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The regulatory functions of mini viral RNAs in influenza virus infections

Project Number
1R21AI147172-01

Contact PI/Project Leader
TE VELTHUIS, AREND JAN

Awardee Organization
UNIVERSITY OF CAMBRIDGE

Description

Abstract Text

SUMMARY Seasonal influenza viruses cause >600 million cases and up to 650 thousand deaths, annually. Moreover, the yearly economic losses associated with these infections run into hundreds of billions of dollars. A greater threat to human health and our economy are **pandemic** and avian influenza viruses, which cause severe disease, organ failure and death by dysregulating the innate immune response. Current evidence suggests that in both seasonal, **pandemic** and avian influenza virus infections, active viral RNA synthesis plays a critical role in triggering and dysregulating this response. The key function of viral RNA synthesis is transcription and replication of the viral genome. However, the process also produces shorter RNA products, of which the function is not fully understood. We recently discovered that **pandemic** and avian influenza A virus infections produce RNA molecules of about 56-125 nucleotides in length, called mini viral RNAs, and that their synthesis is correlated with the upregulation of disease markers. The underlying mechanism is that these mini viral RNAs are bound by cellular pathogen receptor RIG-I and trigger strong innate immune responses in human cells. Mini viral RNAs are produced at high levels by **pandemic** and avian influenza viruses, low levels by seasonal influenza virus strains, and at low levels by lab-adapted influenza virus strains. Currently, the role of mini viral RNAs in the virus replication cycle is unclear. Although mini viral RNAs induce strong innate immune responses, the **pandemic** and avian viruses that produce them are not impaired in their fitness, suggesting that mini viral RNAs may provide a selective advantage during outbreaks and/or that they are part of a regulatory mechanism in virus replication and growth. We will here test the hypothesis that mini viral RNAs play a key role in the viral infection cycle. We will characterise their function in viral replication and host and viral gene expression. In addition, we will investigate how the production of mini viral peptides, encoded by mini viral mRNAs, modulates host responses. In summary, this project will answer fundamental questions about the role of a new type of viral RNA in infections with highly pathogenic influenza viruses and it will contribute to a complete mechanistic understanding of influenza disease.

Public Health Relevance Statement

PROJECT NARRATIVE Pandemic and avian influenza viruses produce short RNA molecules called mini viral RNAs that contribute to severe disease. This project will answer fundamental questions about the role these mini viral RNAs in influenza virus infections and further our mechanistic understanding of influenza disease.

NIH Spending Category

Biodefense Emerging Infectious Diseases Genetics Infectious Diseases Influenza Pneumonia & Influenza

Project Terms

Avian Influenza A Virus Birds Cells Cessation of life Disease Disease Marker Disease Outbreaks Economics Gene Expression Genetic Transcription Growth Health Human Immune response Infection Influenza Influenza A virus Innate Immune Response Length Messenger RNA Nucleotides Organ failure Pathogenicity Peptides Play

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Project Number
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Contact PI/Project Leader
TE VELTHUIS, AREND JAN

Awardee Organization
UNIVERSITY OF CAMBRIDGE

Details

Contact PI/ Project Leader

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Not Applicable

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Organization

Name
UNIVERSITY OF CAMBRIDGE

City
CAMBRIDGE

Country
UNITED KINGDOM (UK)

Department Type
Unavailable

Organization Type
Unavailable

State Code

Congressional District

Other Information

FOA
RFA-AI-18-025

Study Section
Special Emphasis Panel[ZAI1 LR-M (M1)]

Fiscal Year
2019

Award Notice Date
09-September-2019

Administering Institutes or Centers
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

DUNS Number
226552610

CFDA Code
855

Project Start Date
09-September-2019

Project End Date
31-August-2021

Budget Start Date
09-September-2019

Budget End Date
31-August-2020

Project Funding Information for 2019

Total Funding
$118,498

Direct Costs
$109,720

Indirect Costs
$8,778

Year	Funding IC	
2019	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$118,498

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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1R21AI147172-01	TE VELTHUIS, AREND JAN	UNIVERSITY OF CAMBRIDGE

Infectious Diseases; Influenza; Pneumonia & Influenza;

Sub Projects

No Sub Projects information available for 1R21AI147172-01

Publications

No Publications available for 1R21AI147172-01

Patents

No Patents information available for 1R21AI147172-01

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 1R21AI147172-01

Clinical Studies

No Clinical Studies information available for 1R21AI147172-01

News and More

Related News Releases

No news release information available for 1R21AI147172-01

History

No Historical information available for 1R21AI147172-

Thank you for your feedback!

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The regulatory functions of mini viral RNAs in influenza virus infections

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