OMB Number: 4040-0001
Expiration Date: 06/30/2011

APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

3. DATE RECEIVED BY STATE	State Application Identifier

1. * TYPE OF SUBMISSION

☐ Pre-application ☐ Application ☒ Changed/Corrected Application

4. a. Federal Identifier: GRANT11418218

b. Agency Routing Identifier:

2. DATE SUBMITTED: 06/05/2013

Applicant Identifier:

5. APPLICANT INFORMATION

*** Organizational DUNS:** 0770900660000

* Legal Name: EcoHealth Alliance, Inc.

Department: Division:

* Street1: 460 West 34th Street

Street2: 17th Floor

* City: New York County / Parish:

* State: NY: New York Province:

* Country: USA: UNITED STATES * ZIP / Postal Code: 10001-2317

Person to be contacted on matters involving this application

Prefix: Dr. * First Name: Peter Middle Name:

* Last Name: Daszak Suffix:

* Phone Number: (b) (6) Fax Number: +1.212.380.4465

Email: (b) (6)

6. * EMPLOYER IDENTIFICATION *(EIN) or (TIN):* 311726494

7. * TYPE OF APPLICANT: M: Nonprofit with 501C3 IRS Status (Other than Institution of Higher Education)

Other (Specify):

Small Business Organization Type ☐ Women Owned ☐ Socially and Economically Disadvantaged

8. * TYPE OF APPLICATION:

☒ New ☐ Resubmission

☐ Renewal ☐ Continuation ☐ Revision

If Revision, mark appropriate box(es).

☐ A. Increase Award ☐ B. Decrease Award ☐ C. Increase Duration ☐ D. Decrease Duration

☐ E. Other (specify):

* Is this application being submitted to other agencies? Yes ☐ No ☒ What other Agencies?

9. * NAME OF FEDERAL AGENCY: National Institutes of Health

10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER:

TITLE:

11. * DESCRIPTIVE TITLE OF APPLICANT'S PROJECT:

Understanding the Risk of Bat Coronavirus Emergence

12. PROPOSED PROJECT:

* Start Date: 10/01/2013 * Ending Date: 09/30/2018

*** 13. CONGRESSIONAL DISTRICT OF APPLICANT:** NY-010

14. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION

Prefix: Dr. * First Name: Peter Middle Name:

* Last Name: Daszak Suffix:

Position/Title: President

* Organization Name: EcoHealth Alliance, Inc.

Department: Division:

* Street1: 460 West 34th Street

Street2: 17th Floor

* City: New York County / Parish:

* State: NY: New York Province:

* Country: USA: UNITED STATES * ZIP / Postal Code: 10001-2317

* Phone Number: (b) (6) Fax Number: +1.212.380.4465

* Email: (b) (6)

15. ESTIMATED PROJECT FUNDING

a. Total Federal Funds Requested	3,362,338.00
b. Total Non-Federal Funds	0.00
c. Total Federal & Non-Federal Funds	3,362,338.00
d. Estimated Program Income	0.00

16. * IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?

a. YES ☐ THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:

DATE:

b. NO ☐ PROGRAM IS NOT COVERED BY E.O. 12372; OR

☒ PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW

17. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious. or fraudulent statements or claims may subject me to criminal, civil, or administrative penalities. (U.S. Code, Title 18, Section 1001)

☒ *** I agree**

** The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.*

18. SFLLL or other Explanatory Documentation

Add Attachment | Delete Attachment | View Attachment

19. Authorized Representative

Prefix: Mr. * First Name: Aleksei Middle Name:

* Last Name: Chmura Suffix:

* Position/Title: Authorized Organizational Representative

* Organization: EcoHealth Alliance, Inc.

Department: Division:

* Street1: 460 West 34th Street

Street2: 17th Floor

* City: New York County / Parish:

* State: NY: New York Province:

* Country: USA: UNITED STATES * ZIP / Postal Code: 10001-2317

* Phone Number: (b) (6) Fax Number: +1.212.380.4465

* Email: (b) (6)

*** Signature of Authorized Representative**

Winifred Zubin

*** Date Signed**

06/05/2013

20. Pre-application

Add Attachment | Delete Attachment | View Attachment

424 R&R and PHS-398 Specific Table Of Contents

OMB Number: 4040-0010
Expiration Date: 08/31/2011

Project/Performance Site Location(s)

Project/Performance Site Primary Location ☐ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: EcoHealth Alliance, Inc.
DUNS Number: 0770900660000
* Street1: 460 West 34th Street
Street2: 17th Floor
* City: New York County:
* State: NY: New York
Province:
* Country: USA: UNITED STATES
* ZIP / Postal Code: 10001-2317 * Project/ Performance Site Congressional District: NY-010

Project/Performance Site Location 1 ☐ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: Wuhan Institute of Virology
DUNS Number: 5290274740000
* Street1: Xiao Hong Shan, No. 44
Street2: Wuchang District
* City: Wuhan County:
* State:
Province: Hubei
* Country: CHN: CHINA
* ZIP / Postal Code: 430071 * Project/ Performance Site Congressional District:

Project/Performance Site Location a ☐ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: East China Normal University
DUNS Number: 4209454950000
* Street1: 3663 Zhongshan Beilu
Street2:
* City: Shanghai County:
* State:
Province: Shanghai
* Country: CHN: CHINA
* ZIP / Postal Code: 200062 * Project/ Performance Site Congressional District:

Project/Performance Site Location(s)

Project/Performance Site Location 3

☐ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: Yunnan Institute of Endemic Diseases Control and Prevention

DUNS Number:

* Street1: 33 Wenhua Road

Street2:

* City: Dali County:

* State:

Province: Yunnan

* Country: CHN: CHINA

* ZIP / Postal Code: 650201 * Project/ Performance Site Congressional District:

Project/Performance Site Location a

☐ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: Center for Disease Control and Prevention of Guangdong

DUNS Number:

* Street1: 176 Xigang Xilu

Street2:

* City: Guangzhou County:

* State:

Province: Guangdong

* Country: CHN: CHINA

* ZIP / Postal Code: 5103000 * Project/ Performance Site Congressional District:

Additional Location(s) Add Attachment Delete Attachment View Attachment

RESEARCH & RELATED Other Project Information

1. * Are Human Subjects Involved? ☒ Yes ☐ No

1.a If YES to Human Subjects

Is the Project Exempt from Federal regulations? ☐ Yes ☒ No

If yes, check appropriate exemption number. ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6

If no, is the IRB review Pending? ☒ Yes ☐ No

IRB Approval Date:

Human Subject Assurance Number:

2. * Are Vertebrate Animals Used? ☒ Yes ☐ No

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ☐ Yes ☒ No

IACUC Approval Date: 10/15/2010

Animal Welfare Assurance Number A3433-01

3. * Is proprietary/privileged information included in the application? ☐ Yes ☒ No

4.a. * Does this project have an actual or potential impact on the environment? ☐ Yes ☒ No

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ☐ Yes ☐ No

4.d. If yes, please explain:

5. * Is the research performance site designated, or eligible to be designated, as a historic place? ☐ Yes ☒ No

5.a. If yes, please explain:

6. * Does this project involve activities outside of the United States or partnerships with international collaborators? ☒ Yes ☐ No

6.a. If yes, identify countries: China

6.b. Optional Explanation:

7. * Project Summary/Abstract 1234-NIAID_COV_Project_Summary2013.pd Add Attachment Delete Attachment View Attachment

8. * Project Narrative 1235-NIH_COv_Project_Narrative.pdf Add Attachment Delete Attachment View Attachment

9. Bibliography & References Cited 1236-NIAID_COV_2013_Bibliography.pdf Add Attachment Delete Attachment View Attachment

10. Facilities & Other Resources 1237-FACILITIES_AND_OTHER_RESOURCES.p Add Attachment Delete Attachment View Attachment

11. Equipment Add Attachment Delete Attachment View Attachment

12. Other Attachments Add Attachments Delete Attachments View Attachments

Project Summary

This project will examine the risk of future coronavirus (CoV) emergence from wildlife using in-depth field investigations across the human-wildlife interface in China, molecular characterization of novel CoVs and host receptor binding domain genes, mathematical models of transmission and evolution, and *in vitro* and *in vivo* laboratory studies of host range. Zoonotic CoVs are a significant threat to global health, as demonstrated with the emergence of pandemic severe acute respiratory syndrome coronavirus (SARS-CoV) in China in 2002, and the recent and ongoing emergence of Middle East Respiratory Syndrome (MERS-CoV). Bats appear to be the natural reservoir of these viruses, and hundreds of novel bat-CoVs have been discovered in the last two decades. Bats, and other wildlife species, are hunted, traded, butchered and consumed across Asia, creating a largescale human-wildlife interface, and high risk of future emergence of novel CoVs. This project aims to understand what factors increase the risk of the next CoV emerging in people by studying CoV diversity in a critical zoonotic reservoir (bats), at sites of high risk for emergence (wildlife markets) in an emerging disease hotspot (China). The three specific aims of this project are to:

1. Assess CoV spillover potential at high risk human-wildlife interfaces in China. This will include quantifying the nature and frequency of contact people have with bats and other wildlife; serological and molecular screening of people working in wet markets and highly exposed to wildlife; screening wild-caught and market sampled bats from 30+ species for CoVs using molecular assays; and genomic characterization and isolation of novel CoVs.
2. Develop predictive models of bat CoV emergence risk and host range. A combined modeling approach will include phylogenetic analyses of host receptors and novel CoV genes (including functional receptor binding domains); a fused ecological and evolutionary model to predict host-range and viral sharing; and mathematical matrix models to examine evolutionary and transmission dynamics.
3. Test predictions of CoV inter-species transmission. Predictive models of host range (i.e. emergence potential) will be tested experimentally using reverse genetics, pseudovirus and receptor binding assays, and virus infection experiments across a range of cell cultures from different species and humanized mice.

PROJECT NARRATIVE

Most emerging human viruses come from wildlife, and these represent a significant threat to global public health and biosecurity - as demonstrated by the SARS coronavirus pandemic of 2002-03 and an ongoing SARS-like epidemic in the Middle East. This project seeks to understand what factors allow animal Coronaviruses to evolve and jump into the human population by studying virus diversity in a critical group of animals (bats), at sites of high risk for emergence (wildlife markets) in an emerging disease hotspot (China).

FACILITIES AND OTHER RESOURCES

EcoHealth Alliance, New York, USA (Peter Daszak, Jon Epstein, Parviez Hosseini, and Kevin Olival)
EcoHealth Alliance is a 40-year old scientific research NGO that specializes in multidisciplinary research on the causes, origins and spread of zoonotic emerging diseases. EcoHealth Alliance scientists have been working on the emergence of Nipah & Hendra virus, SARS CoV, surveillance for zoonotic agents in wildlife, and spatial modeling for over 15 years, and on modeling of infectious disease emergence and spread for over a decade. EcoHealth Alliance is based in New York City with (b) (4) square feet of office space including a meeting room and basic laboratory – freezer storage and light microscopy. The scientific staff (25 core scientists, 100+ field staff) is supported by a core admin staff of 11 which is available for work on this project and is funded through core funds.

EcoHealth Alliance is equipped with 35 networked PCs including an NIH ARRA-funded International LifeSize Video Conferencing facility. High-speed video conferencing facilities have been installed with key international collaborators in 2011. EcoHealth Alliance has access to a 24-7 server, server support, and all required software including ArcGIS ArcINFO, MatLab, SPSS, R, Microsoft Office, and Adobe CS5 running on both Apple and Windows Operating Systems. Additionally we have a four-processor, public IP addressed Linux and an eight-processor Mac Pro Server - each with 4TB hard drives, which in combination can be used for intensive computational modeling and database processing by all the grantees. Access to the cloud (Amazon) is provided by core funding to EHA.

EcoHealth Alliance is the headquarters of a series of global networks that provide exceptional leverage for the core scientists: 1) The USAID EPT PREDICT consortium. This group conducts human and wildlife surveillance for high-risk pathogens in 24 countries including China. Partners include Dr Ian Lipkin's Center for Infection and Immunity at Columbia University (pathogen discovery), UC Davis, The Smithsonian, GVFI and WCS; 2) The One Health Alliance of South Asia. This is a Rockefeller Foundation funded transboundary disease surveillance program; 3) The EcoHealth Alliance Partners: A global partnership of leading wildlife and global health researchers in tropical and subtropical countries. This gives us unique access to working on-the-ground in countries where surveillance is difficult, such as China, where our group has proven capacity to export samples from; 4) The Consortium for Conservation Medicine: A unique collaborative institution linking Johns Hopkins Bloomberg School of Public Health, Tufts University School of Veterinary Medicine, The University of Pittsburgh Graduate School of Public Health, The University of Wisconsin-Madison Nelson Institute for Environmental Studies, The USGS National Wildlife Health Center, and EcoHealth Alliance. The CCM provides access to hundreds of high caliber scientists, their facilities,

and their students at 6 leading institutes of public health, veterinary medicine, and environmental science in the USA.

East China Normal University, **Shanghai, China** (Shuyi Zhang and Guangjian Zhu)
Dr. Zhang is Dean of the Institutes for Advanced Interdisciplinary Research at East China Normal University. Over (b) (4) square metres is allocated to his research group at ECNU. The lab is fully capable of carrying out molecular, protein, epidemic disease and evolution research. Experimental equipment includes: Roche 454 (GS FLX Titanium System), Bioinformatics Computer Server, Multi-Channel Neurophysiology Workstation TDT, PCR Amplifier, Real time PCR Amplifier, Electrophoresis, Ultra-low Temperature Freezer, Centrifuge, UV-Visible Spectrophotometer, Two-dimensional Electrophoresis, Vertical Electrophoresis System, Incubator, Clean Bench, and Class II-Biosafety Cabinet, Hybridization Oven, Water PurificationSystem, and Shaker.

Wuhan Institute of Virology, Wuhan, China (Zhengli Shi and Xingyi Ge)
The Shi laboratory includes 4 rooms totaling (b) (4), one equipped with two CO2 incubators for tissue culture, one equipped facilities including with high speed centrifuge, 2 -20°C, 3 -80°C freezers, 2 PCR machines, 1 ELISA plate reader, one for molecule diagnosis equipped with two biosafety cabinets, and one normal laboratory equipped various small equipment items (mini-centrifuges, gel electrophoresis units, circulating adjustable water baths, and heat blocks). Also available to Dr. Shi's group is a fully equipped biosafety level 3 laboratory, a newly opened BLS-4 laboratory (the first in China) and Institute-supported facility center, which houses full-time staff and equipment for electronic microscopy, ultracentrifugation, confocal microcopy, and sequencing machine.

The Wuhan Institute of Virology is China's premier institute for virological research. It consists of three research departments and one center: Department of Molecular Virology, Department of Bio-control, Department of Analytical Biochemistry and Biotechnology, and the Virus Resource and Bioinformation Center of China. It also has the Key Laboratory of Molecular Virology of CAS, the Joint-laboratory of Invertebrate Virology, a HIV Pre-screening Lab and Hubei Engineering and Technology Research Center for Viral Diseases. The institute is further divided into 14 research groups, one of which is run by Dr Zhengli Shi. The supporting system of the institute consists of an Analytical Equipment Center, an Experimental Animal Center, an Editorial Office of "Virologica Sinica"and an Computer Network Center. The virus resource and bio-information center of China contains the largest virus bank in Asia, curating around 800 viral strains.
The Institute collaborates with the World Health Organization (WHO), universities and research institutes in more than 30 counties and regions including EcoHealth Alliance in the USA. There are 14 professors, 36 associated professors, 47 assistant professors conducting research on virology and five of these have been awarded honors in the "Hundred Talents Project". The institute has built a BSL-3 lab and a 600 m2 experimental animal center. In 2013, the first BSL-4 lab in China was opened at this

Institute in a purpose-built facility which has been designed with the assistance of the US Centers for Disease Control and the Pasteur Institute.

OMB Number: 4040-0001
Expiration Date: 06/30/2011

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Prefix: Dr. * First Name: Peter Middle Name:
* Last Name: Daszak Suffix:
Position/Title: President Department:
Organization Name: EcoHealth Alliance, Inc. Division:
* Street1: 460 West 34th Street
Street2: 17th Floor
* City: New York County/ Parish:
* State: NY: New York Province:
* Country: USA: UNITED STATES * Zip / Postal Code: 10001-2317
* Phone Number: (b) (6) Fax Number: +1.212.380.4465
* E-Mail: (b) (6)

Credential, e.g., agency login: (b) (6)

*** Project Role:** PD/PI **Other Project Role Category:**

Degree Type: Ph.D.
Degree Year: 1994

***Attach Biographical Sketch** 1244-Peter_Daszak_NIH_biosket Add Attachment Delete Attachment View Attachment
Attach Current & Pending Support Add Attachment Delete Attachment View Attachment

PROFILE - Senior/Key Person 1

Prefix: Dr. * First Name: ZhengLi Middle Name:
* Last Name: Shi Suffix:
Position/Title: Senior Scientist Department:
Organization Name: Wuhan Institute of Virology Division:
* Street1: Xiao Hong Shan, no. 44
Street2: Wuchang District
* City: Wuhan County/ Parish:
* State: Province: Hubei
* Country: CHN: CHINA * Zip / Postal Code: 430071
* Phone Number: (b) (6) Fax Number: +86-27-87198072
* E-Mail: (b) (6)

Credential, e.g., agency login:

*** Project Role:** Co-Investigator **Other Project Role Category:**

Degree Type: Ph.D.
Degree Year: 2000

***Attach Biographical Sketch** 1245-SHI_Zhengli_Biosketch_20 Add Attachment Delete Attachment View Attachment
Attach Current & Pending Support Add Attachment Delete Attachment View Attachment

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Senior/Key Person 2

Prefix: Dr. * First Name: ShuYi Middle Name:

* Last Name: Zhang Suffix:

Position/Title: Dean Department:

Organization Name: East China Normal University Division:

* Street1: B319, Science Building 3663

Street2: North Zhongshan Road

* City: Shanghai County/ Parish:

* State: Province: Shanghai

* Country: CHN: CHINA * Zip / Postal Code: 200062

* Phone Number: (b) (6) Fax Number:

* E-Mail: (b) (6)

Credential, e.g., agency login:

*** Project Role:** Co-Investigator **Other Project Role Category:**

Degree Type: Ph.D.

Degree Year: 1994

***Attach Biographical Sketch** 1246-Zhang_Shuyi_Biosketch_K$ Add Attachment Delete Attachment View Attachment

Attach Current & Pending Support Add Attachment Delete Attachment View Attachment

PROFILE - Senior/Key Person 3

Prefix: Dr. * First Name: Changwen Middle Name:

* Last Name: Ke Suffix:

Position/Title: Director Department:

Organization Name: CDC and Prevention of Guangdong Province Division:

* Street1: Xing Gang West Road, no. 176

Street2:

* City: Guangzhou County/ Parish:

* State: Province: Guangdong

* Country: CHN: CHINA * Zip / Postal Code: 510300

* Phone Number: (b) (6) Fax Number:

* E-Mail: (b) (6)

Credential, e.g., agency login:

*** Project Role:** Co-Investigator **Other Project Role Category:**

Degree Type: Ph.D.

Degree Year: 2001

***Attach Biographical Sketch** 1247-Biosketch_ChangWenKe_COV Add Attachment Delete Attachment View Attachment

Attach Current & Pending Support Add Attachment Delete Attachment View Attachment

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Senior/Key Person 4

Prefix: Dr. * First Name: Jonathan Middle Name: H

* Last Name: Epstein Suffix:

Position/Title: Associate Vice President Department: Conservation Medicine

Organization Name: EcoHealth Alliance Division:

* Street1: 460 W34th Street

Street2: 17th Floor

* City: New York County/ Parish:

* State: NY: New York Province:

* Country: USA: UNITED STATES * Zip / Postal Code: 10001-2317

* Phone Number: (b) (6) Fax Number: +1.212.380.4465

* E-Mail: (b) (6)

Credential, e.g., agency login:

*** Project Role:** Co-Investigator **Other Project Role Category:**

Degree Type: DVM

Degree Year: 2002

***Attach Biographical Sketch** 1248-Epstein_BioSketch_NIH _$ Add Attachment Delete Attachment View Attachment

Attach Current & Pending Support Add Attachment Delete Attachment View Attachment

PROFILE - Senior/Key Person 5

Prefix: Dr. * First Name: Kevin Middle Name:

* Last Name: Olival Suffix:

Position/Title: Senior Research Scientist Department:

Organization Name: EcoHealth Alliance Division:

* Street1: 460 W34th Street

Street2: 17th Floor

* City: New York County/ Parish:

* State: NY: New York Province:

* Country: USA: UNITED STATES * Zip / Postal Code: 10001-2317

* Phone Number: (b) (6) Fax Number: +1.212.380.4465

* E-Mail: (b) (6)

Credential, e.g., agency login:

*** Project Role:** Co-Investigator **Other Project Role Category:**

Degree Type: Ph.D.

Degree Year: 2008

***Attach Biographical Sketch** 1249-Olival_biosketch_NIAID_C Add Attachment Delete Attachment View Attachment

Attach Current & Pending Support Add Attachment Delete Attachment View Attachment

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Senior/Key Person 6

Prefix: Dr. * First Name: Parviez Middle Name:

* Last Name: Hosseini Suffix:

Position/Title: Senior Research Scientist Department:

Organization Name: EcoHealth Alliance Division:

* Street1: 460 W 34th Street

Street2: 17th Floor

* City: New York County/ Parish:

* State: NY: New York Province:

* Country: USA: UNITED STATES * Zip / Postal Code: 10001-2317

* Phone Number: (b) (6) Fax Number: +1.212.380.4465

* E-Mail: (b) (6)

Credential, e.g., agency login:

*** Project Role:** Co-Investigator **Other Project Role Category:**

Degree Type: Ph.D.

