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Development of group 2 influenza A virus entry inhibitors

Project Number Contact PI/Project Leader 1R41AI145727-01 RONG, LIJUN

Awardee Organization
CHICAGO BIOSOLUTIONS, INC.

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Abstract Text

Influenza A viruses belong to the Orthomyxoviridae family with a negative-sense, segmented RNA genome, which can cause seasonal or pandemic flu with high morbidity and significant mortality. Vaccination is the most prevalent prophylactic means for controlling influenza infections. However, an effective vaccine usually takes at least 6 months to develop for the circulating strains. Furthermore, vaccination has limited effectiveness in treatment of immunocompromised patients, and its effectiveness is also limited during a pandemic. The current therapeutic options for flu infections are all based on the NA inhibitors (NAIs), while the influenza M2 ion channel blockers (amantadine and rimantadine) are not recommended anymore since all the circulating influenza strains are resistant to them. However, the rapid emergence of the NAI-resistant strains of influenza A viruses strongly suggests that NAIs alone may not be sufficient as an effective means of the anti-flu therapies, and thus new treatment options targeting the other viral/host factors are urgently needed. This application defines a plan to develop potent, small molecule inhibitors, which block entry of influenza A viruses. We have identified compounds that inhibit entry of infectious influenza A viruses (IC50 values ≤1 µM). These hit compounds exhibit selectivity for H3N2 and H7N1 entry. The overall objective of this Phase I application is to develop these inhibitors as potential anti-flu therapeutics. This application will focus on the following three specific aims: (1) Synthesize structurally diverse analogs of the anti-flu CBS1193 hit series based on structure-activity relationships (SARs) to improve potency and selectivity. (2) Validateothe lead inhibitor candidates in the infectious assay and investigate the mechanism of action (MOA) of the inhibitors. (3) Select flu inhibitors with in vitro ADME properties suitable for i.v. and oral dosing.

Public Health Relevance Statement

Project Narrative This project is to discover and develop small molecule entry inhibitors for influenza viral infection. The proposed research will help to develop potential antiviral therapeutics.

NIH Spending Category

Biodefense Emerging Infectious Diseases Immunization Infectious Diseases Influenza

Pneumonia & Influenza Prevention Vaccine Related

Project Terms

Affect Affinity Amantadine Animal Model Animal Testing Anti-influenza Agent Centers for Disease Control and Prevention (U.S.) Antiviral Agents Biological Assay Cells **Cessation of life Communicable Diseases Development** Dose **Drug Kinetics Effectiveness Epidemic** H7 hemagglutinin Health **Exhibits** Family Genome Goals Grant **Immunocompromised Host** Influenza A virus Hemagglutinin In Vitro Influenza **Influenza Therapeutic Integration Host Factors** Libraries Life **Liver Microsomes** Lead **National Institute of Allergy and Infectious Disease** Mediating Morbidity - disease rate Mutation Orthomyxoviridae Oral Oseltamivir **Permeability Pharmaceutical Preparations Phase Read More**

Details

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Title

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Other Pls

Not Applicable

Program Official

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Contact PI/Project Leader Project Number 1R41AI145727-01 **RONG, LIJUN**

Awardee Organization CHICAGO BIOSOLUTIONS, INC.

Other Information

Fiscal Year

2019

FOA Administering Institutes or Centers **NATIONAL INSTITUTE OF ALLERGY** PA-18-575 Date AND INFECTIOUS DISEASES Study Section Special Emphasis Panel ZRG1 CFDA Code

BCMB-G (10)] 079936940 855

DUNS Number

Project Start

01-April-2019

Project End Date 31-March-2021

Budget Start

01-April-2019

Date

Budget End Date 31-March-2020

Project Funding Information for 2019

Award Notice Date

29-March-2019

Total Funding Direct Costs Indirect Costs \$299,999 \$0 \$0

Year	Funding IC	FY Total Cost by IC
2019	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	\$299.999

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	\$299,999	Biodefense; Emerging Infectious Diseases; Immunization; Infectious Diseases; Influenza; Pneumonia & Influenza; Prevention; Vaccine Related;

品 Sub Projects

No Sub Projects information available for 1R41AI145727-01

Publications

No Publications available for 1R41AI145727-01

Patents

No Patents information available for 1R41AI145727-01

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 1R41AI145727-01

***** Clinical Studies

No Clinical Studies information available for 1R41AI145727-01

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Development of group 2 influenza A virus entry inhibitors

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Project Number 1R41AI145727-01 **Contact PI/Project Leader RONG, LIJUN**

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No Historical information available for 1R41AI145727-01

Similar Projects

No Similar Projects information available for 1R41Al145727-01