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Quantitative Studies of influenza Evolution

Project Number	Former Number	Contact PI/Project Leader	Awardee Organization
3R01GM109018-05S1	5R01GM109018-05	SHAPIRA, SAGI	COLUMBIA UNIVERSITY HEALTH SCIENCES

Description

Abstract Text

Principal Investigator/Program Director (Last, first, middle): Shapira, Sagi An enormous mutation rate, coupled with reassortment (a process analogous to chromosomal segregation) of RNA segments of the viral genome, and natural zoonosis, have lead to influenza epidemics and pandemics in humans. It has been estimated seasonal influenza causes approximately 5 million cases annually, resulting in 250,000 to 500,000 deaths. Deaths resulting from **pandemic** influenza can reach millions and each year, the World Health Organization predicts which strains of the virus are most likely to be circulating in the following year. This approach relies on yearly global surveillance data to monitor ongoing infections in humans and livestock and is prone to significant error. A major shortcoming of these data is that they represent a partial landscape of circulating viruses due to limitations in surveillance and the selective pressures are generated in an uncontrolled setting making it difficult to assess the affect of complex evolutionary processes. However, even when such predictions are accurate, a particular influenza vaccine usually confers protection for no more than a few years due to the high mutation rate of the virus. We propose to overcome these limitations by integrating the experimental expertise of the Shapira and Garcia-Sastre laboratories together with mathematical modeling and computational framework of the Rabadan laboratory, a member of the Center for the Multiscale Analysis of Genomic and Cellular Networks (MAGNet; which provides a core framework for applying systems biology approaches to studying complex biological systems such as influenza evolution). While it is well established that reassortment between influenza isolates from different host species can generate viruses with **pandemic** potential, the relationship between reassortment, viral mutation rates, as well as the selective pressures imposed on this virus remain key questions in influenza biology and are major issues for global public health. Not only does influenza represent an ideal laboratory model for quantitative studies of evolution, understanding the variables that influence antigenic drift, and viral adaptation is paramount. In collaboration with MAGNet, we propose to use modern genomic approaches, coupled with genetically tractable mammalian systems, to determine, in an unprecedented fashion, precisely what evolutionary changes the virus undergoes as it adapts across species, or as it interacts with the host innate and adaptive immune systems, to compute the evolutionary trajectory of individual viral sequences, and to identify selection pressures exerted on the virus. We expect that the experimental and computational platform described in this proposal will foster new insights into the evolutionary constrains that govern viral evolution. Coupled with ongoing surveillance efforts, even modest improvements on the current understanding of the influenza fitness landscape will allow for better assessment of **pandemic** risk potential of circulating strains. Project Description Page 6

Public Health Relevance Statement

Principal Investigator/Program Director (Last, first, middle): Shapira, Sagi PROJECT NARRATIVE In this project, we seek to use modern genomic approaches, coupled with genetically tractable mammalian systems, to determine, in an unprecedented fashion, the genetic changes that influenza virus undergoes as it adapts across species, or as it interacts with the host innate and adaptive immune systems. We aim to study the population structures of actively adapting influenza viruses, compute fitness landscapes of viral sequences, examine selection pressures exerted on the virus, and provide evidence for altered physical and transcriptional interactions that arise during viral adaption. We expect that the experimental and computational platform will foster new insights into the evolutionary constrains that govern influenza evolution. Public Health Relevance Statement Page 7

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Genomic approach Genomics Human Individual Infection Influenza
Laboratories Lead Livestock Modeling Modernization Monitor
Mutation Principal Investigator Process Public Health RNA Risk
Structure System Systems Biology Viral Viral Genome Virus
World Health Organization complex biological systems computational platform
computer framework fitness influenza epidemic influenza virus vaccine
influenzavirus insight mathematical model member **pandemic** disease

Details

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Country
UNITED STATES (US)

Department Type
BIOCHEMISTRY

Organization Type
SCHOOLS OF MEDICINE

State Code
NY

Congressional District
13

Other Information

FOA
PA-18-591

Study Section

Fiscal Year	Award Notice Date
2019	**01-May-2019**

Administering Institutes or Centers
NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

DUNS Number	CFDA Code
621889815	**859**

Project Start Date	**01-February-2014**
Project End Date	**31-December-2019**
Budget Start Date	**01-January-2018**
Budget End Date	**31-December-2019**

Project Funding Information for 2019

Total Funding

Direct Costs

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NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES	$160,159	Emerging Infectious Diseases; Infectious Diseases; Influenza; Pneumonia & Influenza;

Sub Projects

No Sub Projects information available for 3R01GM109018-05S1

Publications

No Publications available for 3R01GM109018-05S1

Patents

No Patents information available for 3R01GM109018-05S1

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 3R01GM109018-05S1

Clinical Studies

No Clinical Studies information available for 3R01GM109018-05S1

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Related News Releases

No news release information available for 3R01GM109018-05S1

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No Similar Projects information available for 3R01GM109018-05S1

Thank you for your feedback!