Degree Year: 2002

***Attach Biographical Sketch** 1250-HOSSEINI_Biosketch_COV20 Add Attachment Delete Attachment View Attachment

Attach Current & Pending Support Add Attachment Delete Attachment View Attachment

PROFILE - Senior/Key Person 7

Prefix: Dr. * First Name: XingYi Middle Name:

* Last Name: Ge Suffix:

Position/Title: Assistant Researcher Department: Department of Emerging Viruses

Organization Name: Wuhan Institute of Virology Division:

* Street1: Xiao Hong Shan, no. 44

Street2: Wuchang District

* City: Wuhan County/ Parish:

* State: Province: Hubei

* Country: CHN: CHINA * Zip / Postal Code: 430071

* Phone Number: (b) (6) Fax Number:

* E-Mail: (b) (6)

Credential, e.g., agency login:

*** Project Role:** Co-Investigator **Other Project Role Category:**

Degree Type: Ph.D.

Degree Year: 2011

***Attach Biographical Sketch** 1251-GE_XingYi_Biosketch_2013 Add Attachment Delete Attachment View Attachment

Attach Current & Pending Support Add Attachment Delete Attachment View Attachment

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Senior/Key Person 8

Prefix: Dr. | * First Name: Guanjin | Middle Name:

* Last Name: Zhu | Suffix:

Position/Title: Assistant Researcher | Department:

Organization Name: Guangdong Entomological Institute | Division:

* Street1: Room 1707, Building 622, 3663 Zhongshanbei Rd

Street2: Putuo District

* City: Shanghai | County/ Parish:

* State: | Province:

* Country: CHN: CHINA | * Zip / Postal Code: 200026

* Phone Number: (b) (6) | Fax Number:

* E-Mail: (b) (6)

Credential, e.g., agency login:

*** Project Role:** Co-Investigator | **Other Project Role Category:**

Degree Type: Ph.D.

Degree Year: 2012

***Attach Biographical Sketch** 1252-Zhu_Gunagjian_Biosketch_ | Add Attachment | Delete Attachment | View Attachment

Attach Current & Pending Support | Add Attachment | Delete Attachment | View Attachment

PROFILE - Senior/Key Person 9

Prefix: Dr. | * First Name: Yun-Zhi | Middle Name:

* Last Name: Zhang | Suffix:

Position/Title: Head of Infectious Disease Surveillance | Department:

Organization Name: Yunnan Center for Disease Control | Division:

* Street1: 33 Wenhua Road

Street2:

* City: Dali City | County/ Parish:

* State: | Province: Yunnan

* Country: CHN: CHINA | * Zip / Postal Code: 671000

* Phone Number: (b) (6) | Fax Number:

* E-Mail: (b) (6)

Credential, e.g., agency login:

*** Project Role:** Co-Investigator | **Other Project Role Category:**

Degree Type: Ph.D.

Degree Year: 2010

***Attach Biographical Sketch** 1253-Biosketch_YunZhiZhang_CO | Add Attachment | Delete Attachment | View Attachment

Attach Current & Pending Support | Add Attachment | Delete Attachment | View Attachment

Program Director/Principal Investigator (Last, First, Middle): Daszak, P.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Peter Daszak	President & Chief Scientist
eRA COMMONS USER NAME (credential, e.g., agency login) (b) (6)	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Bangor University (UK)	BSc. (hons)	07/86	Zoology
University of East London (UK)	Ph.D	03/93	Infectious Diseases

A. Personal Statement

The goal of the proposed research is to investigate the ecology, evolutionary biology and transmission dynamics of bat coronaviruses at the human-wildlife interface. Specifically, we will conduct field studies in China to obtain high quality samples from bats, and identify, characterize and isolate known and novel coronaviruses. We will analyze the patterns of coronavirus transmission among bats and other wildlife, and the risk of spillover to humans. I have been working on the dynamics of emerging viral diseases from wildlife for over 15 years, and have the proven scientific vision, leadership and capacity to lead this team and test the hypotheses laid out here. Since working at the CDC Pathology Activity in 1998 during the Nipah virus outbreak, I have specialized in the ecology of viruses emerging from bats. Under my first Nipah virus R01, I developed a multidisciplinary approach combining fieldwork, phylogenetics, virology, and mathematical modeling to isolate and characterize NiV from bats, analyze transmission dynamics, and identify the cause of its emergence. In 2001, I became director of a research program at a New York-based scientific research NGO. This allowed me to expand my research globally, and in 2005, working with current co-investigators Drs Zhang and Zhengli, we were the first team to identify and characterize SARS-like coronaviruses in bats. I have consolidated this work as PI of: 1) a NIAID R01 to conduct pathogen discovery in bats, and map bat viral diversity; 2) a renewal to my Nipah virus R01 focused on the emergence of NiV in Bangladesh; and 3) a large USAID project (PREDICT) to identify new pathogens in wildlife from emerging disease 'hotspot' regions. The current application builds on this work and leverages my group's unique partnership in China, where we have proven capacity to conduct disease surveillance in humans and wildlife in the markets where SARS emerged, and where we have collaborated at a high level for 12 years. I have a proven record of leading multidisciplinary research teams on emerging viral pathogens from wildlife and have the leadership skills, institutional capacity and network to deliver successful outcomes in the current proposed work.

B. Positions and Honors

Positions and Employment

1993-8 Senior Faculty Research Scientist, Kingston University
1998 Guest Researcher, Centers for Disease Control and Prevention (CDC)
1999-2001 Faculty Research Scientist, University of Georgia
2001- Adjunct Faculty, Tufts Univ. Sch. Veterinary Med.; Univ. Georgia; Columbia Univ.
2001-9 Executive Director, Consortium for Conservation Medicine, EcoHealth Alliance, New York
2009- President & Chief Scientist, EcoHealth Alliance New York.

Other Experience and Professional Membership

Keynote speaker Merieux Foundation Conference on Emerging paramyxoviruses, France (2000); UN Millenium Ecosystem Assessment: Lead Author, human infectious diseases (2006); NIH: ad hoc member, ZRG1 IDM-G 90 study section: Virology, Biodefense & Emerg. Diseases (2003-5); Editorial Board, Conservation Biology (Blackwell); Founding Co-Editor *EcoHealth* (Springer) (2004-10); NAS – Committee Member, Future Needs in Veterinary Research (2004-5); DIVERSITAS (UNESCO-ICSU): Member of Scientific Committee (2004-11; Treasurer 2007-11); NIAID: Steering Committee, workshop on virus-host shifts & emergence of new pathogens (2005); Australian Biosecurity Cooperative Research Center: International Standing Advisory Committee (2005-10); NIH: ad hoc member, ZRG1 IRAP-Q study section (infectious diseases, epidemiology) (2005-7); International EcoHealth Association: Founding board of directors, Treasurer (2006-11); CDC: ad hoc member, ZCD1 SGI, 09PAR07-231, R36 Research Dissertation Awards (2007); European CDC: Keynote speaker, future infectious disease threats (2008); NAS-IOM Committee Member, Global capacity for EID surveillance (2008-9); Scientific Advisory Board, NIAID Center of Excellence, avian influenza (CRISAR), UCLA (2008-9); Reviewer IOM report on Infectious Disease Movements in a Borderless World (2009); NIAID: Steering Committee, workshop on viruses from bats (2009); NAS-IOM Participant, workshop on H1N1, Committee on Emerging Microbial Threats (2009); NIH: ZRG1 IRAP-Q Review panel ARRA Challenge grants (2009); Organizing Committee, 1st International One Health Symposium, Australia (2010); Member, Council of Advisors One Health Commission (2010-); Editor-in-Chief, *EcoHealth* (2010-); Scientific Advisory Board, Oxford Univ. Clinical Research Unit, Vietnam (2010-); Member of IOM Forum on Microbial Threats 2010-; Steering Committeee, NIAID Workshop on Arboviruses 2011; Organizer IOM Forum on Microbial Threats briefing on MERS-CoV 2013.

Honors

Meritorious service award, CDC (1999); CSIRO silver medal for collaborative research (2000); Honored by the naming of a new species of centipede, *Cryptops daszaki* (J Nat Hist 2002; 36: 76-106) (2002); ISI Fast-breaking paper (2002); CBS 60 Minutes documentary on Nipah virus research; 6th Annual Lecturer, Medicine & Humanities, Texas A&M (2003); Editor's choice, *Science* (2006); Zayed International Prize for the Environment (2nd) (2006); Finalist, Director's Pioneer Award (2007); Discovery Channel documentary on Nipah virus research, Bangladesh (2008); Presidential Lecturer, University of Montana (2008) ; Elected member of the Cosmos Club 2012; Honored by the naming of a new species of parasite, *Isospora daszaki* (*Parasitol. Res.* 2013; 111:1463-1466) (2012); Awarded the Hsu-Li Distinguished Lectureship in Epidemiology (2013).

C. Peer-reviewed publications (selected from over 190+); * = Corresponding author

Most relevant to the current application

1. **Daszak P**, Cunningham AA, Hyatt AD (2000). Emerging infectious diseases of wildlife - threats to biodiversity and human health. *Science* 287: 443-449
2. Li W, Shi Z, Yu M, Ren W, Smith C, Epstein JH, Wang H, Crameri G, Hu Z, Zhang H, Zhang J, McEachern J, Field H, **Daszak P**, Eaton BT, Zhang S & Wang L-F (2005). Bats are natural reservoirs of SARS-like coronaviruses. *Science* 310: 676-679.
3. Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL, and **Daszak P* (Corresponding Author)**. (2008). Global trends in emerging infectious diseases. *Nature* 451:990-993
4. Keesing F, Belden LK, **Daszak P**, Dobson A, Harvell CD, Holt RD, Hudson P, Jolles A, Jones KE, Mitchell CE, Myers SS, Bogich T & Ostfeld RS. (2010). Impacts of biodiversity on the emergence and transmission of infectious diseases. *Nature* 468:647-652.
5. Morse SS, Mazet JAK, Woolhouse M, Parrish CR, Carroll D, Karesh WB, Zambrana-Torrelio C, Lipkin WI, **Daszak P* (Corresponding Author)** (2012). Prediction and prevention of the next pandemic zoonosis. *Lancet* 380:1956-1965.
6. **Daszak P** (2012). Anatomy of a pandemic *Lancet* 380: 1883-1884.

7. Quan P-L, Firth C, Conte JM, Williams SH, Zambrana-Torrelio C, Anthony SJ, Ellison JA, Gilbert AT, Kuzmin IV, Niezgoda M, Osinubi MOV, Recuenco S, Markotter W, Breiman R, Kalemba L, Malekani J, Lindblade KA, Rostal MK, Ojeda-Flores R, Suzan G, Davis LB, Blau DM, Ogunkoya AB, Castillo DAA, Moran D, Ngam S, Akaibe D, Agwanda B, Briese T, Epstein JH, **Daszak P**, Rupprecht CE, Holmes EC, Lipkin WI. (2013). Bats are a major natural reservoir for hepaciviruses and pegiviruses. *PNAS* Published ahead of print April 2013.
8. Anthony SJ, Ojeda-Flores R, Rico-Chávez O, Navarrete-Macias I, Zambrana-Torrelio CM, Rostal MK, Epstein JH, Tipps T, Liang E, Sanchez-Leon M, Sotomayor-Bonilla J, Ávila R, Medellín RA, Goldstein T, Suzán G, Daszak P, Lipkin WI. (2013). Coronaviruses in bats from Mexico **Journal of General Virology** Online First.
9. Anthony SJ, Epstein JH, Murray KA, Navarrete-Macias I, Zambrana-Torrelio CM, Solovyov A, Ojeda-Flores R, Arrigo NC, Islam A, Ali Khan S, Hosseini P, Bogich TL, Olival KJ, Sanchez-Leon MD, Karesh W, Goldstein T, Luby SP, Morse SS, Mazet JAK, **Daszak P*(Co-corresponding Author)**, Lipkin WI, Estimating viral diversity in Bats. *PNAS* in review.
10. (b) (6)

Additional recent publications of importance to the field (from 190+ total)

1. Cui J, Han N, Streicker D, Li G, Tang X, Shi Z, Hu Z, Zhao G, Fontanet A, Yi G, Wang L, Jones G, .Field HE, **Daszak P* (Corresponding Author)** & Zhang, S. (2007) Evolutionary relationships between bat coronaviruses and their hosts. *Emerg. Infect. Dis.*13: 1526-1533
2. Epstein JH, Prakash V, Smith CS, **Daszak P**, McLaughlin AB, Meehan G, Field HE, Cunningham AA (2008). Henipavirus infection in fruit bats (*Pteropus giganteus*), India. *Emerg. Infect. Dis.*14: 1309-1311.
3. Smith KF, Behrens M, Schloegel LM, Marano N, Burgiel S, **Daszak P* (Corresponding Author)**. (2009). Reducing the risks of the wildlife trade. *Science* 324:594-595.
4. Epstein J H, Quan PL, Briese T, Street C, Jabado O, Conlan S, Khan SA, Verdugo D, Hossain MJ, Hutchison SK, Egholm M, Luby SP, **Daszak P* (Co-corresponding Author)**, Lipkin WI. (2010). Identification of GBV-D, a Novel GB-like Flavivirus from Old World Frugivorous Bats (*Pteropus giganteus*) in Bangladesh. PLoS Pathogens 6 (7): e1000972.
5. Homaira N, Rahman M, Hossain MJ, Epstein JH, Sultana R, Khan MSU, Podder G, Nahar K, Ahmed B, Gurley ES, **Daszak P**, Lipkin WI, Rollin PE, Comer JA, Ksiazek TG & Luby SP. (2010). Nipah virus outbreak with person-to-person transmission in Thakurgaon, Bangladesh 2007. *Epidemiol & Infection* 138: 1630-1636.
6. Olival KJ, Islam A, Yu M, Anthony SJ, Epstein JH, Khan SA, Khan SU, Crameri G, Wang L-F, Lipkin WI, Luby SP, **Daszak P** (2013). Filovirus antibodies in fruit bats, Bangladesh. *Emerg. Infect. Dis.* 19: 270-273.
7. Sazzad HMS, Hossain MJ, Gurley ES, Ameen KMH, Parveen S, Islam MS, Faruque LI, Podder G, Banu SS, Lo MK, Rollin PE, Rota PA, **Daszak P**, Rahman M, Luby SP. (2013). Nipah virus infection outbreak with nosocomial and corpse-to-human transmission, Bangladesh. *Emerg. Infect. Dis.* 19: 210-217.

D. Research Support

Ongoing Research Support

NSF — Daszak (PI) — 07/01/10-06/30/15
EcoHealthNet - a Research Coordination Network
Funding for student exchange and workshops to fuse veterinary science, ecology and human medical sciences
Role: PI

5R01GM100471 — Perrings (PI) — 09/15/11-06/30/15
NIGMS
Modeling Anthropogenic Effects in the Spread of Infectious Disease
Role: Co-Investigator

1R56TW009502 — Daszak (PI) — 09/17/12-08/31/14
NIH Fogarty International Center
Comparative Spillover Dynamics of Avian Influenza in Endemic Countries
Role: PI

USAID EPT PREDICT Daszak (PI) 10/01/09 – 09/30/14
Modeling hotspots for disease emergence and conducting surveillance in wildlife in hotspots for new emerging zoonoses
Role: PI on Subcontract

2 R01TW005869 Daszak (PI) 09/01/08 – 08/31/13
NIH Ecology of Infectious Diseases (Fogarty International Center)
The Ecology, Emergence and Pandemic Potential of Nipah virus in Bangladesh
To conduct mathematical modeling and fieldwork to understand the dynamics of Nipah virus in Bangladesh
Role: PI

NSF DEB-1257513 Daszak (PI) 08/15/12-07/31/13
US-China Ecology and Evolution of Infectious Diseases Collaborative Workshop; Kunming, China - October, 2012
Role: PI

1 R01AI079231 Daszak (PI) 09/18/08 – 08/31/13
NIAID Non-Biodefense Emerging Infectious Diseases
Risk of viral emergence from bats.
To model hotspots for bat viral diversity, identify & characterize new bat viruses & understand their pathology
Role: PI

HDTRA1-13-C-0029 Preston(PI) 01/11/13-01/10/14
Office of Naval Research, Defense Threat Reduction Agency
Global Rapid Identification Tool (GRIT) for Undiagnosed Emerging Infectious Diseases (EID) Events
Role: Co-Investigator

Completed Research Support

NSF BCS 0826779 Daszak (PI) 10/01/08 – 03/31/12
NSF Human and Social Dynamics
AOC - HSD – Collaborative Research: Human-related factors affecting emerging infectious diseases
To analyze how socio-economic and environmental drivers predict risk of EIDs
Role: PI on lead proposal

R01TW005869 - supplemental Daszak (PI) 09/01/08 – 08/31/11
NIH EID (Fogarty International Center)
Supplemental funding: Predicting the risk of global H5N1 spread
This project will involve mathematical modeling and fieldwork in Bangladesh and China to understand risk of H5N1 spread.
Role: PI

NSF EF-062239 Kilpatrick (PI) 09/01/06 - 08/30/11
NSF/NIH: Ecology & Evolution of Infectious Diseases
Predicting spatial variation in West Nile virus transmission
Study interaction among WNV vector, reservoir host populations across an urban-to-rural gradient.
Role: Co-PI

R01 TW05869 Daszak (PI) 08/01/02 - 05/31/07
NIH/Fogarty International Center
Anthropogenic change & emerging zoonotic paramyxoviruses
To identify the cause of emergence of Nipah and Hendra viruses in Malaysia and Australia.
Role: PI

HSD 0525216 Daszak (PI) 10/15/05 - 10/14/06
National Science Foundation: Human and Social Dynamics
Collaborative Research: Socio-Economic and Environmental Drivers of Emerging Diseases
To analyze patterns of disease emergence globally and produce a broad risk assessment.
Role: PI

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Zhengli Shi	Senior scientist
eRA COMMONS USER NAME (credential, e.g., agency login) (b) (6)	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Department of Biology, Wuhan University, China	B.S.	1987	GENETICS
Wuhan Institute of Virology, Chinese Academy of Sciences, China	M.S.	1990	VIROLOGY
University Montpellier II, Montpellier, France	Ph.D.	2000	VIROLOGY

A. Personal Statement

The focus of this project is to understand the risk of coronavirus spillover from bats to people in China, using ecological analyses, fieldwork, receptor binding assays, and modeling approaches. I have worked in lab-based virology for 23 years, specializing in SARS-CoV and SARS-like CoVs since 2002. This includes the discovery of a wide-array of SARS-like coronaviruses in mainland China, including two isolates able to bind to the ACE2 receptor. My lab has established several bat primary cell lines and immortalized cell lines, capacity for pseudovirus generation and SARS-specific binding assays and we have expertise in every laboratory technique in this proposal. I have collaborated with the PI for over 10 years, and have spent time in laboratories in the USA and Europe. My lab will be responsible for diagnosis, genomics and isolation of coronavirus from wild and domestic animals in Southern China and for analyzing their receptor binding domains.

B. Positions and Honors.

Positions and Employment

1990-1993 Research assistant, Wuhan Institute of Virology, Chinese Academy of Sciences, China
1993-1995 Research scientist, Wuhan Institute of Virology, Chinese Academy of Sciences, China
2000- Senior Scientist, Wuhan Institute of Virology, Chinese Academy of Sciences, Wuhan, China

Other Experience and Professional Memberships

2008- Member, American Society of Microbiology
2001- Member, Chinese Society of Microbilogy
2001- Member, Chinese Society of Biochemistry and Molecular Biology
2004- Editor board, Chinese Journal of Virology
2004-2009 Editor board, Virologica Sinica
2010- Associate Editor, Virologica Sinica

Honors

1996 Chinese Government Graduate Scholarship, the Ministry of Education, PR China.
2003 Natural Science Award (the second rank) of Hubei province, China.
2004 Outstanding supervisor of graduate student of Hubei province, China.
2005 Visitor scholarship from the Chinese Academy of Sciences.
2006 Outstanding scientist of the Chinese Academy of Sciences.

C. Selected peer-reviewed publications (Selected from 82 peer-reviewed)

Most relevant to the current application

1. Li, W., Shi Z., Yu M., Ren W., Smith C., Epstein H. J., Zhang S., Wang H., Crameri G., Hu Z., Zhang H., Zhang J., Mceachern J., Field H., Daszak P., Eaton T.B. and Wang L. F. (2005). Bats are natural reservoirs of SARS-like coronaviruses. Science, 310(5748), 676-679.
2. Hon, C. C., Lam, T. Y., Shi, Z., Drummond, A. J., Yip, C. W., Zeng, F., Lam, P. Y. and Leung, F. C.. (2008). Evidence of the recombinant origin of a bat severe acute respiratory syndrome (SARS)-like coronavirus and its implications on the direct ancestor of SARS coronavirus. Journal of Virology, 82(4), 1819-1826.
3. Yuan, J., Hon,C. C., Li, Y., Wang, D., Xu, G., Zhang, H., Zhou, P., Poon, L. M., Lam, T. T. Leung, F. C. and Shi, Z. (2010). Intra-species Diversity of SARS-Like Coronaviruses (CoVs) in Rhinolophus sinicus and Its Implications on the Origin of SARS-CoVs in human. Journal of General Virology, 91(4),1058-1062.
4. Hou, Y., Peng, C., Yu, M., Li,Y., Han, Z., Wang, L-F., Li, F., Shi, Z. (2010). Bat Angiotensin Converting Enzyme-2 Displays Different Receptor Activity to Severe Acute Respiratory Syndrome Coronavirus Entry. Archives of Virology, 155(10), 1563-1569.
5. Wang, J., Wang, L-F. and Shi, Z. (2008). Construction of a non-infectious SARS coronavirus replicon for application in drug screening and analysis of viral protein function. Biochemical and Biophysical Research Communications, 374(1),138-142.

