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Impact of selective genome packaging on influenza A virus reassortment

Project Number
5R01AI125268-04

Contact PI/Project Leader
LOWEN, ANICE C

Awardee Organization
EMORY UNIVERSITY

Description

Abstract Text

Summary Influenza A viruses (IAV) are constantly changing. This change occurs rapidly, on a similar time scale to influenza epidemics. For this reason, the epidemiology and evolution of IAV are closely linked, and an in depth understanding of viral evolution is critical for public health efforts aimed at controlling influenza. We are working to understand the mechanisms of IAV genomic diversification, which underlie its evolution. The current proposal focuses on reassortment, the process by which influenza and other viruses with segmented genomes exchange gene segments. The potential for reassortment to purge the viral genome of deleterious mutations and bring together multiple beneficial changes makes it a powerful catalyst of viral evolution. Reassortant viruses that derive gene segments from human and avian or swine-adapted IAV can furthermore overcome host restrictions to cause zoonoses or pandemics. Indeed, reassortment enabled all four IAV pandemics of the last century. However, reassortment between heterologous IAVs is subject to strong constraints, due to the potential for incompatibility among divergent viral proteins or RNAs. Herein, we propose to measure the impact on reassortment efficiency of sequence divergence within viral RNA packaging signals. In this way, we will test the hypothesis that selective genome packaging limits reassortment. We expect that the severity of the restriction on reassortment will correlate inversely with sequence identity within packaging signal regions and that, for this reason, certain segment combinations will be more likely to arise than others. We furthermore predict that the genotypes that emerge from heterologous reassortment will reflect the physical interactions among viral RNA segments during virion assembly. We will therefore use our data to construct testable models of how the eight segments are organized within the virion. This approach brings a novel methodology to the perennially difficult problem of how the genome is packaged into viral particles. Finally, to gauge the importance of packaging signal mismatch relative to protein mismatch, we will evaluate the impact of sequence divergence within viral protein coding sequences on reassortment outcomes. Ultimately, we aim to define the conditions in nature that are permissive for reassortment and the factors that determine the efficiency of reassortment. This knowledge will significantly advance our understanding of IAV evolution and the mechanisms that shape the emergence of zoonotic and **pandemic** IAVs.

Public Health Relevance Statement

Project Narrative Through regular epidemics and infrequent pandemics, influenza virus causes mild to severe disease in a significant proportion of the population every year. Reassortment, the process by which two differing influenza viruses exchange genes, is one mechanism by which novel strains capable of causing these outbreaks arise. By defining the circumstances under which reassortment can proceed, our research enables public health efforts aimed at predicting and limiting the emergence of new influenza virus strains.

NIH Spending Category

Biodefense | Emerging Infectious Diseases | Genetics | Infectious Diseases | Influenza | Pneumonia & Influenza

Project Terms

Birds | Cells | Code | Complex | Data | Defect | Detection | Disease | Disease Outbreaks | Dose | Epidemic | Epidemiology | Evaluation | Evolution | Family suidae | Gene Exchanges | Genes | Genetic | Genome | Genomics | Genotype | Goals | Human | Infection | Influenza | Influenza A Virus, H1N1 Subtype | Influenza A Virus, H5N1 Subtype | Influenza A Virus, H7N9 Subtype | Influenza A virus | Knowledge | Link | Measures | Methodology | Modeling | Mutation | Nature | Netherlands | North America | Open Reading Frames | Outcome | Panama | Pathogenicity | Pathway Analysis | Population | Process | Proteins | Public Health | RNA | Reassortant Viruses | Research | Role | Severities | Shapes | Signal Transduction | Signaling Protein | Silent Mutation

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Project Number
5R01AI125268-04

Contact PI/Project Leader
LOWEN, ANICE C

Awardee Organization
EMORY UNIVERSITY

Organization

Name
EMORY UNIVERSITY

City
ATLANTA

Country
UNITED STATES (US)

Department Type
MICROBIOLOGY/IMMUN/VIROLOGY

Organization Type
SCHOOLS OF MEDICINE

State Code
GA

Congressional District
05

Other Information

FOA
PA-13-302

Study Section
Virology - B Study Section[VIRB]

Fiscal Year
2019

Award Notice Date
03-July-2019

Administering Institutes or Centers
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

DUNS Number
066469933

CFDA Code
855

Project Start Date **04-August-2016**

Project End Date **31-July-2021**

Budget Start Date **01-August-2019**

Budget End Date **31-July-2021**

Project Funding Information for 2019

Total Funding
$386,618

Direct Costs
$250,000

Indirect Costs
$136,618

Year	Funding IC	FY Total Cost by IC
2019	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$386,618

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	$386,618	Biodefense; Emerging Infectious Diseases; Genetics; Infectious Diseases; Influenza; Pneumonia & Influenza;

Sub Projects

No Sub Projects information available for 5R01AI125268-04

Publications

No Publications available for 5R01AI125268-04

Patents

No Patents information available for 5R01AI125268-04

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 5R01AI125268-04

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Related News Releases

No news release information available for 5R01AI125268-04

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No Historical information available for 5R01AI125268-04

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No Similar Projects information available for 5R01AI125268-04