenic potential of these novel viruses. A prime example of a sequence-based novel virus is Lloviu virus (LLOV), the newest member of the filovirus family. LLOV is closely related to the highly pathogenic ebola- and marburgviruses that cause severe disease in humans with extraordinarily high case fatality rates. The genomic viral RNA of LLOV was isolated from dead **bats** in Spain and is rudimentary. Important sequence elements located at the LLOV genome ends are missing. These include the antigenomic promoter that is essential for viral genome replication. Therefore, studies addressing LLOV genome replication and transcription, or pathogenesis have been impossible to date. In this proposal, we bring together expertise in the field of filoviral replication and transcription, rescue of filovirus clones, filovirus pathogenesis, and statistical modeling to generate infectious LLOV clones for in vitro and in vivo studies. By complementing the missing LLOV sequence with homologous sequences from related filoviruses, we have successfully established a hybrid LLOV minigenome system, enabling studies of LLOV replication and transcription for the first time. Based on this system, we will utilize LLOV minigenome systems in combination with statistical modeling to optimize the complemented promoter sequences (Aim 1). These optimized minigenome systems build the foundation for the generation and rescue of infectious full-length LLOV clones. The generated LLOV clones will then be characterized in in vitro studies. We will determine replication kinetics and host response signatures in primary human cells (Aim 2). Finally, we will perform pathogenesis studies with LLOV using a small animal model of filovirus infection (Aim 3). These studies will be instrumental to get a better understanding of the virulence of LLOV and its potential to cause disease in animals and humans. The platform developed in this project to assess the pathogenic potential of novel viruses can be adapted to other nonsegmented negative-sense RNA viruses and would therefore be of great benefit to the scientific community.

Public Health Relevance Statement

Filoviruses are highly pathogenic viruses with the potential to cause unpredicted outbreaks. Recently, a new filovirus, Lloviu virus, has been discovered. The goal of this project is to gain a better understanding of the virulence of this virus and its pathogenic potential. .

NIH Spending Category

Biodefense Biotechnology Emerging Infectious Diseases Genetics Infectious Diseases Rare Diseases

Project Terms

Address Animal Model Animals Base Sequence Biological Assay Case Fatality Rates Cell Culture Techniques Cells Chiroptera Communities Complement Complementary DNA Computer Simulation Disease Disease Outbreaks Ebola virus Elements Family Filoviridae Infections

Back to Search Results

Description
Details
Sub-Projects
Publications
Patents
Outcomes
Clinical Studies
News and More
History
Similar Projects

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Awardee Organization
BOSTON UNIVERSITY MEDICAL CAMPUS

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City
BOSTON
Country
UNITED STATES (US)

Department Type
MICROBIOLOGY/IMMUN/VIROL(
Organization Type
SCHOOLS OF MEDICINE

State Code
MA
Congressional District
07

Other Information

FOA
PA-16-161
Study Section
Virology - A Study Section[VIRA]

Fiscal Year
2019
Award Notice Date
25-January-2019

Administering Institutes or Centers
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
DUNS Number
604483045
CFDA Code
855

Project Start Date
13-February-2018
Project End Date
31-January-2022
Budget Start Date
01-February-2019
Budget End Date
31-January-2022

Project Funding Information for 2019

Total Funding
$247,500
Direct Costs
$150,000
Indirect Costs
$97,500

Year	Funding IC	
2019	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$247,500

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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Back to Search Results

Description

Details

Sub-Projects

Publications

Patents

Outcomes

Clinical Studies

News and More

History

Similar Projects

Deciphering the pathogenic potential of Lloviu virus, a novel filovirus

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Genetics; Infectious Diseases; Rare Diseases;

Sub Projects

No Sub Projects information available for 5R21AI137793-02

Publications

No Publications available for 5R21AI137793-02

Patents

No Patents information available for 5R21AI137793-02

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 5R21AI137793-02

Clinical Studies

No Clinical Studies information available for 5R21AI137793-02

News and More

Related News Releases

No news release information available for 5R21AI137793-02

History

No Historical information available for 5R21AI137793-02

Back to Search Results

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Description
Details
Sub-Projects
Publications
Patents
Outcomes
Clinical Studies
News and More
History
Similar Projects

Project Number	Contact PI/Project Leader	Awardee Organization
5R21AI137793-02	MUHLBERGER, ELKE C	BOSTON UNIVERSITY MEDICAL CAMPUS