Additional recent publications of importance to the field (in chronological order)

1. Ren, W., Li, W., Yu, M., Hao, P., Zhang, Y., Zhou, P., Zhang, S., Zhao, G., Zhong, Y., Wang, S., Wang, L. F. and Shi, Z. (2006). Full genome sequences of two SARS-like coronaviruses in horseshoe bats and genetic variation analysis. Journal of General Virology, 87(11), 3355-3359.
2. Li,Y., Wang, J., Hickey, A. C., Zhang, Y., Li, Y., Wu, Y., Zhang, H., Yuan, J., Han, Z., McEachern, J., Broder, C. C., Wang, L. F. and Shi, Z. (2008). Potential nipah virus infection in Chinese bats. Emerging Infectious Diseases, 14(12),1974-1976.
3. Ren, W., Qu, X., Li, W., Han, Z., Yu, M., Zhang, S., Wang, L. F., Deng, H., Shi, Z. (2008). Difference in receptor usage between SARS coronavirus and SARS-like coronavirus of bat origin. Journal of Virology, 82(4), 1899–1907.
4. Zhou, P., Han, Z., Wang, L.F. and Shi, Z. (2009). Immunogenicity difference between the SARS coronavirus and the bat SARS-like coronavirus spike (S) proteins. Biochemical and Biophysical Research Communications, 387(2), 326-329.
5. Li, Y., Ge X., Hon C. C., Zhang H., Zhou P., Zhang Y., Wang L. F. and Shi Z. (2010). Prevalence and Genetic Diversity of Adeno-Associated Viruses in Bats, China. Journal of General Virology, 91(10), 2601-2609.
6. Zhang Y., Zhang H., Dong X., Yuan J., Zhang H., Yang X., Zhou Peng., Ge X., Li Y., Wang L-F, and Shi Z (2010). Hantavirus Outbreak Associated with Laboratory Rats in Yunnan, China. Infection, Genetics and Evolution, 10(5): 638–644.
7. Li, Y., Ge X., Zhang H., Zhou P., Zhu Y., Zhang Y., Yuan J., Wang L-F., Shi Z. (2010). Host Range, Prevalence and Genetic Diversity of Adenoviruses in Bats. Journal of Virology, 84(8), 3889–3897.
8. Yu, M., Tachedjian, M., Crameri, G., Shi, Z. and Wang, L.F. (2010). Identification of key amino acid residues required for horseshoe bat angiotensin-I converting enzyme 2 to function as a receptor for severe acute respiratory syndrome coronavirus. Journal General Virology, 91(7), 1708-1712.
9. Ge, X., Li, Y., Yang, X., Zhang, H., Zhou, P., Zhang, Y. & Shi, Z. (2012). Metagenomic analysis of viruses from bat fecal samples reveals many novel viruses in insectivorous bats in china. Journal of Virology, 86, 4620-4630.
10. Zhou, P., Li, H., Wang, H., Wang, L. F., Shi, Z. (2012). Bat severe acute respiratory syndrome-like coronavirus ORF3b homologues display different interferon antagonist activities. Journal General Virology, 93, 275-281.

D. Research Support

Ongoing Research Support

30970137 National Natural Science Foundation of China Shi (PI) 01/01/2010-12/31/2012
Metagenomic analysis of bat intestinal viruses
Role: PI

2011CB504700 National Basic Research program of China Shi (PI) 01/01/2011-12/31/2015

Mechanism of interspecies transmission of zoonotic viruses
Role: PI

81290341 National Natural Science Foundation of China Shi (PI) 01/01/2013-12/31/2017
Genetic diversity, identification and pathogenesis of bat viruses
Role: PI

Completed Research Support

2005CB523004 National Basic Research program of China Shi (PI) 01/01/2006-12/31/2010
Interspecies transmission mechanism of zoonotic viruses
Role: PI

2009ZX10004-109 Key project of infectious diseases Shi (PI) 01/01/2009-12/31/2010
Rapid and high throughput diagnostic methods for emerging infectious viral pathogens
Role: PI

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Zhang, Shuyi	Dean
eRA COMMONS USER NAME (credential, e.g., agency login) (b) (6)	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Northeast Normal University, China	B.Sc	07/87	Biology
University of Paris XIII, France	D.E.A.	10/90	Ethology
University Pierre & Marie Curie, France	Ph.D.	12/94	Primatology, Tropical Ecology

A. Personal Statement

The goal of the current proposal is to work on the ecology and evolutionary biology of a coronaviruses from wildlife, with special emphasis on China. My background is ideally suited to this work because I am originally trained as a wildlife biologist, but have been working on the ecology and evolutionary biology of zoonoses in wildlife for the past decade. My career as a wildlife biologist began with a Ph.D in France on the behavioral ecology of capuchin monkeys (*Cebus apella*) in primary forest of French Guiana. In 1995, I returned to China, working on golden monkeys (*Rinopithecus*) at the Institute of Zoology, Chinese Academy of Sciences. At the same time, I began to work on the behavioral ecology of bats and rapidly became the leading bat researcher in China, building a large, well-funded group working on the phylogeny, genetics and ecology of bats. In 2003, during the early outbreak of SARS epidemic, I was one of the few Chinese researchers hypothesizing that SARS must have originated from wild birds or mammals, and I became closely involved in the work of the WHO veterinary team investigating potential wildlife reservoirs for SARS. I continued this work with Drs Zhengli Shi, Peter Daszak and Jon Epstein after the WHO team had left, and discovered that bats are the natural reservoir of SARS-like CoVs. After we published our results in *Science* in 2005, I continued to work on bat CoVs, bat genetics, molecular biology and immunology. I have worked actively with the EcoHealth Alliance and with the Wuhan Institute of Virology, and am involved in most of the preliminary data that is listed in the current application. I also act as the main, on-the-ground contact for EcoHealth Alliance research in China, and am Country Coordinator for the USAID-EPT PREDICT program. During the past decade, I have demonstrated my capacity to provide access to some of the most sensitive fieldwork sites in China and collaborate with US institutions in this work. This includes: collaborative work at Xinghai Lake, where we successfully isolated the first H5N1 from wild birds; work on hunter-trader cohorts in the wet markets of Guangzhou, where we are collaborating with EcoHealth Alliance to identify novel pathogens spilling over from wildlife to people; and the work we conducted on bat SARS-like CoVs in 20034, which involved the export of samples from wildlife into foreign collaborators labs for sequencing and pathogen discovery. In my current capacity as Dean of a 3-institute collaboration at ECNU, I have unique capability to mobilize resources, and work within my large network of collaborators to facilitate the current project.

B. Positions and Honors

Positions and Employment

2011- Dean, Institutes for Advanced Interdisciplinary Research, East China Normal University, China
2010- Country Coordinator, USAID-EPT PREDICT
2006-2008 Professor, School of Life Science, East China Normal University, China
1997-2006 Research Professor, Institute of Zoology, Chinese Academy of Sciences, China
1995-1997 Associate Research Professor, Institute of Zoology, Chinese Academy of Sciences, China
1995 Assistant Research Professor, Institute of Zoology, Chinese Academy of Sciences, China

Other Experience and Professional Memberships

1997- Chairman of China's Primate Specialist Group, Species Survival Commission, World

Conservation Union (IUCN-SSC)
1999- Secretary General of Bat Specialists Group of China's Mammalogical Society
2000- Member of Chinese National Committee for International Union of Biological Sciences

Honors

1989 Fellowship from the China's Education Ministry for students abroad
1991 Fellowship from the French Government for Chinese students
1995 Research grant under the "100 Talent Programme" sponsored by the Chinese Academy of Sciences
1998 Allowance of the State Department for research and technology
1999 Research grant under the "Young Scientist" sponsored by the Chinese Academy of Sciences
2000 "Excellent Young Researcher Grant" of the National Natural Science Foundation of China
2001 "Young Scientist" award of the Chinese Academy of Sciences
2006 Nation Award (class II) for Science and Technology

C. Peer-reviewed publications (selected from over 180 peer-reviewed publications)

Most relevant to the current application

1. He, J.F., Peng, G.W., Min, J., Yu, D.W., Liang, W.J., Zhang, S.Y., Xu, R.H., Zheng, H.Y., Wu, X.W., Xu, J., Fang, L., Zhang, X., Li, H., Yan, X.G., Lu, J.H., Hu, Z.H., Huang, J.C., Wan, Z.Y., Lin, J.Y., Song, H.D., Wang, S.Y., Zhou, X.J., Zhang, G.W., Guo, B.W., Zheng, H.J., Zhang, X.L., Zheng, K., Wang, B.F., Fu, G., Hou, J.L., Wang, X.N., Chen, S.J., Hao, P., Tang, H., Ren, S.X., Zhong, Y., Guo, Z.M., Liu, Q., Miao, Y.G., Kong, X.Y., He, W.Z., Li, Y.X., Chen, Z., Wu, C-I, Zhao, G.P., Chiu, R.W.K., Chim, S.S.C., Tong, Y.K., Chan, P.K.S., Tan, J.S., Lo, Y.M.D. (2004). Molecular evolution of the SARS-coronavirus during the course of the SARS epidemic in China. Science, 303, 1666-1669.
2. Li, W.D., Shi, Z.L., Yu, M., Ren, W.Z., Smith, C., Epstein, J., Wang, H.Z., Crameri, G., Hu, Z.H., Zhang, H.J., Zhang, J.H., McEachern, J., Field, H., Daszak, P., Eaton, B.T., Zhang, S.Y., Wang, L.F. (2005). Bats are natural reservoirs of SARS-like coronaviruses. Science, 310, 676-679.
3. Tang, X.C., Zhang, J.X., Zhang, S.Y., Wang, P., Fan, X.H., Li, L.F., Li, G., Dong, B.Q., Liu, W., Cheung, C.L., Xu, K.M., Song, W.J., Vijaykrishna, D., Poon, L.L.M., Peiris, J.S.M., Smith, G.J.D., Chen, H., Guan, Y. (2006). Prevalence and genetic diversity of coronaviruses in bats from China. Journal of Virology, 80, 7481-7490.
4. Ren, W.Z., Qu, X.X., Li, W.D., Han, Z.G., Yu, M., Zhou, P., Zhang, S.Y., Wang, L.F., Deng, H.K., Shi, Z.L. (2008). Difference in receptor usage between SARS coronavirus and SARS-like coronavirus of bat origin. Journal of Virology, 82, 1899-1907.
5. Tang, X.C., Li, G., Vasilakis, N., Zhang, Y., Shi, Z.L., Zhong, Y., Wang, L.F., Zhang, S.Y. (2009). Differential stepwise evolution of SARS Coronavirus functional proteins in different host species. BMC Evolutionary Biology 9, 52, doi:10.1186/1471-2148-9-52.

Additional recent publications of importance to the field

1. Wang, L.F., Shi, Z.L., Zhang, S.Y., Field, H., Daszak, P., Eaton, B.T. (2006). Review of Bats and SARS. Emerging and Infectious Disease, 12, 1834 -1840.
2. Li, G., Jones, G., Rossiter, S., Chen, S.F., Parsons, S., Zhang, S.Y. (2006). Phylogenetics of small horseshoe bats from East Asia based on mitochondrial DNA sequence variation. Journal of Mammalogy, 87, 1234-1240.
3. Ren, W.Z., Li, W.D., Yu, M., Hao, P., Zhou, P., Zhang, S.Y., Zhao, G.P., Zhong, Y., Wang, S.Y., Wang, L.F., Shi, Z.L. (2006). Full-length genome sequences of two SARS-like coronaviruses in 4 horseshoe bats and genetic variation analysis. Journal of General Virology, 87, 3355–3359.
4. Cui, J., Han, N.J., Streicker, D., Li, G., Tang, X.C., Shi, Z.L., Hu, Z.H., Zhao, G.P., Guan, Y., Wang, L.F., Field, H., Jones, G., Daszak, P., Zhang, S.Y. (2007). Evolutionary relationships between bat coronaviruses and their hosts. Emerging and Infectious Disease, 13, 1526-1532.
5. Rossiter, S.J., Benda, P., Dietz, C., Zhang, S.Y., Jones, G. (2007). Rangewide phylogeography in the greater horseshoe bat inferred from microsatellites: implications for population history, taxonomy and conservation. Molecular Ecology, 16, 4699-4714.
6. Cui, J., Counor, D., Shen, D., Sun, G.Y., Deubel, V., Zhang, S.Y. (2008). Detection of Japanese

encephalitis virus antibodies in bats, Southern China. American Journal of Tropical Medicine and Hygiene, 78, 1007-1011.
7. Zhang, J.S., Jones, G., Zhang, L.B., Zhu, G.J., Zhang, S.Y. (2010). Recent surveys of bats (*Mammalia: Chiroptera*) from China II. Pteropodidae. Acta Chiropterologica, 12, 103-116.
8. Liu, Y., Cotton, J.A., Shen, B., Han, X.Q., Rossiter, S.J., Zhang, S.Y. (2010). Convergent sequence evolution between echolocating bats and dolphins. Current Biology, 20, R53-54.
9. Zhang, L.B., Parson, S., Daszak, P., Wei, L., Zhu, G.J., Zhang, S.Y. (2010). Variation in the abundance of ectoparasite mites in relation to the reproduction status, age, sex and size of flat-headed bats. Journal of Mammalogy, 91, 136–143.
10. Shen, B., Han, X.Q., Jones, G., Rossiter, S.J., Zhang, S.Y. (2013). Adaptive evolution of Myo6 Gene in Old World Fruit Bats (Family: Pteropodidae). PLOS ONE, 8(4), doi: 10.1371/journal.pone.0062307

D. Research Support

Ongoing Research Support

(b) (4) Morse (PI) 10/01/09-09/30/14
PREDICT-Wildlife SMART Surveillance/PREDICT Project to pre-empt at the earlier stages possible, zoonotic diseases that impose significant threat to public health.
Role: Collaborator

(b) (4) Zhang (PI) 01/01/11-12/30/13
(b) (4): Surveillance Emerging Infectious Diseases This project is to conduct surveillance in wildlife in hotspots for new emerging zoonoses.
Role: PI

(b) (4) Zhang (PI) 01/01/11-12/30/13
(b) (4): Study of the Evolution of SARS Coronavirus This project is to study the evolutionary relationships between bat coronaviruses and their hosts.
Role: PI

Completed Research Support

(b) (4) Zhang (PI) 01/01/09-12/30/12
(b) (4)
: Research on biological characteristics of Bats.
Role: PI

(b) (4) Zhang (PI) 01/01/10-12/30/12
Changjiang Scholars and Innovative Research Team in University in China: Studying and Monitoring Wildlife and Zoonosis in Eastern China This project is to identify new viruses from wildlife in Eastern China, and to examine the pathogenicity and infectiousness for these novel pathogens.
Role: PI

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Ke, ChangWen	Director, Institute of Pathogenic Microbiology Guangdong Center for Disease Control and Prevention
eRA COMMONS USER NAME (credential, e.g., agency login)	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
West China Medical University	M.P.H.	1984	Public Health
West China Medical University	B.S.	1989	Medicine
Sun Yensen University	M.D.	2001	Biochemistry and Molecular Biology

A. Personal Statement.

I have worked in public health and infectious disease research for more than 10 years. As Director of the Institute of Pathogenic Microbiology at Guangdong CDC I have been involved in the study and control of several emerging zoonitic infections, including SARS CoV and most recently, H7N9 avian influenza. Our work under the Guangdong Department of Health and with several Chinese universities and international collaborators has established several syndromic disease surveillance programs and collaborative infectious disease research programs including Chikungunya, enterovirus 71, Avian influenza H7N9 and H5N1, and SARS CoV. Most recently, through partnership with the USAID PREDICT program, we have augmented our lab's ability to identify zoonotic agents in people highly exposed to wildlife such as those working in live animal markets. This ongoing surveillance program has led to the identification of people who have been exposed to animal pathogens, including SARS CoV, and supports the initiative to extend this type of surveillance to other provinces in China. I believe that there is strong evidence that spillover of animal pathogens to people is occurring in China and MERS CoV in the Middle East shows that we should pay more attention to bat coronaviruses. Given the technical expertise and capacity for disease detection at the microbiology lab at Guangdong CDC, I have high confidence that we will be able to contribute to our understanding of coronavirus circulation in human populations and to determine the risk of new CoVs emerging in China.

B. Positions and Honors

Positions and Employment

1989-2000	Doctor in Charge, Health & Epidemic Prevention Station of Guangdong Province
1994-1996	Participant, Department II of Virology, National Institute of Infectious Diseases, Japan
2003-2004	Visiting researcher, Virology Department, National Institute of Infectious Diseases,Japan
2004-	Director, Institute of Microbiology Center for Disease prevention and Control, Guangdong province, China

Other Experience and Professional Memberships

2004-	Member of National expert committee of Influenza
2006-	Member of National Biosafety expert Committee

C. Selected Peer-reviewed Publications

Most relevant to the current application

1. Mo, H., Zeng, G., Ren, X., Li, H., Ke, C.W., Tan, Y., Cai, C., Lai, K., Chen, R., Chan-Yeung, M., Zhong, N. (2006). Longitudinal profile of antibodies against SARS-coronavirus in SARS patients and their clinical significance. Respirology. Jan; 11(1):49-53.
2. Qiaoli, Z.*,Jianfeng, H., De, W., Zijun, W., Xinguang, Z., Haojie, Z., Fan, D., Zhiquan, L., Shiwen, W., Zhenyu, H., Yonghui, Z., Ke, C.W., Yuan D., Liang W., Li D., Chen, P. (2012). Maiden Outbreak of Chikungunya in Dongguan City, Guangdong Province, China: Epidemiological Characteristics. PLOS ONE, 7(8):1-8
3. Wu, D., Zheng H., Li, H., Monagin, C., Guo, X., Liu, L., Zeng, H., Fang, L., Mo, Y., Zhou, H., Zhang, H., Kou, J., Long, C., Hiromu, Y., & Ke, C.W. (2012). Phylogenetic and molecular characterization of Coxsackievirus A24 variant isolates from a 2010acute hemorrhagic conjunctivitis outbreak in Guangdong, China Virology Journal, 9.41: 1-9
4. Guan, D., van der Sanden, S., Zeng, H., Li, W., Zheng, H., Ma, C., Su, J., Liu, Z., Guo, X., Zhang, X., Liu, L., Koopmans, M., Ke, C.W.* (2012) Population Dynamic and Genetic Diversity of C4 Strains of Human Enterovirus 71 in Mainland China, 1998-2010. PLOS ONE, 7(9):1-8
5. Yang, F., He, J.*, Zhong, H., Ke, C.W., Zhang, X., Hong, T., Ni, H., Lin, J. (2012). Temporal Trends of Influenza A (H1N1) Virus Seroprevalence following 2009 Pandemic Wave in Guangdong, China: Three Cross-Sectional Serology Surveys. PLOS ONE, 7(6):1-8

Additional recent publications of importance to the field (in chronological order)

1. Ke, C.W., Li T.C., Takeda, N. (2005). Positively Charged Amino Acid Residues of VP1 Capsid Protein of Human Polyomavirus BK Influence on the Formation of Virus-like Particles Generated by Recombinant Baculoviruses. Virologica Sinica, 21(1)20-23
2. Ke C.W., Zheng, K., Zhang, X., Zhou H.Q., Duan J.H., Lin L.F. (2005). Detection of Dengue virus by real-time polymerase chain reaction with TaqMan MGB probe. Chinese J Zoonosis, 21(8)716-720
3. Yan, J., Ke, C.W., Zheng, H., et al. (2006). Rapid diagnosis and Identification of Human Enteroviruses by sequencing VP4 gene. Chinese Journal of Vaccines and Immunization. 12(6)469-471
4. Zheng, H.Y., Liu L., Guo, X., Ke, C.W. (2006). A Comparative Study of Three IgM ELISA Kits for Measles Detection. Journal of Tropical Medicine, (08) 897-899
5. Ke, C.W., Deng, F. (2007). Surveillance system based on hospital and laboratory network to discover emerging viral diseases Journal Pathogen Biology, 2(1): 75-76
6. Ke, C.W., Zou, L.R., Yan, J. (2007). Control strategy for emerging Zoonosis. Chinese J Zoonosis, 23(1)92-93.
7. Li, B., Tan, H., Wang, D., et al. (2010). Phenotypic and genotypic characterization of vibrio Cholera O139 of clinical and aquatic isolation in China. Curr. Microbiol.
8. Ding, X., Jiang, L., Ke, C.W. et al. (2010). Amino acid sequence analysis and identification of mutations under positive selection in Hemagglutinin of 2009 influenza A (H1N1) isolates. Virus Genes, 41:329-340
9. Sun, L.M., Zheng, H.Y., Zheng, X.Z. et al. (2011). An enterovirus 71 epidemic in Guangdong province of China, 2008: Epidemiological, Clinical, and Virogenic manifestations. Jpn. J. Ifect. Dis., 64:13-18
10. Su, S., Ning, Z.Y., Zhu, W.J., Jiao, P.R., Ke, C.W., Qi, W.B., Huang, Z., Tian, J., Cao, L., Tan, L.K., Shao, Z.W., Liang, H.B., Huang, W.M., Liao, M., Li, S.J., Zhang, G.H. (2013). Lack of evidence of avian-to-human transmission of avian influenza A (H5N1) virus among veterinarians, Guangdong, China, 2012. Journal of Clinical Virology. 56(4), 365-366.

D. Research Support

Ongoing Research Support

(b) (4) 2012-2015

National Major Projects of Major Infectious Disease Control and Prevention: the Ministry of Science and Technology of the People's Republic of China

Completed Research Support

China–U.S. 2009-2012
Collaborative Program on Emerging and Re-Emerging Infectious Diseases
Enhanced surveillance on Salmonella in Guangdong province.

30972591
National Natural Science Foundation of China 2010-2011
Epidemiology and molecular mechanism of virulence mutation of dengue viruses in Guangdong

World Bank 2005
Establish Laboratory Network for Emergency Response and Surveillance of Infectious Diseases in Guangdong Province and Training.

WHO 07.03.01.AW.01.
Epidemiological study on Transmission on Influenza A Virus from Animals to Human

WHO grant: 07.02.01.AW.01.
Surveillance on emerging and reemerging infectious diseases pathogen in Guangdong Province

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Jonathan H. Epstein	Associate Vice President & Asia Regional Coordinator
eRA COMMONS USER NAME (credential, e.g., agency login) (b) (6)	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Brandeis University, MA	BA	1996	Biology
Tufts University, Sch. Vet. Med., Boston, MA	DVM	2002	Wildlife Med., Intl. Med.
Tufts University, Sch. Vet. Med., Boston, MA	MPH	2002	Epidemiology
Tufts University, Sch. Vet. Med., Boston, MA	Cert Intl Med	2002	Zoonotic Diseases

A. Personal Statement

The goal of the proposed research is to investigate the ecology, evolutionary history and transmission dynamics of mammalian coronaviruses at the human-animal interface. Specifically, we will conduct field studies in China to obtain high quality samples from bats and other mammals found in wet market systems and identify and characterize known and novel coronaviruses. We will analyze the patterns of coronavirus transmission among bats and other wildlife, and the risk of spillover to humans. This research will address fundamentally important issues about the diversity of coronaviruses in mammalian hosts and the risk of inter-species transmission and emergence in human populations. My research has focused on the epidemiology and ecology of emerging zoonotic viruses carried by bats (Nipah virus, Ebolavirus, and SARS CoV), and other wildlife, and the drivers that lead to emergence. My work on SARS CoV ecology, in collaboration with co-investigators Daszak (PI), Zhang and Shi led to the discovery of several SARS-Like coronaviruses in bats, which appear to be ancestral to SARS-CoV and most recently which utilize the same ACE2 receptor as SARS CoV, suggesting direct spillover to humans is possible. Recently, I led a field team in Saudi Arabia in collaboration with the KSA Ministry of Health, to identify the animal origins of the newly discovered **MERS CoV**. I continue to be involved in this ongoing investigation along with co-investigators Daszak and Olival. I have also conducted pathogen discovery work in bats, utilizing next generation sequencing technologies, which led to the discovery of a novel flavivirus related to Hepatitis C virus (GBV D). This team brings a high level of expertise in disease ecology, epidemiology, and pathogen discovery, and includes China's leading experts on wildlife zoonoses in partnership with key provincial CDCs. Our team has maintained a highly productive collaboration under several NIH and non-federally funded research projects, generating peer-reviewed papers in high impact journals (including *Science, PNAS,* and *PLoS Pathogens*). We have proven through previous work that we can manage logistically challenging projects involving people, wildlife, and animals in the wet markets in China, which gives this proposal a high likelihood of success. Under several federal awards, I have successfully managed the field and molecular investigations of zoonotic viruses in bats in several countries including Saudi Arabia, China, India, Malaysia, Thailand, and Bangladesh, all of which have logistical and political challenges. Using the bat and human samples we have already collected; and new animal samples we propose to collect; we will have the resources available to achieve the aims of this proposal.

B. Positions and Honors

Positions and Employment

1999 Intern, Brisbane South Public Health Unit & DPI Queensland Animal Research Institute, AUS.
2002 Extern, Division of Viral and Rickettsial Diseases, CDC, Atlanta, GA
2002 Veterinary Intern, Small animal emergency and critical care, Ocean State Vet. Spec., RI
2003- Senior Research Scientist, EcoHealth Alliance, New York, NY.
2003- Adjunct Faculty, Ecology, Columbia Univ., NY & Tufts University Sch. of Vet. Med., MA.
2006- Adjunct Faculty, Mailman School of Public Health, Columbia Univ, NY
2007- Adjunct Asst. Clinical Professor, Public Health & Family Med, Tufts Univ School of Medicine, MA

2008- Postdoctoral fellow, Center for Infection and Immunity, Columbia University, NY, Adjunct Associate Professor, Mt. Sinai School of Medicine
2008- Review Editor - *EcoHealth*
2009- Associate Vice President, Conservation Medicine Program EcoHealth Alliance, NY
2009- Executive Director, Consortium for Conservation Medicine, EcoHealth Alliance, NY
2009- Asia Regional Coordinator, USAID EPT (PREDICT)
2011- Admissions committee, Tufts University Masters in Conservation Medicine degree program
2012- Board of Directors, International Association of Ecology and Health; Scientific Advisory Board, Lubee Bat Conservancy

Other Experience and Professional Memberships

1998- Member: American Veterinary Medicinal Association, American Association of Zoo Vets, Wildlife Disease Association, New York Academy of Sciences,
2003- Member, IUCN Veterinary Specialist Group
2004 Invited speaker, WHO, Emerging Zoonotic Diseases Working Group meeting
2004 Member and Health Advisor, IUCN Bat Specialist Group; Advisory committee, Suffolk Country Board of Public Health; International Assoc. Ecology and Health
2006 Member, Delta Omega Public Health Honors Society
2007- Leader, Vertebrate Health Task Force, Smithsonian Institution Geological Earth Observatory Program (SIGEO)
2010- Scientific Committee Member, DIVERISTAS ecoHEALTH cross-cutting network (ICSU-UNESCO)
2008-13. (selected) Invited presentations: University of Malaysia, Sarawak – Emerging zoonoses; **IOM-NAS** Committee on Achieving sustainable global capacity for surveillance and response to emerging infectious diseases; Nipah virus colloquium, University Malaya, Kuala Lumpur, Malaysia, Nipah virus symposium, American Society for Tropical Medicine & Hygiene; International Bat Research Symposium, Prague; American Society of Microbiology, Washington, DC; Australian Animal Health Laboratory (AAHL), Geelong; International Meeting on Emerging Diseases (IMED), Vienna; **IOM** meeting on MERS CoV and H7N9, Washington DC.

Honors

2002 First recipient, Certificate of International Veterinary Medicine, Tufts University Sch. Vet. Med.
2002 Hills award for excellence in veterinary clinical nutrition
2002 Sylvia Mainzer award for outstanding achievement in the field of public health
2004 NIH Loan Repayment Award (competitive award for Nipah virus research)
2006 Inducted into Delta Omega Honor Society for Public Health (Alpha Rho Chapter – 1st alumni inductee; 1st Inaugural Keynote Speaker)
2007 Outstanding Alumnus award, Tufts Cummings School of Veterinary Medicine
2012 Young Alumni Achievement Award, Tufts University (selected from all alumni who graduated in past 10 yrs)

D. Selected peer-reviewed publications (from 45). * indicates corresponding author

Most relevant to the application (in chronological order)

1. Li, W., Shi, Z., Yu, M., Ren, W., Smith, C., Epstein, J.H., Wang, H., Crameri, G., Hu, Z., Zhang, H., Zhang, J., McEachern, J., Field, H., Daszak, P., Eaton, B.T., Zhang, S. & Wang, L-F. (2005). Bats are natural reservoirs of SARS-like coronaviruses. Science 310: 676-679.
2. Epstein, J.H.*, Quan, P.L., Briese, T., Street, C., Jabado, O., Conlan, S., Khan, S.A., Verdugo, D., Hossain, M.J., Hutchison, S.K., Egholm, M., Luby, S.P., Daszak, P., & Lipkin, W.I. (2010). Identification of GBV-D, a Novel GB-like Flavivirus from Old World Frugivorous Bats (Pteropus giganteus) in Bangladesh. PLoS Pathogens 6(7): e1000972. doi:10.1371/journal.ppat.1000972.
3. Anthony, S.J, Ojeda-Flores, R., Rico-Chávez, O., Navarrete-Macias, I., Zambrana-Torrelio, C.M., Rostal, M.K., Epstein, J.H., Tipps, T., Liang, E., Sanchez-Leon, M., Sotomayor-Bonilla, J., Aguirre, A.A., Ávila, R., Medellín, R.A., Goldstein, T., Suzán, G., Daszak, P., Lipkin, W.I. (2013). Coronaviruses in bats from Mexico. J. Gen Virol. Published ahead of print January 30, 2013, doi:10.1099/vir.0.049759-0

4. Wacharapluesadee, S., Sintunawa, C., Kaewpom, T., Khongnomnan, K., Olival, K.J., Epstein, J.H., et al. (2013). Group C betacoronavirus from bat guano 11 fertilizer, Thailand. Emerg Infect Dis. Aug. 12 http://dx.doi.org/10.3201/eid1908.130119
5. Quan, P.L., Firth, C., Conte, J.M., Williams, S.H., Zambrana-Torrelio, C.M., Anthony, S.J., Ellison, J.A., Gilbert, A.T., Kuzmin, I.V., Niezgoda, M., Osinubi, M.O.V., Recuenco, S., Markotter, W., Breiman, R.F., Kalemba, L., Malekani, J., Lindblade, K.A., Rostal, M.K., Ojeda-Flores, R., Suzan, G., D., Lora B., Blau, D.M., Ogunkoya, A.B., Alvarez C., Danilo A., Moran, D., Ngam, S., Akaibe, D., Agwanda, B., Briese, T., Epstein, J.H., Daszak, P., Rupprecht, C.E., Holmes, E.C., & Lipkin, W.I. (2013). Bats are a major natural reservoir for hepaciviruses and pegiviruses. PNAS. doi:10.1073/pnas.1303037110

Additional recent publications of importance to the field (in chronological order)

1. Epstein, J.H.*, Field, H.E., Luby, S., Pulliam, J., & Daszak, P. (2006). Nipah Virus: Impact, Origins, and Causes of Emergence. Current Infectious Disease Reports 8: 59-65.
2. Epstein, J.H.*, Rahman, S.A., Zambriski, J.A., Halpin, K., Meehan, G., Jamaluddin, A.A., Hassan, S.S., Field, H.E., Hyatt, A.D., Daszak, P. & HERG. (2006). Feral cats (Felis catus) as possible vectors for Nipah virus. Emerging Infectious Diseases. 12: 1178-1179.
3. Field, H.E., Wang, L.F., Zhang, S., Daszak, P., Smith, C.S., Epstein, J.H., Shi, Z. (2007). Searching for the natural reservoir of the SARS virus. Preventive Veterinary Medicine. 81(1-3): 216-216 Sp. Issue.
4. Epstein, J.H.*, Prakash, V., Smith, C.S., Daszak, P., McLaughlin, A.B., Meehan, G., Field, H.E., and Cunningham, A.A. (2008). Evidence for Henipavirus infection in Indian Pteropus giganteus (Chiroptera; Pteropodidae) fruit bats. Emerging Infectious Diseases 14(8). 1309-11.
5. Epstein, J.H.*, Olival, K.J., Pulliam, J.R.C., Smith, C., Westrum, J., Hughes, T., et al. (2009). Pteropus vampyrus, a hunted migratory species with a multinational home-range and a need for regional management. Journal of Applied Ecology. 46(5):991-1002.
6. Epstein, J.H.*, Price, J.T. (2009). The Significant but Understudied Impact of Pathogen Transmission from Humans to Animals. Mount Sinai Journal of Medicine 76(5):448-55.
7. Homaira, N., Rahman, M., Hossain, M. J., Epstein, J.H., Sultana, R., Khan, M.S.U., Podder, G., Nahar, K., Gurley, E.S., Daszak, P., Lipkin W.I., Rollin, P.E., Comer, J.A., Ksiazek, T.G., Luby, S.P. (2010). Nipah outbreak with person-to-person transmission in Thakurgaon, Bangladesh, 2007. Epidemiology and Infection. 138: 1630-1636.
8. Sohayati, A., Rahman, Hassan, S.S, Olival, K.J., Mohamed, M., Chang, L-Y., Hassan, L., Suri, A.S., Saad, N.M., Shohaimi, S.A., Mamat, Z.C., Epstein, J.H., Field, H.E., Daszak, P., & HERG. (2010). Genetic characterization of Nipah virus isolated from naturally infected Pteropus vampyrus in Malaysia. Emerging Infectious Diseases.16(12).1990-3.
9. Pulliam, J.R., Epstein, J.H., Dushoff, J., Rahman, S.A., Meehan, G., Bunning, M., HERG, Jamaluddin, A.A., Hyatt, A.D., Field, H.E., Dobson, A.P. & Daszak, P. (2011). Agricultural intensification, priming for persistence, and the emergence of Nipah virus: a lethal bat-borne zoonoses. Journal of the Royal Society, Interface. Doi:10.1098/rsif.2011.0223 (journal's most cited article in 2012)
10. Halpin, K., Hyatt, A.D., Fogarty, R., Middleton, D., Bingham, J., Epstein, J.H., Rahman, S.A., Hughes, T., Smith, C., Field, H.E., Daszak, P., & the Henipavirus Ecology Research Group. (2011). Pteropid Bats are Confirmed as the Reservoir Hosts of Henipaviruses: A Comprehensive Experimental Study of Virus Transmission. Am J Trop Med Hyg. 85:946-951; doi:10.4269/ajtmh.2011.10-0567
11. Sohayati, R., Hassan, L., Sharifah, S.H., Lazarus, K., Zaini, C.M., Epstein, J.H., Naim, N.S., Field, H. E., Arshad, S.S., Aziz, J.A., & Daszak, P. (2011). Evidence for Nipah virus recrudescence and serological patterns of captive Pteropus vampyrus. Epidemiology and Infection. 139, pp 1570-1579 doi:10.1017/S0950268811000550
12. Daszak, P., Zambrana-Torrelio, C., Bogich, T.L., Fernandez, M., Epstein, J.H., Murray, K.A. & Hamilton, H. (2012). Interdisciplinary approaches to understanding disease emergence: The past, present and future drivers of Nipah virus emergence. PNAS doi:10.1073/pnas.1201243109

D. Research Support

Ongoing Research Support

Ongoing Research Support

USAID Daszak (PI) 10/01/09 – 09/30/14
Emerging Pandemic Threats: PREDICT
Modeling hotspots for disease emergence and conducting surveillance in wildlife for new emerging zoonoses.
Role: Asia Regional Coordinator: coordinating field and lab activities in Bangladesh, India, Thailand, Malaysia, Indonesia and China; Surveillance Team and Molecular Diagnostic team member.

2 R01TW005869 Daszak (PI) 09/01/08 – 08/31/14
NIH Ecology of Infectious Diseases (Fogarty International Center)
The Ecology, Emergence and Pandemic Potential of Nipah virus in Bangladesh
To conduct mathematical modeling and fieldwork to understand the dynamics of Nipah virus in Bangladesh
Role: Co-PI

1 R01AI079231 Daszak (PI) 09/18/08 – 08/31/13
NIAID Non-Biodefense Emerging Infectious Diseases
Risk of viral emergence from bats. This project is to model hotspots for viral diversity and emergence in bats, to identify new viruses from bats, and to examine the pathogenicity and infectiousness for these novel pathogens. Role: Co-PI

0955897 NSF Research Coordination Network Daszak (PI) 07/01/10-06/30/15
EcoHealthNet: Environmental Science and Health Research Network
The major goal of this research is to run a series of workshops and student research exchange programs focused on collaborations among the human medical, veterinary, ecological and economic sciences.
Role: Co-PI, Program Director

USFWS, F12AP01117 Epstein (PI).
Development of a Great Ape Health Unit in Sabah, Malaysia 09/13/12 - 09/13/14

USFWS, 4500036150 Epstein (PI) 09/15/12 - 09/14/14
Characterization of Climatic Parameters within Bat Hibernacula, their Influence on Environmental Loads of *Geomyces destructans*, and Implications for the Migration of White-Nose Syndrome in Bats

Completed Research Support

1K08AI067549 Epstein (PI) 07/1/07 – 07/30/11
Understanding the Ecology of Nipah Virus in Bangladesh (NIAID)
Modeling the dynamics of Nipah virus in *Pteropus giganteus* and risk of spillover to humans.
Role: PI (collecting Nipah virus epidemiological data from Bats in Bangladesh)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Olival, Kevin James	Senior Research Scientist
eRA COMMONS USER NAME (credential, e.g., agency login) (b) (6)	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Colorado State University	B.S.	05/97	Biology
Columbia University	MA	10/03	Conservation Biology
Columbia University	PhD	05/08	Ecology and Evolutionary Biology
American Museum of Nat. History	Postdoctoral	08/09	Molec. Parasitology
NIH Fogarty US Global Health Fellow	Postdoctoral	08/11	Int'l. Emerg. Inf. Dis

A. Personal Statement

The goal of our proposal is to study the ecology, evolution, and spillover potential of bat coronaviruses. Specifically, we will use a combination of fieldwork, mathematical modeling, and phylogenetic and molecular methods to test several hypotheses related to zoonotic spillover risk and the limits to host range for bat coronaviruses. My research experiences are strongly complementary to these aims. I have been conducting research on bat evolution, ecology, population genetics, and viral discovery for the past 11 years. During my dissertation at Columbia University, I used host population genetics and phylogeography to understand the dynamics of Nipah virus in Southeast Asian fruit bats. As a post-doc at AMNH I discovered several novel malaria parasites in bats, and used molecular systematics to understand the co-evolution and origins of non-human *Plasmodium*. I developed new approaches that combine phylogenetic, ecological and species life-history variables to predict viral diversity in bats, and have tested these using data from the literature. As an NIH Global Health Fellow, I expanded our knowledge of Nipah virus ecology in Bangladesh through population genetic analyses of the putative primary reservoir host, *Pteropus giganteus*, led field investigations on role of non-*Pteropus* fruit bats in Nipah virus circulation, and discovered a number of novel bat pathogens in these species. I have led field research projects and training workshops to conduct viral discovery throughout Asia, including Malaysia, Bangladesh, India, Vietnam, Cambodia, Thailand, and the Philippines. This included several expeditions to collect Nipah virus samples in Bangladesh and Malaysia, and a three-week long Ebola Reston investigation of bats in the Philippines. Most recently I have led field teams on two 3-week expeditions in Saudi Arabia to identify the animal reservoir of MERS-CoV; this work is ongoing. My latest research is focused on: 1) global viral discovery in bats; 2) integrating phylogenetic and molecular evolution analyses with ecological information to better understand the risk of bat viral spillover. In summary, for the past decade my research has been focused on the evolution and ecology of bats and their associated pathogens, and my current focus of using phylogenetic and evolutionary approaches model viral spillover risk in bats is highly complementary to the aims in this proposal.

B. Positions and Honors

Positions and Employment

2000-02 Mentor, NSF Undergraduate Mentoring in Environmental Biology (UMEB) for Pacific Islander undergraduates, University of Hawaii
2002-08 Research Collaborator, Consortium for Conservation Medicine, New York
2003- Member, Henipavirus Ecology Research Group
2003 Lecturer in Disease Ecology, Columbia University Continuing Education course
2003-08 Visiting researcher – bat genetics, Veterinary Research Institute, Malaysia
2005 Visiting researcher – bat genetics, Institute for Ecology and Biological Resources, Vietnam
2005 Visiting researcher – bat genetics, Pasteur Institute, Cambodia
2005 Judge, NY Science and Engineering Fair
2006-07 Mentor, Conservation Genetics High School Internship Program, AMNH, New York
2006-13 Instructor, Columbia University Secondary School Summer Program, New York
2007 Steering Committee, Small Matters: Microbes and Their Role in Conservation, New York
2007 Symposium Organizer, Bat Hunting and Bushmeat, Phuket, Thailand
2009 Symposium Organizer, Bat migration and disease, 1st Int'l Workshop on Bat Migration, Germany
2009 Organizer and Scientific Review Committee, Exploring the Dynamic Relationship Between Health and the Environment, AMNH Spring Symposium, New York
2009- Review Editor, EcoHealth
2009- Adjunct Research Faculty, Center for Environmental Sustainability, Columbia University, New York.
2009- Visiting Research Scientist, American Museum of Natural History, Mammalogy Department.
2010 Mentor and Scientific Review Committee, Student Conference on Conservation Science New York
2010- Key Personnel and Lead Country Liaison: Thailand, Bangladesh, and Vietnam - USAID PREDICT
2010- Lead Field Researcher, FAO-EHA investigation of Ebola Reston reservoirs in Philippines
2011- Steering Committee, NSF RCN grant, South-east Asian Bat Conservation Research Group
2011- Internship Mentor, NSF RCN grant EcoHealthNet, graduate training in One Health
2013- EHA Team lead; MERS-CoV animal reservoir investigations with MoH in Saudi Arabia

Honors

1993-97 Colorado State University Distinguished Scholar Award
2003 NSF Graduate Student Fellowship, Honorable Mention
2005-07 Bat Conservation International Student Award and Scholarship
2004-07 US Environmental Protection Agency STAR Fellowship Award
2008 PhD Dissertation with Distinction, Columbia University
2013 Plenary talk on bat virus modeling at 11th Annual ASM Biodefense and EID Research Meeting
2013 Invitation to participate in Institute of Medicine panel on novel Coronavirus

C. Selected Peer-reviewed Publications (Selected from 25 peer-reviewed publications)

Most relevant to the current application

1. Turmelle, A. & Olival, K.J. (2009). Correlates of viral richness in bats (Order Chiroptera). EcoHealth 6(4): 522-39.
2. Rahman, S.A., Hassan, SS, Olival, K.J., Mohamed, M., Chang, L.Y., Hassan, L., Saad, N.M., Shohaimi, S.A., Mamat, Z.C., Naim, M.S., Epstein, J.H., Suri, A.S., Field, H.E., Daszak, P. & HERG. (2010). Characterization of Nipah virus from Naturally Infected *Pteropus vampyrus* Bats, Malaysia. Emerging Infectious Diseases 16(12): 1990-93.
3. Olival, K.J., Epstein, J.H., Wang, L.F., Field, H.E., & Daszak, P. (2012). Are bats unique viral reservoirs? in A. A. Aguirre, R. S. Ostfeld, and P. Daszak, editors. New Directions in Conservation Medicine: Applied Cases of Ecological Health. Oxford University Press, Oxford. pp. 195-212.
4. Levinson, J., Bogich, T.L., Olival, K.J., Epstein, J.H., Johnson, C.K., Karesh, W. & Daszak, P. (2013). Targetting surveillance for zoonotic virus discovery. Emerging Infectious Diseases 19(5): 743-47.
5. (b) (4)

Identification of Group C Betacoronavirus from Bat guano fertilizer, Thailand. Emerging Infectious Diseases.

Additional recent publications of importance to the field (in chronological order)

1. Olival, K.J. & Daszak, P. (2005). The ecology of emerging neurotropic viruses. Journal of NeuroVirology 11: 440-45.
2. Pulliam, J.R.C., Field, H.E., Olival, K.J. & HERG. (2005). An alternative explanation of Nipah virus strain variation. Emerging Infectious Diseases 11(12): 1978-1979.
3. Daszak, P., Plowright, R., Epstein, J.H., Pulliam, J.R.C., Rahman, S.A., Field, H.E., Smith, C.S., Olival, K.J., Luby, S., Halpin, K., Hyatt, A.D., & HERG. (2006). The emergence of Nipah and Hendra virus: pathogen dynamics across a wildlife-livestock-human continuum. In: Disease Ecology: Community structure and pathogen dynamics, In Collinge and Ray, ed. Oxford University Press: Oxford. pp. 188-203.
4. Olival, K.J., Stiner, E.O., & Perkins, S.L. (2007). Detection of *Hepatocystis* sp. in Southeast Asian Flying Foxes (Pteropodidae) using Microscopic and Molecular Methods. Journal of Parasitology 93(6): 1538-1540.
5. Epstein, J.H., Olival, K.J., Pulliam, J.R.C., Smith, C.S., Westrum, J., Hughes, T., Dobson, A., Zubaid, A., Rahman, S.A., Basir, M.M., Field, H.E., & Daszak, P. (2009). Management of *Pteropus vampyrus*, a hunted migratory species with a multinational home-range. Journal of Applied Ecology 46(5): 991-1002.
6. Murdock, C., Olival, K.J. & Perkins, S.L. (2010). Feeding preference of snow-melt mosquitoes (Culicidae: Culiseta and Ochelerotatus) show a link between cervid amplifying hosts for Jamestown Canyon Virus (Bunyaviridae: Orthobunyavirus) and humans. Journal of Medical Entomology 47(2): 226-229
7. Smith, C.S., Epstein, J.H., Breed, A., Plowright, R., Olival, K.J., de Jong, C., Daszak, P. & Field, H.E. (2011). Satellite Telemetry and Long-Range Bat Movements. PloS One 6(2): e14696.
8. Bogich, T.L., Olival, K.J., Hosseini, P., Mazet, J., Morse, S., Karesh, W.B., Jones, K.E., Levy, M., Funk, S., Brito, I., Epstein, J.H., Brownstein, J., Joly, D., & Daszak, P. (2012). Using Mathematical Models in a Unified Approach to Predicting the Next Emerging Infectious Disease. New Directions in Conservation Medicine: Applied Cases of Ecological Health. In Aguirre, Ostfeld and Daszak, ed. Oxford University Press. pp. 607-18.
9. Morse, S.F., Olival, K.J., Kosoy, M., Billeter, S.A., Patterson, B.D., Dick, C.W., & Dittmar, K. (2012). Global distribution and genetic diversity of Bartonella in bat flies (Hippoboscoidea, Streblidae, Nycteribiidae). Infection, Genetics and Evolution 12(8): 1717-23.
10. Olival, K.J. (2012). Correlates and evolutionary consequences of population genetic structure in bats. In Gunnell and Simmons, ed. Evolutionary History of Bats: Fossils, Molecules, and Morphology. Cambridge University Press, Cambridge. pp. 267-316.
11. Olival, K.J., Islam, A., Yu, M., Anthony, S.J., Epstein, J.H., Khan, S.A., Khan, S.U., Crameri, G., Wang, L.F., Lipkin, W.I., Luby S.P., & Daszak, P. (2013). Ebolavirus Antibodies in Fruit Bats, Bangladesh. Emerging Infectious Diseases 19(2): 270-273.
12. (b) (4)
13. (b) (4)

D. Research Support

Ongoing Research Support

NIH 1 R01AI079231 Daszak (PI) 09/18/08 – 08/31/13
NIAID Non-Biodefense Emerging Infectious Diseases. "Risk of viral emergence from bats".
This project is to model hotspots for viral diversity and emergence in bats, to identify new viruses from bats, and to examine the pathogenicity and infectiousness for these novel pathogens.
Role: Key Personnel: lead project implementation, study design, and phylogenetic modeling

USAID EPT PREDICT Daszak (PI) 10/01/09 – 09/30/14
Modeling hotspots for disease emergence and conducting surveillance in wildlife for new emerging zoonoses.
Role: Key Personnel: Modeling disease risk and managing projects in Asian countries

US Geological Survey (USGS) Olival (Co-PI) 06/18/12-06/17/13
"Genetic Approaches to Defining Taxonomic and conservation Units for the Hawaiian Hoary Bat"
Using molecular tools to conserve the endangered Hawaiian Hoary bat.
Role: Co-PI

USFWS 4500036150 Epstein (PI) 09/01/12-12/31/14
Characterization of Climatic Parameters within Bat Hibernacula, their Influence on Environmental Loads of *Geomyces destructans*, and Implications for the Migration of White-Nose Syndrome in Bats.
Role: Co-PI

Completed Research Support

NIH 3R01TW005869-06S1 Daszak (PI) 09/01/09 – 8/31/11
NIH Ecology of Infectious Diseases ARRA supplement to "The Ecology, Emergence and Pandemic Potential of Nipah virus in Bangladesh". Examined the ecology of Nipah virus in Bangladesh; population genetic structure of *P. giganteus*; and the pathogen discovery from a diverse range of bats. Over the course of this award I published >10 papers including 4 in the prestigious journal *Emerging Infectious Diseases*; presented at >20 national and int'l conferences; and media coverage in the *New York Times* Science section.

Role: Fogarty US Global Health Fellow; lead for ARRA reserach

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Parviez R Hosseini	POSITION TITLE Senior Research Fellow
eRA COMMONS USER NAME (b) (6)	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Brown University	Sc. B.	12/94	Applied Math – Biology
University of California, Santa Barbara	Ph.D	06/02	Biological Sciences

A. Personal Statement

The aims of the proposed research include disease ecology, evolutionary biology, and understanding the transmission dynamics of coronaviruses among wildlife hosts and their spillover to people. The latter includes analyzing patterns of viral prevalence, building and parameterizing mathematical models of pathogen transmission and evolution, and field research on these dynamics. In my career, I have used my training as theoretical ecologist and my broad experience in mathematics, statistics and ecology to focus on analyzing and explaining the process of disease emergence. I have studied disease ecology, with a strong focus on analytical and computation modeling approaches for the past 9 years. This work has involved leading the modeling component of several major research projects across a wide array of disease systems including *Mycoplasma gallisepticum* in House Finches, Barley and Cereal Yellow Dwarf viruses in California grasslands, Chikungunya virus, Rift Valley fever, and avian influenza. I am now the lead researcher on the modeling component for Influenza and Arbovirus Dynamics at EcoHealth Alliance. My strong interest in the impact of population structure on the emergence of novel pathogens, and my experience in working with computational modeling of emerging diseases give me a perfect background for the current proposed work. I also have considerable experience in working within national and international collaborative groups which will prove invaluable in the current project.

B. Positions and Honors

Positions and Employment

2002-2005 Post-doctoral Associate, Cornell University, Lab of Ornithology, Ithaca, NY

2005-2009 Associate Research Scholar, Princeton University, Dept. of Ecology and Evolutionary Biology. Princeton, NJ

2009- Senior Research Fellow, EcoHealth Alliance, NY

Professional Activities:

2003 – 2005 Participant, Seasonality and the Population Dynamics of Infectious Diseases, NCEAS, Santa Barbara, CA

2004 Invited Speaker, Ecology of Infectious Disease Meeting, Emory University, Atlanta

2004 Invited Speaker, Dept. of Zoology, Oregon State University

2006 Invited Speaker, Dept. of Biology, EEOB Seminar Series, University of North Carolina

2007 Invited Speaker, Dept. of Ecology and Evolutionary Biology, University of Tennessee

2008 Invited Speaker, Dept. of Zoology, Oxford University, UK

2008 Invited Speaker, Dept. of Biology, Stanford University, CA
2009 – present Member of modeling team, USAID-EPT PREDICT
2010 – present Review Editor, EcoHealth

Selected Honors:

2003 NSF RTG/GRT Fellowship on Spatial ecology
2004 Invited to speak at EEID in 2004 and 2011
2004 Member NCEAS group on Recovery plans and de-listing
2005 Member NCEAS group on designing ecological protected areas research
2005 Member NCEAS group on complex population dynamics
2007 *PNAS* 2007 paper cited by Faculty of 1000 Biology as "Must Read"
2007 *PNAS* paper listed as Science Editor's choice, 6th April 2007

C. Peer-reviewed publications

Most relevant to the current application

1. Hosseini, P.R. (2003). How localized consumption stabilizes predator-prey systems with finite frequency of mixing. American Naturalist 161:567-585. doi:10.1086/368293
2. Hosseini, P.R., Dobson, A. & Dhondt, A.A. (2004). Seasonality and wildlife disease: How seasonal birth, aggregation and variation in immunity affect the dynamics of Mycoplasma gallisepticum in House Finches. Proceedings of the Royal Society of London: Biological Sciences. 271:2569-2577. doi:10.1098/rspb.2004.2938
3. Hosseini, P.R. (2006) Pattern Formation and Individual-Based Models: The Importance of Understanding Individual-Based Movement. Ecological Modeling 194: 357-371. doi:10.1016/j.ecolmodel.2005.10.041
4. Seabloom, E.W., Hosseini, P.R., Power, A.G., Borer, E.T. (2009). Causes and implications of co-infection by RNA viruses in natural grasslands. American Naturalist. 173:E79-E98. doi: 10.1086/596529
5. Hosseini, P.R., Sokolow, S.H., Vandegrift, K.J., Kilpatrick, A.M. & Daszak, P. (2010). Predictive power of air travel and socio-economic data for early pandemic spread PLoS One. 5(9):e12763. doi:10.1371/journal.pone.0012763.

Additional recent publications of importance to the field

1. Campbell, S.P., Clark, A., Crampton, L., Guerry, A.D., Hatch, L.T., Hosseini, P.R., Lawler, J.J., O'Connor R.J. (2002). An assessment of monitoring efforts in endangered species recovery plans. Ecological Applications. 12:674-681. doi:10.1890/1051-0761(2002)012[0674:AAOMEI]2.0.CO;2
2. Kollias, G.V., Sydenstricker, K.V., Kollias, H.W., Ley, D.H., Hosseini, P.R., Connolly, V. & Dhondt, A.A. (2004). Experimental infection of individually caged House Finches with Mycoplasma gallisepticum. J. Wildlife Diseases. 40: 79-86.
3. Dhondt, A.A., Altizer, S., Cooch, E.G., Davis, A.K., Dobson, A., Driscoll, M.J.L., Hartup, B.K., Hawley, D. M., Hochachka, W.M., Hosseini, P.R., Jennelle, C.S., Kollias, G.V., Ley, D.H., Swarthout, E.C.H., Sydenstricker, K.V. (2005). Dynamics of a novel pathogen in an avian host: Mycoplasmal conjunctivitis in house finches. Acta Tropica 94(1):77-93. doi:10.1016/j.actatropica.2005.01.009
4. Altizer, S., Dobson, A., Hosseini, P., Hudson, P. Pascual, M., & Rohani, P. (2006). Seasonality and the dynamics of infectious diseases. Ecology Letters 9:467-484. doi:doi:10.1111/j.1461-0248.2005.00879.x
5. Hosseini, P.R., Dhondt, A.A., & Dobson, A.P. (2006). Spatial Spread of an Emerging Infectious Disease: Conjunctivitis in House Finches – Seasonal Rates and Geographic Barriers, Ecology. 87: 3037–3046. esajournals.org.
6. Borer, E., Hosseini, P.R., Seabloom, E., & Dobson, A.P. (2007). Pathogen-induced reversal of native dominance in a grassland community PNAS. 104:5473-5478 doi:10.1073/pnas.0608573104
7. Ballantyne, F.,Menge, D., Ostling, A., & Hosseini, P.R. (2008). Nutrient recycling affects autotroph and ecosystem stoichiometry, American Naturalist. 171:511-523. doi:10.1086/528967
8. Barseghian, D., Altintas, I., Jones, M. B., Crawl, D., Potter, N., Gallagher, J., Cornillon, P., Schildhauer, M., Borer, E.T., Seabloom, E.W. & Hosseini, P.R. (2009). Workflows and extensions to the Kepler scientific

workflow system to support environmental sensor data access and analysis. Ecological Informatics. 5(1):42-50 doi:10.1016/j.ecoinf.2009.08.008

9. Brandt, A.J., Seabloom, E.W., & Hosseini, P.R. (2009). Phylogeny and provenance affect plant-soil feedbacks in invaded California grasslands. Ecology 90:1063-1072.
10. Moore, S.M., Borer, E.T., Hosseini, P.R. (2010). Predators indirectly control vector-borne disease: linking predator-prey and host-pathogen models, Journal of the Royal Society Interface. 7:161-176 doi:10.1098/rsif.2009.0131

D. Research Support

Ongoing Research Support

NSF EF-1015791 Mitchell (PI) 07/01/10 – 6/30/15
National Science Foundation/National Institutes of Health: Ecology of Infectious Diseases program. The community ecology of viral pathogens – Causes and consequences of coinfection in hosts and vectors. To conduct mathematical modeling and fieldwork to understand implications in a wild grass, aphid-vectored disease system.
Role: Co-PI

NSF Daszak (PI) 06/21/10 - 06/20/15
Collaborative research: the community ecology of viral pathogens - causes and consequences of coinfection in hosts and vectors.
Role: Co-PI

GHN-A-00-09-00010-00 Morse (PI) 10/1/09-09/30/14
USAID Emerging Pandemic Threats
PREDICT - Wildlife SMART Surveillance
Modeling hotspots for disease emergence and conducting surveillance in wildlife in hotspots for new emerging zoonoses
Role: Hotspots Modeler

National Institutes Of Health Daszak (PI) 09/17/12 - 08/31/13
Fogarty International Center
Comparative Spillover Dynamics of Avian Influenza in Endemic Countries
Role: Co-PI

Completed Research Support

NIH 3R01TW005869-07S1 Daszak (PI) 07/01/10 – 06/30/11
Research: The Ecology, Emergence and Pandemic Potential of Nipah virus in Bangladesh, Supplement: Understanding and predicting the spread of H5N1 in Bangladesh, China and Globally, Modeling Research Award. To conduct model development and research to understand the role of wild and domestic poultry and livestock in creating the conditions that allow sustained spillover of human-pathogenic influenza viruses into people.
Role: Key Personnel

NIH 3R01TW005869-07S2 Daszak (PI) 07/01/10 – 06/30/11
Research: The Ecology, Emergence and Pandemic Potential of Nipah virus in Bangladesh, Supplement: Understanding and predicting the spread of H5N1 in Bangladesh, China and Globally, Field Research Award. To conduct fieldwork to understand the role of wild and domestic poultry and livestock in creating the conditions that allow sustained spillover of human-pathogenic influenza viruses into people.
Role: Key Personnel

NIH 3R01TW005869-06S4 Daszak (PI) 07/01/09 – 06/30/10
Research: The Ecology, Emergence and Pandemic Potential of Nipah virus in Bangladesh, Supplement: Understanding and predicting the spread of H5N1 in Bangladesh, China and Globally, Modeling Research

Award. To conduct model development and research to understand the role of wild and domestic poultry and livestock in creating the conditions that allow sustained spillover of human-pathogenic influenza viruses into people.
Role: Key Personnel

NIH 3R01TW005869-06S3 Daszak (PI) 07/01/09 – 06/30/10
Research: The Ecology, Emergence and Pandemic Potential of Nipah virus in Bangladesh, Supplement: Understanding and predicting the spread of H5N1 in Bangladesh, China and Globally, Field Research Award. To conduct field work to understand the role of wild and domestic poultry and livestock in creating the conditions that allow sustained spillover of human-pathogenic influenza viruses into people.
Role: Key Personnel

NSF EID 05-25666 Borer (PI) 09/01/05 – 8/31/10
Research: Predicting the effects of environmental change and host diversity on the dynamics of insect-vectored generalist pathogens.
Role: Key Personnel
The goal of this project was to assess a community-based strategy for reducing alcohol abuse among older individuals.
Role: PI

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Ge, Xing Yi	Assistant Researcher
eRA COMMONS USER NAME (credential, e.g., agency login)	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Huazhong Agricultural University, Wuhan, China		07/05	Biotechnology
Huazhong Agricultural University, Wuhan, China		07/08	Preventive Veterinary Medicine
Wuhan Institute of Virology, Chinese Academy of Sciences, Wuhan, China	Ph.D	12/11	Biochemistry and Molecular Biology

A. Personal Statement

Throughout my career, I have received extensive molecular training, including deep sequencing, and collaborated in multiple publications in the field of viral genetic diversity in bats in China. I have investigated the genetic diversity of bat adeno-associated viruses and their virus-host interactions, and isolated 22 novel ssDNA viruses from bat fecal samples using inverse PCR, which were then identified to belong in the Circoviridae family. Additionally, using metagenomic analyses, I participated in the characterization of a totivirus from bat feces in China, which showed its capacity of infecting various insect cell lines, thus having a wide geographical distribution. Our most recent work on SARS-like coronaviruses in bats has shown that there are SARS-like CoVs in bats that use the ACE2 receptor, and therefore could be directly transmissible to humans. The discovery of MERS CoV shows that there are other coronaviruses, most likely from bats, that use different receptors to infect people. For this reason, we should understand the diversity of bat coronaviruses in China and determine whether they can infect people. In the current proposal, which aims to study coronaviruses in China, I will be responsible for the diagnosis, genomics and isolation of coronaviruses and for analyzing their receptor binding domains, in order to understand their viral spillover risk and geographic distribution. We have shown that our lab at Wuhan has the ability to identify and test these viruses for receptor usage, and I am confident that this study will allow us to find many other coronaviruses in nature with zoonotic potential.

B. Positions and Honors

Positions and Employment

2005-2008 Master's Training, College of Veterinary Medicine, Huazhong Agricultural University, China
2008-2011 Doctoral Training, Wuhan Institute of Virology, Chinese Academy of Sciences, China
2010 Doctoral Training, Unit of Molecular Genetics of RNA Viruses, Department of Virology, Institute Pasteur, Paris, France
2012- Assistant Researcher, Wuhan Institute of Virology, Wuhan, China

Honors

2005 Excellent Thesis of Bachelor Degree of Hubei province
2005 Innovation Award of Huazhong Agricultural University
2007 First Prize of Excellent Graduate student
2012 CAS Presidential Scholarship (Excellence Prize)

C. Selected Peer-reviewed Publications

Most relevant to the current application

1. Li, Y., Ge X.Y., Hon C.C., Zhang, H., Zhou P., Zhang Y., Wang L.F., Shi Z. (2010). Prevalence and genetic diversity of adeno-associated viruses in bats, China. Journal of General Virology, 91(10), 2601-9.
2. Ge* X.Y., Rameix-Welti*, M.A., Gault* E., Chase, G., dos Santos Afonso, E., Picard D., Schwemmle, M., Naffakh, N. (2011). Influenza Virus Infection Induces the Nuclear Relocalization of the Hsp90 Co-Chaperone p23 and Inhibits the Glucocorticoid Receptor Response. *PLoS One*, 6(8), e23368. (*equal contribution)
3. Moisy, D., Jacob, Y., Laoide, B.M., Ge, X.Y., Baudin, F., Naffakh, N., Jestin, J.L. (2012). The HMGB1 protein binds to influenza virus nucleoprotein and promotes viral replication. Journal of Virology, 86(17), 9122-33.
4. Ge, X.Y., Li, Y., Yang X., Zhang H., Zhou P., Zhang Y., & Shi Z. (2012). Metagenomic Analysis of Viruses from the Bat Fecal Samples Reveals Many Novel Viruses in Insectivorous Bats in China. Journal of Virology, 86(8), 4620-30.
5. Wu L., Zhou, P., Ge X.Y., Wang, L.F., Baker M., Shi Z. (2013). Deep RNA sequencing reveals a complex transcriptional landscape of a bat adenovirus. Journal of Virology, 87(1), 503-11.

Additional recent publications of importance to the field (in chronological order)

1. Li, Y., Ge, X.Y., Zhang, H., Zhou, P., Zhu, Y., Zhang, Y., Yuan, J., Wang, L.F., Shi, Z. (2010). Host range, prevalence, and genetic diversity of adenoviruses in bats. Journal of Virology, 84(8), 3889-97.
2. Zhang, Y., Zhang, H., Dong, X., Yuan, J., Zhang, H., Yang, X., Zhou, P., Ge, X.Y., Li, Y., Wang, L.F., Shi, Z. (2010). Hantavirus outbreak associated with laboratory rats in Yunnan, China. Infection, Genetics and Evolution, 10(5), 638-44.
3. Ge, X.Y., Li, J., Peng, C., Wu, L., Yang, X., Wu, Y., Zhang, Y., Shi, Z. (2011). Genetic diversity of novel circular ssDNA viruses in bats in China. Journal of General Virology, 92, 2646–2653.
4. Yang, X., Zhang, Y., Ge, X.Y., Yuan, J., Shi, Z. (2012). A novel totivirus-like virus isolated from bat guano. Archives of Virology, 157(6), 1093-9.

D. Research Support

Ongoing Research Support

Completed Research Support

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Zhu, Gunagjian	Assistant Researcher
eRA COMMONS USER NAME (credential, e.g., agency login) XXXX	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
East China Normal University, Shanghai, China	B.S.	07/03	Biology Science
Hainan Normal University, Haikou, China	M.S.	07/03	Ecology
East China Normal University, Shanghai, China	Ph.D	6/12	Biochemistry and Molecular Biology

A. Personal Statement

Throughout my graduate studies and work with East China Normal University, I have carried out molecular biology and field ecology research focused on bat genetics and viral diversity. I have co-authored multiple publications in the field of viral genetics and bat ecology under the mentorship of Dr. Shuyi Zhang. I have also worked actively with EcoHealth Alliance on the USAID- EPT PREDICT program as a field team leader for China. For this program I have been responsible for the identification of high-risk interfaces between wildlife and people, where close contact might allow for zoonotic pathogen spillover (e.g. live animal markets). I have also led wildlife surveys which involved bat and rodent capture and sampling for viral discovery. Through this work we have conducted site-selection and wild and domestic animal sampling in Guangxi, Yunnan, Guangdong and Shanghai, and have compiled archived and current samples from birds in Shanghai Chongming Reserve for H7N9 avian influenza analyses. Under the USAID PREDICT program I collected several hundred bat samples which have been tested for coronaviruses (and several other viral families) at the Wuhan Institute of Virology. Under this current proposal, I would be responsible for developing and leading a wildlife team to sample bats, rodents, and other small mammals in the live animal markets of southern China. Through my graduate and professional work I have developed expertise in collecting high-quality, non-destructive samples from wildlife as well as expertise in molecular diagnostics. This combination of experiences allows me to understand the whole process of bringing samples from field to lab with an understanding of how to maximize opportunity for viral detection. I think that the aims of this proposal are important for providing the most current information about viral dynamics in live animal markets in China, particularly in rural areas where wildlife trade still occurs and where there is little data on spillover. I am very enthusiastic about participating in this study and confident that it has the right experts and study plan to succeed.

B. Positions and Honors

Positions and Employment

2007- Assistant Researcher, Guangdong Entomological Institute, China

Other Experiences and Professional Memberships

Honors

2009 Biology Prize of the 2009 Ig Nobel Prize

C. Selected Peer-reviewed Publications

Most relevant to the current application

1. Zhu, G., Han, N., Hong, T., Tan, M., Yu, D., Zhang, L. (2008). Echolocation Call, Roost and ND 1 Sequence Analysis of New Record of Nyctalus plancyi （Chiroptera： Vespertilionidae) on Hainan Island. Zoological Research, 29(4), 447-451. （in Chinese）
2. Zhu, G., Li, D., Ye, J., Hong, T., Zhang, L. (2008). New Record of Ia io in Hainan Island, its Echolocation Pulses and ND1 Analysis. Chinese Journal of Zoology, 43(5), 69-75. （in Chinese）
3. Sun, Y., Yu, D., Zhu, G., Liu, X., Zhang, S.Y., Chen, J. (2009). Isolation and characterization of 11 microsatellite loci in *Scotophilus kuhlii* (Lesser Asiatic Yellow House Bat). Conservation Genetics, 10, 1857-1859.
4. Mao, X., Zhu, G., Zhang, S.Y., Rossiter, S.J. (2010). Pleistocene climatic cycling drives intra-specific diversification in the intermediate horseshoe bat (*Rhinolophus affinis*) in Southern China. Molecular Ecology, 19(13), 2754-2769.
5. Hua, P., Zhang, L., Zhu G., Jones, G., Zhang, S., Rossiter, S.J. (2011). Hierarchical polygyny in multiparous lesser flat-headed bats. Molecular Ecology, 20(17), 3669-3680.

Additional recent publications of importance to the field (in chronological oder)

1. Zhu, G, Tang, Z., Liang, B., Zhang, X. (2007). Diet and Roost Site of Cynopterus sphinx in Winter in Haikou. Chinese Journal of Zoology, 42(4), 22-27. （in Chinese）
2. Zhang, L., Zhu, G, Jones, G., Zhang, S.Y. (2009). Conservation of bats in China: problems and recommendations. ORYX, 43(2), 179-182.
3. Tan, M., Jones, G., Zhu, G., Ye, J., Hong, T., Zhou, S., Zhang, S., Zhang, L. (2009). Fellatio by fruit bats prolongs copulation time. PLoS One, 4(10), e7595.
4. Ma, J., Jones, G., Zhu, G., Metzner, W. (2010). Echolocation behaviours of the Japanese pipistrelle bat *Pipistrellus abramus* during foraging flight. Acta Theriologica, 55(4), 315-332.
5. Zhu, G., Chmura, A., Zhang, L. (2011). Morphology, echolocation calls and diet of *Scotophilus kuhlii* (Chiroptera: Vespertilionidae) on Hainan Island, south China. Acta Chiropterologica, 14(1), 175-181.
6. (b) (4)

D. Research Support

styles 6/5/13 2:21 PM
Comment [1]: Other support?

Ongoing Research Support

GHN-A-00-09-00010-00 Morse (PI) 10/01/09-09/30/14
PREDICT-Wildlife SMART Surveillance/PREDICT Project to pre-empt at the earlier stages possible, zoonotic diseases that impose significant threat to public health.
Role: Field Team Leader

Completed Research Support

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Zhang, Yun-Zhi	Chief Physician, Professor
eRA COMMONS USER NAME (credential, e.g., agency login)	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
School of Life Sciences, Yunnan University	B.S.	1990	Endemic Diseases
Kunming Medical University	M.D.	2005	Medicine
Wuhan Institute of Virology, Chinese Academy of Sciences	PhD	2010	Virology

A. Personal Statement My career in public health is focused on virology and surveillance for zoonotic infections, including hantaviruses, henipaviruses and coronaviruses. As head of infectious disease surveillance at Yunnan CDC, I am particularly interested in the risk of new pathogens emerging through the wildlife trade, which Yunnan is on the front line of in China. Through collaborative research with Wuhan Institute of Virology (Zhengli Shi) and EcoHealth Alliance (Peter Daszak, Jon Epstein and Kevin Olival), we have conducted specific surveillance in bats, rodents and primates in Yunnan Province, and on the border with Myanmar, Laos and Vietnam. This has led to our discovery of numerous CoVs in mammals, including bats, and including the recent finding of a bat SL-CoV that uses ACE2. Given my collaboration with this group, and our capacity to do extensive surveillance of wildlife and people in Yunnan, I believe that this project will generate substantial results and help us understand the risk of CoV emergence from wildlife much better in the future.

B. Positions and Honors

Positions and Employment

2003-6	Deputy chief physician, Public Health Branch of the Chinese Medical Association Youth Committee
2006-9	Head of infectious disease surveillance, Yunnan Center for Disease Control, Peoples' Republic of China.
2009-Present	Head of Infectious disease surveillance, Yunnan Institute of Endemic Disease Control and Prevention, Peoples' Republic of China

Other Experience and Professional Memberships

2002-2004	Participant, international Field Epidemiology Training Program (FETP)

C. Selected Peer-reviewed Publications

Most relevant to the current application

1. Li, Y., Wang, J.M., Hickey, A.C., Zhang, Y.Z., Li, Y., Wu, Y., Zhang, H., Yuan, J., Han, Z.G., McEachern, J., Broder, C.C., Wang, L.F. & Shi, Z. (2008). Antibodies to Nipah or Nipah-like viruses in bats, China. Emerging Infectious Diseases,14(12):1974-1976

2. Zhang, Y.Z., Zhang, H.L., Dong, X.Q., Yuan, J.F., Zhang, H.J., Yang, X.L., Zhou, P., Ge, X.Y., Li, Y., Wang, L.F., Shi, Z.L. (2010). Hantavirus outbreak associated with laboratory rats in Yunnan, China. Infection, Genetics and Evolution, 10(5):638-644
3. Li, Y., Ge, X., Zhang, H., Zhou, P., Zhu, Y., Zhang, Y.Z., Yuan, J., Wang, L.F. & Zhengli, S. (2010). Host range, prevalence, and genetic diversity of adenoviruses in bats. Journal of Virology, 84(8):3889-3897
4. Li, Y., Ge, X., Hon, C.C., Zhang, H., Zhou, P., Zhang, Y.Z., Wu, Y., Wang, L.F. & Shi, Z. (2010). Prevalence and genetic diversity of adeno-associated viruses in bats, China. Journal of General Virology, 91(10):2601-2609
5. Zhang, Y.Z., Yuan, J., Yang, X., Zhou, J., Yang, W., Peng, C., Zhang, H.L., Shi, Z. (2011). Novel Hantavirus detected in Yunnan Red-backed Vole Eothenomys miletus, China. Journal of General Virology, 92(3):1454-1457.

Additional recent publications of importance to the field (in chronological order)

1. Yuan, J.F., Zhang, Y.J., Li, J.L., Zhang, Y.Z., Wang, L.F., Shi, Z.L. (2012). Serological evidence of ebolavirus infection in bats, China. Virology Journal, 9: 236; doi: 10.1186/1743-422X-9-236
2. Yang, X.L., Zhang, Y.Z., Ge, X.Y., Yuan, J.F., Shi, Z.L. (2012). A novel totivirus-like virus isolated from bat guano. Archives of Virology, 157 (6), 1093-1099 , doi: 10.1007/s00705-012-1278-y
3. Ge, X.Y., Li, Y., Yang, XL, Zhang, H.J., Zhou, P., Zhang, Y.Z., Shi, Z.L. (2012). Metagenomic Analysis of Viruses from Bat Fecal Samples Reveals Many Novel Viruses in Insectivorous Bats in China. Journal of Virology. 86(8). 4620-4630, doi. 10.1128/JVI.06671-11

D. Research Support

Ongoing Research Support

Ministry of Science 01/01/2013- 12/01/2017
Yunnan region is an important natural reservoir of the virus and the insect vector, pathogen survey

Grant No.: 81260437 01/01/2013 -12/01/2016
National Natural Science Foundation of China
Yunnan murine viral metagenome important viral epidemic status and related research

(b) (4) 11/01/ 2012- 11/01/2015

Grant No.: (b) (4) 09/01/2011 -12/01/2014
Yunnan Talented young technology leaders

Completed Research Support

Grant No.: 81060132 01/01/2011-12/01/2013
National Natural Science Foundation of China,
Yunnan novel hantavirus distribution, pathogenicity and receptor research

Grant number: (b) (4) 01/01/2011-12/01/2013
Yunnan applied basic research projects

OMB Number: 4040-0001
Expiration Date: 06/30/2011

* ORGANIZATIONAL DUNS: 0770900660000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: EcoHealth Alliance, Inc.

Delete Entry * Start Date: 10/01/2013 * End Date: 09/30/2014 Budget Period 1

A. Senior/Key Person

	Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary ($)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
1.	Dr.	Peter		Daszak		PD/PI		(b) (4), (b) (6)					
2.	Dr.	Jonathan	H.	Epstein		Senior/Key Personne							
3.	Dr.	Kevin	J.	Olival		Senior/Key Personne							
4.	Dr.	Parviez	R.	Hosseini		Senior/Key Personne							
5.													
6.													
7.													
8.													

9. Total Funds requested for all Senior Key Persons in the attached file

Total Senior/Key Person 99,498.00

Additional Senior Key Persons: Add Attachment Delete Attachment View Attachment

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Scientist (tbd)	(b) (4), (b) (6)					
1	Program Coordinator						
2	Total Number Other Personnel				Total Other Personnel		122,378.00

Total Salary, Wages and Fringe Benefits (A+B) 221,876.00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1

* ORGANIZATIONAL DUNS: 0770900660000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: EcoHealth Alliance, Inc.

Delete Entry * Start Date: 10/01/2013 * End Date: 09/30/2014 Budget Period 1

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

	Equipment item	* Funds Requested ($)
1.		
2.		
3.		
4.		
5.		
6.		
7.		
8.		
9.		
10.		
11.	**Total funds requested for all equipment listed in the attached file**	
	Total Equipment	

Additional Equipment: Add Attachment | Delete Attachment | View Attachment

D. Travel

		Funds Requested ($)
1.	Domestic Travel Costs (Incl. Canada, Mexico and U.S. Possessions)	3,605.00
2.	Foreign Travel Costs	32,313.00
	Total Travel Cost	35,918.00

E. Participant/Trainee Support Costs

		Funds Requested ($)
1.	Tuition/Fees/Health Insurance	
2.	Stipends	
3.	Travel	
4.	Subsistence	
5.	Other	
	Number of Participants/Trainees **Total Participant/Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION F-K, BUDGET PERIOD 1

Next Period

* ORGANIZATIONAL DUNS: 0770900660000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: EcoHealth Alliance, Inc.

Delete Entry * Start Date: 10/01/2013 * End Date: 09/30/2014 Budget Period

F. Other Direct Costs

		Funds Requested ($)
1.	Materials and Supplies	21,400.00
2.	Publication Costs	
3.	Consultant Services	
4.	ADP/Computer Services	
5.	Subawards/Consortium/Contractual Costs	227,663.00
6.	Equipment or Facility Rental/User Fees	
7.	Alterations and Renovations	
8.	Shipping & Communications	10,000.00
9.		
10.		
	Total Other Direct Costs	259,063.00

G. Direct Costs

	Funds Requested ($)
Total Direct Costs (A thru F)	516,857.00

H. Indirect Costs

	Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1.	EcoHealth Alliance F&A Rate	44.10	289,195.00	127,535.00
2.	EcoHealth Alliance F&A on 2 Subawar	44.10	50,000.00	22,050.00
3.				
4.				
	Total Indirect Costs			149,585.00

Cognizant Federal Agency

(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs

	Funds Requested ($)
Total Direct and Indirect Institutional Costs (G + H)	666,442.00

J. Fee

Funds Requested ($)

K. * Budget Justification 1239-EHA_NIAID_COV_BUDGETJUSTIFICATION Add Attachment Delete Attachment View Attachment

(Only attach one file.)

OMB Number: 4040-0001
Expiration Date: 06/30/2011

Previous Period

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

* ORGANIZATIONAL DUNS: 0770900660000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: EcoHealth Alliance, Inc.

Delete Entry * Start Date: 10/01/2014 * End Date: 09/30/2015 Budget Period 2

A. Senior/Key Person

	Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary ($)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
1.	Dr.	Peter		Daszak		PD/PI		(b) (4), (b) (6)					
2.	Dr.	Jonathan	H.	Epstein		Senior/Key Personne							
3.	Dr.	Kevin	J.	Olival		Senior/Key Personne							
4.	Dr.	Parviez	R.	Hosseini		Senior/Key Personne							
5.													
6.													
7.													
8.													
9.	Total Funds requested for all Senior Key Persons in the attached file												

Total Senior/Key Person 105,265.00

Additional Senior Key Persons: Add Attachment Delete Attachment View Attachment

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Scientist	(b) (4), (b) (6)					
1	Program Coordinator						
2	Total Number Other Personnel						

Total Other Personnel 129,468.00

Total Salary, Wages and Fringe Benefits (A+B) 234,733.00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2

* ORGANIZATIONAL DUNS: 0770900660000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: EcoHealth Alliance, Inc.

Delete Entry * Start Date: 10/01/2014 * End Date: 09/30/2015 Budget Period 2

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

	Equipment item	* Funds Requested ($)
1.		
2.		
3.		
4.		
5.		
6.		
7.		
8.		
9.		
10.		
11.	**Total funds requested for all equipment listed in the attached file**	
	Total Equipment	

Additional Equipment: Add Attachment | Delete Attachment | View Attachment

D. Travel

		Funds Requested ($)
1.	Domestic Travel Costs (Incl. Canada, Mexico and U.S. Possessions)	3,605.00
2.	Foreign Travel Costs	32,313.00
	Total Travel Cost	35,918.00

E. Participant/Trainee Support Costs

		Funds Requested ($)
1.	Tuition/Fees/Health Insurance	
2.	Stipends	
3.	Travel	
4.	Subsistence	
5.	Other	
	Number of Participants/Trainees **Total Participant/Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION F-K, BUDGET PERIOD 2

Next Period

* ORGANIZATIONAL DUNS: 0770900660000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: EcoHealth Alliance, Inc.

Delete Entry * Start Date: 10/01/2014 * End Date: 09/30/2015 Budget Period 2

F. Other Direct Costs	Funds Requested ($)
1. Materials and Supplies	19,250.00
2. Publication Costs	2,600.00
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	211,699.00
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Shipping and Communications	10,000.00
9. Local Reimbursement	950.00
10.	
Total Other Direct Costs	244,499.00

G. Direct Costs	Funds Requested ($)
Total Direct Costs (A thru F)	515,150.00

H. Indirect Costs

	Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1.	EcoHealth Alliance F&A	44.10	303,450.00	133,822.00
2.	EcoHealth Alliance F&A on 2 Subawar	44.10	50,000.00	22,050.00
3.				
4.				
	Total Indirect Costs			155,872.00

Cognizant Federal Agency

(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)
Total Direct and Indirect Institutional Costs (G + H)	671,022.00

J. Fee	Funds Requested ($)

K. * Budget Justification 1239-EHA_NIAID_COV_BUDGETJUSTIFICATION Add Attachment Delete Attachment View Attachment

(Only attach one file.)

OMB Number: 4040-0001
Expiration Date: 06/30/2011

Previous Period

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

* ORGANIZATIONAL DUNS: 0770900660000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: EcoHealth Alliance, Inc.

Delete Entry * Start Date: 10/01/2015 * End Date: 09/30/2016 Budget Period 3

A. Senior/Key Person

	Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary ($)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
1.	Dr.	Peter		Daszak		PD/PI							(b) (4), (b) (6)
2.	Dr.	Jonathan	H.	Epstein		Senior/Key Personne							
3.	Dr.	Kevin	J.	Olival		Senior/Key Personne							
4.	Dr.	Parviez	R.	Hosseini		Senior/Key Personne							
5.													
6.													
7.													
8.													
9.	Total Funds requested for all Senior Key Persons in the attached file												

Total Senior/Key Person 111,357.00

Additional Senior Key Persons: Add Attachment Delete Attachment View Attachment

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Scientist						(b) (4), (b) (6)
1	Program Coordinator						
2	Total Number Other Personnel						

Total Other Personnel 136,961.00

Total Salary, Wages and Fringe Benefits (A+B) 248,318.00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3

* ORGANIZATIONAL DUNS: 0770900660000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: EcoHealth Alliance, Inc.

Delete Entry * Start Date: 10/01/2015 * End Date: 09/30/2016 Budget Period 3

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

	Equipment item	* Funds Requested ($)
1.		
2.		
3.		
4.		
5.		
6.		
7.		
8.		
9.		
10.		
11.	**Total funds requested for all equipment listed in the attached file**	
	Total Equipment	

Additional Equipment: Add Attachment | Delete Attachment | View Attachment

D. Travel

		Funds Requested ($)
1.	Domestic Travel Costs (Incl. Canada, Mexico and U.S. Possessions)	3,605.00
2.	Foreign Travel Costs	32,313.00
	Total Travel Cost	35,918.00

E. Participant/Trainee Support Costs

		Funds Requested ($)
1.	Tuition/Fees/Health Insurance	
2.	Stipends	
3.	Travel	
4.	Subsistence	
5.	Other	
	Number of Participants/Trainees **Total Participant/Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION F-K, BUDGET PERIOD 3

Next Period

* ORGANIZATIONAL DUNS: 0770900660000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: EcoHealth Alliance, Inc.

Delete Entry * Start Date: 10/01/2015 * End Date: 09/30/2016 Budget Period 3

F. Other Direct Costs	Funds Requested ($)
1. Materials and Supplies	7,250.00
2. Publication Costs	2,600.00
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	213,238.00
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Shipping and Communications	7,500.00
9. Local Reimbursement	950.00
10.	
Total Other Direct Costs	231,538.00

G. Direct Costs	Funds Requested ($)
Total Direct Costs (A thru F)	515,774.00

H. Indirect Costs

	Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1.	EcoHealth Alliance F&A Rate	44.10	302,536.00	133,418.00
2.	EcoHealth Alliance F&A Rate on 2 Sub	44.10	50,000.00	22,050.00
3.				
4.				
	Total Indirect Costs			155,468.00

Cognizant Federal Agency

(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)
Total Direct and Indirect Institutional Costs (G + H)	671,242.00

J. Fee	Funds Requested ($)

K. * Budget Justification 1239-EHA_NIAID_COV_BUDGETJUSTIFICATION Add Attachment Delete Attachment View Attachment

(Only attach one file.)

OMB Number: 4040-0001
Expiration Date: 06/30/2011

Previous Period

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

* ORGANIZATIONAL DUNS: 0770900660000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: EcoHealth Alliance, Inc.

Delete Entry * Start Date: 10/01/2016 * End Date: 09/30/2017 Budget Period 4

A. Senior/Key Person

	Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary ($)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
1.	Dr.	Peter		Daszak		PD/PI							(b) (4), (b) (6)
2.	Dr.	Jonathan	H.	Epstein		Senior/Key Personne							
3.	Dr.	Kevin	J.	Olival		Senior/Key Personne							
4.	Dr.	Parviez	R.	Hosseini		Senior/Key Personne							
5.													
6.													
7.													
8.													
9.	Total Funds requested for all Senior Key Persons in the attached file												

Total Senior/Key Person 116,925.00

Additional Senior Key Persons: Add Attachment Delete Attachment View Attachment

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Scientist						(b) (4), (b) (6)
1	Program Coordinator						
2	Total Number Other Personnel						

Total Other Personnel 143,808.00

Total Salary, Wages and Fringe Benefits (A+B) 260,733.00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD

* ORGANIZATIONAL DUNS: 0770900660000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: EcoHealth Alliance, Inc.

Delete Entry * Start Date: 10/01/2016 * End Date: 09/30/2017 Budget Period 4

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

	Equipment item	* Funds Requested ($)
1.		
2.		
3.		
4.		
5.		
6.		
7.		
8.		
9.		
10.		
11.	Total funds requested for all equipment listed in the attached file	
	Total Equipment	

Additional Equipment: Add Attachment Delete Attachment View Attachment

D. Travel	**Funds Requested ($)**
1. Domestic Travel Costs (Incl. Canada, Mexico and U.S. Possessions)	3,605.00
2. Foreign Travel Costs	32,313.00
Total Travel Cost	35,918.00

E. Participant/Trainee Support Costs	**Funds Requested ($)**
1. Tuition/Fees/Health Insurance	
2. Stipends	
3. Travel	
4. Subsistence	
5. Other	
Number of Participants/Trainees — Total Participant/Trainee Support Costs	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION F-K, BUDGET PERIOD 4

Next Period

* ORGANIZATIONAL DUNS: 0770900660000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: EcoHealth Alliance, Inc.

Delete Entry * Start Date: 10/01/2016 * End Date: 09/30/2017 Budget Period 4

F. Other Direct Costs	Funds Requested ($)
1. Materials and Supplies	7,000.00
2. Publication Costs	2,600.00
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	201,422.00
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Shipping & Communications	6,250.00
9. Local Reimbursement	950.00
10.	
Total Other Direct Costs	218,222.00

G. Direct Costs	Funds Requested ($)
Total Direct Costs (A thru F)	514,873.00

H. Indirect Costs

	Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1.	EcoHealth Alliance F&A	44.10	313,452.00	138,232.00
2.	EcoHealth Alliance F&A on 2 Subawar	44.10	50,000.00	22,050.00
3.				
4.				
	Total Indirect Costs			160,282.00

Cognizant Federal Agency

(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)
Total Direct and Indirect Institutional Costs (G + H)	675,155.00

J. Fee	Funds Requested ($)

K. * Budget Justification 1239-EHA_NIAID_COV_BUDGETJUSTIFICATION Add Attachment Delete Attachment View Attachment

(Only attach one file.)

OMB Number: 4040-0001
Expiration Date: 06/30/2011

Previous Period

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5

* ORGANIZATIONAL DUNS: 0770900660000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: EcoHealth Alliance, Inc.

Delete Entry * Start Date: 10/01/2017 * End Date: 09/30/2018 Budget Period 5

A. Senior/Key Person

	Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary ($)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
1.	Dr.	Peter		Daszak		PD/PI		(b) (4), (b) (6)					
2.		Jonathan	H.	Epstein		Senior/Key Personne							
3.		Kevin	J.	Olival		Senior/Key Personne							
4.		Parviez	R.	Hosseini		Senior/Key Personne							
5.													
6.													
7.													
8.													

9. Total Funds requested for all Senior Key Persons in the attached file

Total Senior/Key Person 122,772.00

Additional Senior Key Persons: Add Attachment Delete Attachment View Attachment

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Scientist	(b) (4), (b) (6)					
1	Program Coordinator						
2	Total Number Other Personnel						

Total Other Personnel 150,999.00

Total Salary, Wages and Fringe Benefits (A+B) 273,771.00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5

* ORGANIZATIONAL DUNS: 0770900660000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: EcoHealth Alliance, Inc.

Delete Entry * Start Date: 10/01/2017 * End Date: 09/30/2018 Budget Period 5

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

	Equipment item	* Funds Requested ($)
1.		
2.		
3.		
4.		
5.		
6.		
7.		
8.		
9.		
10.		
11.	**Total funds requested for all equipment listed in the attached file**	
	Total Equipment	

Additional Equipment: Add Attachment | Delete Attachment | View Attachment

D. Travel

		Funds Requested ($)
1.	Domestic Travel Costs (Incl. Canada, Mexico and U.S. Possessions)	3,605.00
2.	Foreign Travel Costs	32,313.00
	Total Travel Cost	35,918.00

E. Participant/Trainee Support Costs

		Funds Requested ($)
1.	Tuition/Fees/Health Insurance	
2.	Stipends	
3.	Travel	
4.	Subsistence	
5.	Other	
	Number of Participants/Trainees **Total Participant/Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION F-K, BUDGET PERIOD 5

* ORGANIZATIONAL DUNS: 0770900660000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: EcoHealth Alliance, Inc.

Delete Entry * Start Date: 10/01/2017 * End Date: 09/30/2018 Budget Period 5

F. Other Direct Costs	Funds Requested ($)
1. Materials and Supplies	3,500.00
2. Publication Costs	2,600.00
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	191,576.00
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Shipping & Communications	6,250.00
9. Local Reimbursement	550.00
10.	
Total Other Direct Costs	204,476.00

G. Direct Costs	Funds Requested ($)
Total Direct Costs (A thru F)	514,165.00

H. Indirect Costs

	Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1.	EcoHealth Alliance F&A	44.10	322,588.00	142,262.00
2.	EcoHealth Alliance F&A on 2 Subawar	44.10	50,000.00	22,050.00
3.				
4.				
	Total Indirect Costs			164,312.00

Cognizant Federal Agency

(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)
Total Direct and Indirect Institutional Costs (G + H)	678,477.00

J. Fee	Funds Requested ($)

K. * Budget Justification 1239-EHA_NIAID_COV_BUDGETJUSTIFICATION Add Attachment Delete Attachment View Attachment

(Only attach one file.)

ECOHEALTH ALLIANCE BUDGET JUSTIFICATION

A. Key personnel:

The PD/PI, Dr. Peter Daszak, will commit (b) (4), (b) (6) per year in each year of this budget. He will be primarily responsible for overseeing the project, general management, communication and collaboration with subawardees, as well as contributing to data analysis and manuscript writing.

Senior/Key Personnel, Dr. Epstein, will commit (b) (4), (b) (6) per year. Dr. Epstein will lead the design and implementation of the bat epidemiology fieldwork; supervise field teams, lab data analyses as well as conduct field training. He will participate in regular conference calls, help with data analysis, and draft manuscripts.

Senior/Key Personnel, Dr. Olival, will commit (b) (4), (b) (6) per year. Dr. Olival will direct the bat population genetics work, assist with data analyses, and manuscript writing. He will also advise on the modeling and provide training for field teams.

Senior/Key Personnel, Dr. Hosseini, will commit (b) (4), (b) (6) per year. Dr. Hosseini will perform spatial analyses and data mapping in collaboration with of Dr. Epstein and Dr. Olival.

B. Other personnel:

A research scientist will be hired at 12 months time per year to provide direct assistance and oversight of field activities in China; maintain equipment and logistics; and coordinate animal and human sample shipment to the labs in China and in the US. This person will be based at EcoHealth Alliance, but will spend significant time in the field.

Mr. Aleksei Chmura (b) (4), (b) (6) per year) in Y1-Y5 will fulfill program assistance duties as well as conduct field research in China. Mr Chmura will coordinate regular calls, reports, maintain EcoHealth Alliance budget and financial reporting, draft subcontracts, and set-up project database advise field activities and assist with statistical analysis.

Once we secure IRBs for human sampling in Y1, we will hire three medical officers from China provincial CDCs as consultants to work in Guangxi, Hunan, and Fujian during Y2-Y5. These medical officers will be responsible for all IRB approved human sampling as well as maintaining cold chain for storage and shipping of samples.

For all EcoHealth Alliance personnel that will have salary covered by this grant, we have included the EcoHealth Alliance 5% per annum increase in salary.

C. Fringe benefits.

Fringe benefits are calculated for EcoHealth Alliance's federally approved rate of 30% of base salary.

D. Consultant: Once all permits are in place in Y2-5, EcoHealth Alliance will contract three technician-consultants trained in phlebotomy – one in each province: Guangxi, Hunan, and Fujian. The technicians will conduct interviews as part of the human wildlife contact survey as well as collect blood samples from volunteers in animal markets. These will be given daily rate of $67 for 5 months work per year (3 technicians x 5

months x 20 days per month x $67 = $20,000 per year) as well as funds to cover shipping and maintaining cold-chain ($333 x 3 months x 3 provinces = $3,000 per year) from provincial areas to Wuhan Institute of Virology. We also will support the technician's allowable room/transportation/food costs expected to average monthly at food ($62), room ($100), and transportation ($100): $262 x 3 technicians x 5 months = $3,923 per year.

E. Equipment: N/A

F. Supplies: For Y1-Y5, we request annual support for tubes, syringes (5k); computer, phone, GPS (8k); lab reagents and buffer (10k); shipping (10k); PPE (10k); bat catching equipment (10k); food/accomodation for field team (10k); dry shippers, liquid Nitrogen (8k)

G. Travel
Domestic travel: $4,400 is requested for years 1-5, comprising $2,200 each for the PI (Dr. Daszak) and Senior/Key Personnel (Dr. Epstein) for travel to collaborating labs, to group meetings, and domestic scientific conferences to present results of our work.

International travel: $33,000 is requested p.a. in Years 1-5. This will support 4 RT flights p.a. from New York to Shanghai or Guangzhou for the field veterinarian; 3 for the Senior/Key Personnel and 1 for the PI (Daszak) @ $2500 ea; Food and accommodation at $8,500 p.a. for Senior/Key Personnel and the field team in China including field activities. Field vehicle rental & driver hire $500/wk x 9 wks.

H. Participant support costs: We are requesting consortium/contractual support for our two partners: East China Normal University and Wuhan Institute of Virology. We are requesting $34,560 per year for Y1-Y5 for East China Normal University and for Wuhan Institute of Virology $93,960 in Y1 and $81,000 in Y2-Y5. These amounts are justified as follows:

EAST CHINA NORMAL UNIVERSITY

EcoHealth Alliance Budget Justification, H. Participant Support Costs (ctd)

a) Senior Personnel: Dr. Shuyi Zhang (b) (4), (b) (6) per year in Y1-Y5 Dr. Zhang will oversee the field sample collection and coordination of sample transfer to Wuhan or US partners. He will not request any salary from this grant. His salary will be covered by his instiutional discretionary funds.

b) Other personnel: A full time field biologist, Dr. GuanJian Zhu (b) (4), (b) (6) per year), will implement field site visits, sample collection, and sample shipment to Wuhan or to Co-PIs. A full time field technician, Mr. Junpeng Zhang (b) (4), (b) (6) per year), will assist with sample collection, handling, and transport from field to lab as well as with sample shipping from East China Normal University to Wuhan or US partners. Both Mr. Zhang and Dr. Zhu will work full-time for in Y1-Y5.

c) Fringe Benefits: Fringe benefits are provided at ECNU rate of 5% to Dr. Zhu and Mr. Zhang in Y1-Y5.

d) Equipment: N/A

e) Supplies: $560 are allocated per year in Y1-Y5 to support Field Biologist and Field Technician costs for telephone internet, and GPS: Phone = 15x2= 30; Internet = 5x2 = 10, GPS (batteries) = 3.5x2 = 10; total per month = $47.

f) Travel: Dr. Zhang will provide travel costs for Field Biologist and Field Technician from discretionary funding. We request $2,000 per year to support Dr. Zhang and Dr. Zhu to travel to US for Co-Investigator meetings in either Boston or New York. Support will provide room and board for the two at per diem rate of $250 for 4 days (= 250x4x2 = $2,000). Dr. Zhang is already supported for travel funds of his own in those years.

g) Participant support costs: N/A

h) Other direct costs: N/A

i) Indirect Costs. All administrative costs are charged directly.

WUHAN INSTITUTE OF VIROLOGY

a) Key personnel. Dr. Zhengli Shi, Senior Virologist. (b) (4), (b) per year in Y1-Y5. Dr. Shi will oversee the coronavirus screening for all samples collected in China. She will work with the PI, Co-Investigators, and Senior/Key Personnel to analyze data and write manuscripts. She will also coordinate data and material sharing with the co-Investigators. Dr. Shi will not take salary on this grant and is funded by discretionary sources at her Institute.

b) Other personnel:
Mr. Jialu Li, Lab technician. (b) (4), (b) (6) p.a. in Y1-Y5. The lab technician will test all bat and other animal samples collected in China for coronaviruses and will conduct molecular characterization and phylogenetic analyses of new coronavirus strains identified as well as catalog and ship samples and maintain a sample database.

EcoHealth Alliance Budget Justification, H. Participant Support Costs (ctd)

c) Fringe benefits: Wuhan Institute of Virology benefit rate of 5% is applied to salary for Mr. Jialu Li in Y1-Y5.

d) Equipment: The subcontractor will purchase one ultracold -80˚C freezer for dedicated sample storage for this project. $12,960.

e) Supplies: Annual costs for Laboratory reagents (20k); shipping to US (twice per year x 2.5k = 5k); testing costs (30k); expendable equipment costs (5k) are requested in Y1-Y5.

f) Travel: Round-trip airfare to Boston/NYC for Co-Investigator (Dr. Shi) for attending PD/PI meetings once-per year in Y1-Y5: $2,600. Dr. Shi has discretionary funds to supplement travel expenditures. We also request $2,400 to cover in-country transportation costs of supplies and samples.

g) Participant support costs: N/A

h) Other direct costs: We request annual support costs for Telephone ($180), Printing ($144), Conference Calls ($504), and local shipping charges ($172) for Dr. Shi's laboratory and Mr. Li in Y1-Y5.

i) Indirect Costs. All administrative costs are charged directly.

H. Other direct costs: We request $71,000 in year one for sample collection materials including bat catching equipment, syringes, tubes, and reagents, and 2 liquid nitrogen dry shippers at $3,000each. We also request $10,000 for shipping supplies from NY to China in yr 1, then $5,000 p.a. for shipping in years 2-5. We also request $4,000 in years 3 and 4 for lab reagents to complete population genetics tests.

Other expenses for publishing and communications including video conferencing facilities will be covered by EcoHealth Alliance.

I. Indirect Costs

We are requesting the EcoHealth Alliance federally-approved indirect cost rate of 30.0% on all applicable direct costs. Indirect is taken only on the first $25,000 for each consortium/contractual agreement. As there are 2 (one to Wuhan Insititute of Virology and the other to East China Normal University), a total of $15,000 ($7,500x2) is taken as indirect on consortium/contractual agreements only in Y1 and included as part of direct cost calculations. In Y2-Y5 no indirect is taken on consortium/contractual agreements.

RESEARCH & RELATED BUDGET - Cumulative Budget

		Totals ($)
Section A, Senior/Key Person		555,817.00
Section B, Other Personnel		683,614.00
Total Number Other Personnel	10	
Total Salary, Wages and Fringe Benefits (A+B)		1,239,431.00
Section C, Equipment		
Section D, Travel		179,590.00
1. Domestic	18,025.00	
2. Foreign	161,565.00	
Section E, Participant/Trainee Support Costs		
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other		
6. Number of Participants/Trainees		
Section F, Other Direct Costs		1,157,798.00
1. Materials and Supplies	58,400.00	
2. Publication Costs	10,400.00	
3. Consultant Services		
4. ADP/Computer Services		
5. Subawards/Consortium/Contractual Costs	1,045,598.00	
6. Equipment or Facility Rental/User Fees		
7. Alterations and Renovations		
8. Other 1	40,000.00	
9. Other 2	3,400.00	
10. Other 3		
Section G, Direct Costs (A thru F)		2,576,819.00
Section H, Indirect Costs		785,519.00
Section I, Total Direct and Indirect Costs (G + H)		3,362,338.00
Section J, Fee		

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1

*** ORGANIZATIONAL DUNS:** 5290274740000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: Wuhan Institute of Virology

*** Start Date:** 10-01-2013 *** End Date:** 09-30-2014 **Budget Period: 1**

A. Senior/Key Person

	Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary ($)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
1.	Dr.	Zhengli		Shi		Co-Investigator							(b) (4), (b) (6)
2.	Dr.	Xingyi		Ge		Senior Research Technician							

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name: Mime Type: **Total Senior/Key Person** (b) (4), (b)

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits	* Funds Requested ($)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Laboratory Technician100						(b) (4), (b) (6)
1	**Total Number Other Personnel**					**Total Other Personnel**	(b) (4), (b) (6)

Total Salary, Wages and Fringe Benefits (A+B)

RESEARCH & RELATED Budget (A-B) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1

*** ORGANIZATIONAL DUNS:** 5290274740000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: Wuhan Institute of Virology

*** Start Date:** 10-01-2013 *** End Date:** 09-30-2014 **Budget Period: 1**

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	* Funds Requested ($)
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name: Mime Type:

D. Travel	Funds Requested ($)
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,060.00
2. Foreign Travel Costs	
Total Travel Cost	**2,060.00**

E. Participant/Trainee Support Costs	Funds Requested ($)
1. Tuition/Fees/Health Insurance	
2. Stipends	
3. Travel	
4. Subsistence	
5. Other:	
Number of Participants/Trainees	**Total Participant/Trainee Support Costs**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1

*** ORGANIZATIONAL DUNS:** 5290274740000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: Wuhan Institute of Virology

*** Start Date:** 10-01-2013 *** End Date:** 09-30-2014 **Budget Period: 1**

F. Other Direct Costs	Funds Requested ($)
1. Materials and Supplies	95,737.00
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	**95,737.00**

G. Direct Costs	Funds Requested ($)
Total Direct Costs (A thru F)	**123,699.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1. Wuhan Institute of Virology F&A	8.00	123,699.00	9,896.00
		Total Indirect Costs	**9,896.00**

Cognizant Federal Agency

(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)
Total Direct and Indirect Institutional Costs (G + H)	**133,595.00**

J. Fee	Funds Requested ($)

K. * Budget Justification	File Name: 1242-WIV NIAID COV BUDGET JUSTIFICATION.pdf (Only attach one file.)	Mime Type: application/pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

*** ORGANIZATIONAL DUNS:** 5290274740000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: Wuhan Institute of Virology

*** Start Date:** 10-01-2014 *** End Date:** 09-30-2015 **Budget Period: 2**

A. Senior/Key Person

	Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary ($)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
1.	Dr.	Zhengli		Shi		Co-Investigator							(b) (4), (b) (6)
2.	Dr.	Xingyi		Ge		Senior Research Technician							

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name: Mime Type: **Total Senior/Key Person** (b) (4), (b)

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits	* Funds Requested ($)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Laboratory Technician						(b) (4), (b) (6)
1	**Total Number Other Personnel**					**Total Other Personnel**	(b) (4), (b) (6)
						Total Salary, Wages and Fringe Benefits (A+B)	

RESEARCH & RELATED Budget (A-B) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2

*** ORGANIZATIONAL DUNS:** 5290274740000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: Wuhan Institute of Virology

*** Start Date:** 10-01-2014 *** End Date:** 09-30-2015 **Budget Period: 2**

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	* Funds Requested ($)
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name: Mime Type:

D. Travel	Funds Requested ($)
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,060.00
2. Foreign Travel Costs	
Total Travel Cost	**2,060.00**

E. Participant/Trainee Support Costs	Funds Requested ($)
1. Tuition/Fees/Health Insurance	
2. Stipends	
3. Travel	
4. Subsistence	
5. Other:	

Number of Participants/Trainees **Total Participant/Trainee Support Costs**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2

*** ORGANIZATIONAL DUNS:** 5290274740000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: Wuhan Institute of Virology

*** Start Date:** 10-01-2014 *** End Date:** 09-30-2015 **Budget Period: 2**

F. Other Direct Costs	Funds Requested ($)
1. Materials and Supplies	100,756.00
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	**100,756.00**

G. Direct Costs	Funds Requested ($)
Total Direct Costs (A thru F)	**128,718.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1. Wuhan Institute of Virology F&A Rate	8.00	128,718.00	10,297.00
		Total Indirect Costs	**10,297.00**

Cognizant Federal Agency

(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)
Total Direct and Indirect Institutional Costs (G + H)	**139,015.00**

J. Fee	Funds Requested ($)

K. * Budget Justification	File Name: 1242-WIV NIAID COV BUDGET JUSTIFICATION.pdf (Only attach one file.)	Mime Type: application/pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

*** ORGANIZATIONAL DUNS:** 5290274740000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: Wuhan Institute of Virology

*** Start Date:** 10-01-2015 *** End Date:** 09-30-2016 **Budget Period: 3**

A. Senior/Key Person

	Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary ($)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
1.	Dr.	Zhengli		Shi		Co-Investigator							(b) (4), (b) (6)
2.	Dr.	Xingyi		Ge		Senior Research Technnician							

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name: Mime Type: **Total Senior/Key Person** (b) (4), (b)

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits	* Funds Requested ($)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Laboratory Technician						(b) (4), (b) (6)
1	**Total Number Other Personnel**					**Total Other Personnel**	(b) (4), (b) (6)

Total Salary, Wages and Fringe Benefits (A+B)

RESEARCH & RELATED Budget (A-B) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3

*** ORGANIZATIONAL DUNS:** 5290274740000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: Wuhan Institute of Virology

*** Start Date:** 10-01-2015 *** End Date:** 09-30-2016 **Budget Period: 3**

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	* Funds Requested ($)
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name: Mime Type:

D. Travel	Funds Requested ($)
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,060.00
2. Foreign Travel Costs	
Total Travel Cost	**2,060.00**

E. Participant/Trainee Support Costs	Funds Requested ($)
1. Tuition/Fees/Health Insurance	
2. Stipends	
3. Travel	
4. Subsistence	
5. Other:	

Number of Participants/Trainees **Total Participant/Trainee Support Costs**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3

*** ORGANIZATIONAL DUNS:** 5290274740000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: Wuhan Institute of Virology

*** Start Date:** 10-01-2015 *** End Date:** 09-30-2016 **Budget Period: 3**

F. Other Direct Costs	Funds Requested ($)
1. Materials and Supplies	119,373.00
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	**119,373.00**

G. Direct Costs	Funds Requested ($)
Total Direct Costs (A thru F)	**147,335.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1. Wuhan institute of Virology F&A Rate	8.00	147,335.00	11,787.00
		Total Indirect Costs	**11,787.00**

Cognizant Federal Agency

(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)
Total Direct and Indirect Institutional Costs (G + H)	**159,122.00**

J. Fee	Funds Requested ($)

K. * Budget Justification	File Name: 1242-WIV NIAID COV BUDGET JUSTIFICATION.pdf (Only attach one file.)	Mime Type: application/pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

*** ORGANIZATIONAL DUNS:** 5290274740000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: Wuhan Institute of Virology

*** Start Date:** 10-01-2016 *** End Date:** 09-30-2017 **Budget Period: 4**

A. Senior/Key Person

	Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary ($)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
1.	Dr.	Zhengli		Shi		Co-Investigator							(b) (4), (b) (6)
2.	Dr.	Xingyi		Ge		Senior Research Technician							

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name: Mime Type: **Total Senior/Key Person** (b) (4), (b) (6)

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits	* Funds Requested ($)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Laboratory Technician						(b) (4), (b) (6)
1	**Total Number Other Personnel**					**Total Other Personnel**	(b) (4), (b) (6)

Total Salary, Wages and Fringe Benefits (A+B)

RESEARCH & RELATED Budget (A-B) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4

*** ORGANIZATIONAL DUNS:** 5290274740000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: Wuhan Institute of Virology

*** Start Date:** 10-01-2016 *** End Date:** 09-30-2017 **Budget Period: 4**

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	* Funds Requested ($)
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name: Mime Type:

D. Travel	Funds Requested ($)
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,060.00
2. Foreign Travel Costs	
Total Travel Cost	**2,060.00**

E. Participant/Trainee Support Costs	Funds Requested ($)
1. Tuition/Fees/Health Insurance	
2. Stipends	
3. Travel	
4. Subsistence	
5. Other:	

Number of Participants/Trainees **Total Participant/Trainee Support Costs**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4

*** ORGANIZATIONAL DUNS:** 5290274740000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: Wuhan Institute of Virology

*** Start Date:** 10-01-2016 *** End Date:** 09-30-2017 **Budget Period: 4**

F. Other Direct Costs	Funds Requested ($)
1. Materials and Supplies	119,373.00
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	**119,373.00**

G. Direct Costs	Funds Requested ($)
Total Direct Costs (A thru F)	**147,335.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1. Wuhan Institute of Virology F&A Rate	8.00	147,335.00	11,787.00
		Total Indirect Costs	**11,787.00**

Cognizant Federal Agency

(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)
Total Direct and Indirect Institutional Costs (G + H)	**159,122.00**

J. Fee	Funds Requested ($)

K. * Budget Justification	File Name: 1242-WIV NIAID COV BUDGET JUSTIFICATION.pdf (Only attach one file.)	Mime Type: application/pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5

*** ORGANIZATIONAL DUNS:** 5290274740000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: Wuhan Institute of Virology

*** Start Date:** 10-01-2017 *** End Date:** 09-30-2018 **Budget Period: 5**

A. Senior/Key Person

	Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary ($)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
1.	Dr.	Zhengli		Shi		Co-Investigator							(b) (4), (b) (6)
2.	Dr.	Xingyi		Ge		Senior Research Technician							

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name: Mime Type: **Total Senior/Key Person** (b) (4), (b) (6)

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits	* Funds Requested ($)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Laboratory Technician						(b) (4), (b) (6)
1	**Total Number Other Personnel**					**Total Other Personnel**	(b) (4), (b) (6)
						Total Salary, Wages and Fringe Benefits (A+B)	

RESEARCH & RELATED Budget (A-B) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5

*** ORGANIZATIONAL DUNS:** 5290274740000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: Wuhan Institute of Virology

*** Start Date:** 10-01-2017 *** End Date:** 09-30-2018 **Budget Period: 5**

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	* Funds Requested ($)
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name: Mime Type:

D. Travel	Funds Requested ($)
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,060.00
2. Foreign Travel Costs	
Total Travel Cost	**2,060.00**

E. Participant/Trainee Support Costs	Funds Requested ($)
1. Tuition/Fees/Health Insurance	
2. Stipends	
3. Travel	
4. Subsistence	
5. Other:	
Number of Participants/Trainees	**Total Participant/Trainee Support Costs**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5

*** ORGANIZATIONAL DUNS:** 5290274740000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: Wuhan Institute of Virology

*** Start Date:** 10-01-2017 *** End Date:** 09-30-2018 **Budget Period: 5**

F. Other Direct Costs	Funds Requested ($)
1. Materials and Supplies	119,373.00
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	**119,373.00**

G. Direct Costs	Funds Requested ($)
Total Direct Costs (A thru F)	**147,335.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1. Wuhan Institute of Virology F&A Rate	8.00	147,355.00	11,787.00
		Total Indirect Costs	**11,787.00**

Cognizant Federal Agency

(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)
Total Direct and Indirect Institutional Costs (G + H)	**159,122.00**

J. Fee	Funds Requested ($)

K. * Budget Justification	File Name: 1242-WIV NIAID COV BUDGET JUSTIFICATION.pdf (Only attach one file.)	Mime Type: application/pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals ($)	
Section A, Senior/Key Person		**79,325.00**
Section B, Other Personnel		**50,185.00**
Total Number Other Personnel	5	
Total Salary, Wages and Fringe Benefits (A+B)		**129,510.00**
Section C, Equipment		
Section D, Travel		**10,300.00**
1. Domestic	10,300.00	
2. Foreign		
Section E, Participant/Trainee Support Costs		
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other		
6. Number of Participants/Trainees		
Section F, Other Direct Costs		**554,612.00**
1. Materials and Supplies	554,612.00	
2. Publication Costs		
3. Consultant Services		
4. ADP/Computer Services		
5. Subawards/Consortium/Contractual Costs		
6. Equipment or Facility Rental/User Fees		
7. Alterations and Renovations		
8. Other 1		
9. Other 2		
10. Other 3		
Section G, Direct Costs (A thru F)		**694,422.00**
Section H, Indirect Costs		**55,554.00**
Section I, Total Direct and Indirect Costs (G + H)		**749,976.00**
Section J, Fee		

WUHAN INSTITUTE OF VIROLOGY BUDGET JUSTIFICATION, SUBAWARD

A. Senior/Key Personnel:

Co-Investigator, Dr. Zhengli Shi, a Senior Research Scientist at the Chinese Academy of Science's Wuhan Institute of Virology will commit (b) (4), (b) (6) per year (b) (4), (b) (6) to this project to refine study protocols, coordinate research, oversee implementation of all activities, analyze data, lead regular meetings with other PD/PI and Other Senior/Key Personnel as well as draft papers. Dr. Xingyi Ge, Senior Research Technician, will commit (b) (4), (b) (6) per year to perform all laboratory work and directly supervise the laboratory technician.

B. Other Personnel

One laboratory technician will commit (b) (4), (b) (6) per year (b) (4), (b) (6) each to this project to perform all required laboratory assays and maintenance as well as participate in selected meetings, perform research for papers, and assist Dr. Shi in performing the work under this award.

All Wuhan Institute of Virology salaries include the US "overhead" or "fringe", so this is not calculated separately.

C. Equipment

No equipment over $5,000 will be purchased.

D. Travel

We are requesting $2,060 per year for all years for Senior/Key Personnel Dr. Shi and Dr. Ge to travel to Shanghai to visit partner laboratory at East China Normal Univeristy (ECNU) and meet with the PD/PI as well as with collaborators on this proposal: these include EcoHealth Alliance, East China Normal University, Yunnan CDC, Shanghai CDC, and Guangdong CDC. Travel is calculated at one round trip airfare from Wuhan to Shanghai ($300), three-night hotel in Shanghai ($150 per night), and four days per diem (at $70 per day)

F. Other Direct Costs

We are requesting support for laboratory experiments and related costs.

RNA Extractions

We will be running RNA Extractions for 1,000 bats per year (three samples per bat: oral, anal, and blood) in each year of the project. This will cost $13,922 per year (QIAamp ViralRNA Mini Kit with Axygen Pipette Tips and Filter Tubes at $4.64 per sample). Extracted RNA per animal will be pooled.

RT-PCR

Costs for 1-Step RT-PCR assays for Coronavirus conducted on 1,000 samples per year for each year of the project total $7,123 and are detailed as follows: Superscript III one step kit ($5.18 per sample); Platinum Tag DNA Polymerase ($0.57 per sample); nuclease-free water ($0.16 per sample); and Axygen Pipette Tips and Filter Tubes ($1.21 per sample).

DNA Sequencing

In each year of the project, DNA Sequencing will be performed on 3,200 samples at a cost of $2.91 per reaction. We request a total of $9,325 per year in each year.

Laboratory Supplies
We request support for *in vitro* infection experiments using pseudoviruses carrying the spike proteins (wild type or mutants) or live viruses in cell lines of different origins, binding affinity assays between the spike proteins (wild type or mutants) and different cellular receptor molecules, and humanized mouse experiments.

In Year 1, $65,367 is requested: Lipofectamine2000 transfection reagent at a cost of $2,428; cell lines from bats and other mammals including primates and humans at a cost of $971; *in vitro* infection experiments require GIBCO Fetal Bovine Serum ($3,562), GIBCO antibiotic antimycotic ($563), GIBCO medium ($2,914) as well as $19,426 for Corning Cell culture; receptor-mutant pseudovirus binding assays require Luciferase assay system E1500 ($858), pseudovirus package ($3,885), and sequencing ($22,664); $8,094 is required for protein expression from the binding affinity assays.

In Year 2, $70,385 is requested: Lipofectamine2000 transfection reagent at a cost of $2,428; cell lines from bats and other mammals including primates and humans at a cost of $971 – sufficient cell lines will be established by the end of Year 2, so this cost requirement will discontinue in Years 3-5; increased number of *in vitro* infection experiments require slightly more funding for GIBCO Fetal Bovine Serum ($4,047) as well as GIBCO antibiotic antimycotic ($563), GIBCO medium ($2,914) as well as $19,426 for Corning Cell culture; receptor-mutant pseudovirus binding assays require Luciferase assay system E1500 ($858), pseudovirus package requirements will approximately double from Y1 ($6,799), and sequencing ($22,664); $9,713 is required for protein expression from the increased Year 2 number of binding affinity assays at a slightly higher cost than year one as well.

In Years 3, 4 and 5, $89,002 is requested per year: Lipofectamine2000 transfection reagent at a cost of $2,428 per year; increased number of *in vitro* infection experiments require slightly more funding for GIBCO Fetal Bovine Serum ($5,828 per year) as well as GIBCO antibiotic antimycotic ($563 per year), GIBCO medium ($2,914 per year) as well as $19,426 per year for Corning Cell culture; receptor-mutant pseudovirus binding assays require Luciferase assay system E1500 ($858 per year), pseudovirus package requirements will be $6,799 per year, sequencing ($22,664 per year) and gene synthesis ($12,915 per year) will also be required; $9,713 per year is required for protein expression from binding affinity assays; in only years 3, 4, and 5 humanized mouse *in vivo* experimental animals will be raised at an annual cost of $4,857 per year.

H. Indirect Costs

We are requesting an extremely indirect cost of 8% on all direct costs.

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1

*** ORGANIZATIONAL DUNS:** 4209454950000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: East China Normal University

*** Start Date:** 10-01-2013 *** End Date:** 09-30-2014 **Budget Period: 1**

A. Senior/Key Person

	Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary ($)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
1.	Dr.	Shuyi		Zhang		Co-Investigator							(b) (4), (b) (6)
2.	Dr.	Guangjian		Zhu		Research Technician							

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name: Mime Type: **Total Senior/Key Person** (b) (4), (b) (6)

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits	* Funds Requested ($)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	**Total Number Other Personnel**					**Total Other Personnel**	
						Total Salary, Wages and Fringe Benefits (A+B)	25,000.00

RESEARCH & RELATED Budget (A-B) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1

*** ORGANIZATIONAL DUNS:** 4209454950000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: East China Normal University

*** Start Date:** 10-01-2013 *** End Date:** 09-30-2014 **Budget Period: 1**

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	* Funds Requested ($)
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name: Mime Type:

D. Travel	Funds Requested ($)
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,700.00
2. Foreign Travel Costs	
Total Travel Cost	**2,700.00**

E. Participant/Trainee Support Costs	Funds Requested ($)
1. Tuition/Fees/Health Insurance	
2. Stipends	
3. Travel	
4. Subsistence	
5. Other:	

Number of Participants/Trainees **Total Participant/Trainee Support Costs**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1

*** ORGANIZATIONAL DUNS:** 4209454950000

*** Budget Type:** ○ Project ● Subaward/Consortium

Enter name of Organization: East China Normal University

*** Start Date:** 10-01-2013 *** End Date:** 09-30-2014 **Budget Period: 1**

F. Other Direct Costs	Funds Requested ($)
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Fieldwork Support Costs	59,400.00
Total Other Direct Costs	**59,400.00**

G. Direct Costs	Funds Requested ($)
Total Direct Costs (A thru F)	**87,100.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1. East China Normal University F&A Rate	8.00	87,100.00	6,968.00
		Total Indirect Costs	**6,968.00**

Cognizant Federal Agency

(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)
Total Direct and Indirect Institutional Costs (G + H)	**94,068.00**

J. Fee	Funds Requested ($)

K. * Budget Justification	File Name: 1243-ECNU NIAID COV BUDGET JUSTIFICATION.pdf (Only attach one file.)	Mime Type: application/pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

*** ORGANIZATIONAL DUNS:** 4209454950000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: East China Normal University

*** Start Date:** 10-01-2014 *** End Date:** 09-30-2015 **Budget Period: 2**

A. Senior/Key Person

	Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary ($)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
1.	Dr.	Shuyi		Zhang		Co-Investigator							(b) (4), (b) (6)
2.	Dr.	Guangjian		Zhu		Research Technician							

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name: Mime Type: **Total Senior/Key Person** (b) (4), (b) (6)

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits	* Funds Requested ($)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	**Total Number Other Personnel**					**Total Other Personnel**	

Total Salary, Wages and Fringe Benefits (A+B) (b) (4), (b) (6)

RESEARCH & RELATED Budget (A-B) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2

*** ORGANIZATIONAL DUNS:** 4209454950000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: East China Normal University

*** Start Date:** 10-01-2014 *** End Date:** 09-30-2015 **Budget Period: 2**

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	* Funds Requested ($)
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name: Mime Type:

D. Travel	Funds Requested ($)
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,700.00
2. Foreign Travel Costs	
Total Travel Cost	**2,700.00**

E. Participant/Trainee Support Costs	Funds Requested ($)
1. Tuition/Fees/Health Insurance	
2. Stipends	
3. Travel	
4. Subsistence	
5. Other:	
Number of Participants/Trainees	**Total Participant/Trainee Support Costs**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2

*** ORGANIZATIONAL DUNS:** 4209454950000

*** Budget Type:** ○ Project ● Subaward/Consortium

Enter name of Organization: East China Normal University

*** Start Date:** 10-01-2014 *** End Date:** 09-30-2015 **Budget Period: 2**

F. Other Direct Costs	Funds Requested ($)
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Field Work Support Costs	39,600.00
Total Other Direct Costs	**39,600.00**

G. Direct Costs	Funds Requested ($)
Total Direct Costs (A thru F)	**67,300.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1. East China Normal University F&A Rate	8.00	67,300.00	5,384.00
		Total Indirect Costs	**5,384.00**

Cognizant Federal Agency

(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)
Total Direct and Indirect Institutional Costs (G + H)	**72,684.00**

J. Fee	Funds Requested ($)

K. * Budget Justification	File Name: 1243-ECNU NIAID COV BUDGET JUSTIFICATION.pdf (Only attach one file.)	Mime Type: application/pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

*** ORGANIZATIONAL DUNS:** 4209454950000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: East China Normal University

*** Start Date:** 10-01-2015 *** End Date:** 09-30-2016 **Budget Period: 3**

A. Senior/Key Person

	Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary ($)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
1.	Dr.	Shuyi		Zhang		Co-Investigator							(b) (4), (b) (6)
2.	Dr.	Guangjian		Zhu		Research Technician							

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name: Mime Type: **Total Senior/Key Person** (b) (4), (b) (6)

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits	* Funds Requested ($)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	**Total Number Other Personnel**					**Total Other Personnel**	

Total Salary, Wages and Fringe Benefits (A+B) (b) (4), (b) (6)

RESEARCH & RELATED Budget (A-B) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3

*** ORGANIZATIONAL DUNS:** 4209454950000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: East China Normal University

*** Start Date:** 10-01-2015 *** End Date:** 09-30-2016 **Budget Period: 3**

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	* Funds Requested ($)
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name: Mime Type:

D. Travel	Funds Requested ($)
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,700.00
2. Foreign Travel Costs	
Total Travel Cost	**2,700.00**

E. Participant/Trainee Support Costs	Funds Requested ($)
1. Tuition/Fees/Health Insurance	
2. Stipends	
3. Travel	
4. Subsistence	
5. Other:	

Number of Participants/Trainees **Total Participant/Trainee Support Costs**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3

*** ORGANIZATIONAL DUNS:** 4209454950000

*** Budget Type:** ○ Project ● Subaward/Consortium

Enter name of Organization: East China Normal University

*** Start Date:** 10-01-2015 *** End Date:** 09-30-2016 **Budget Period: 3**

F. Other Direct Costs	Funds Requested ($)
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Field Work Support Costs	29,700.00
Total Other Direct Costs	**29,700.00**

G. Direct Costs	Funds Requested ($)
Total Direct Costs (A thru F)	**50,108.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1. East China Normal University F&A Rate	8.00	50,108.00	4,009.00
		Total Indirect Costs	**4,009.00**

Cognizant Federal Agency

(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)
Total Direct and Indirect Institutional Costs (G + H)	**54,117.00**

J. Fee	Funds Requested ($)

K. * Budget Justification	File Name: 1243-ECNU NIAID COV BUDGET JUSTIFICATION.pdf (Only attach one file.)	Mime Type: application/pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

*** ORGANIZATIONAL DUNS:** 4209454950000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: East China Normal University

*** Start Date:** 10-01-2016 *** End Date:** 09-30-2017 **Budget Period: 4**

A. Senior/Key Person

	Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary ($)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
1.	Dr.	Shuyi		Zhang		Co-Investigator							(b) (4), (b) (6)
2.	Dr.	Guangjian		Zhu		Research Technician							

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name: Mime Type: **Total Senior/Key Person** (b) (4), (b) (6)

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits	* Funds Requested ($)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	**Total Number Other Personnel**					**Total Other Personnel**	

Total Salary, Wages and Fringe Benefits (A+B) (b) (4), (b) (6)

RESEARCH & RELATED Budget (A-B) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4

*** ORGANIZATIONAL DUNS:** 4209454950000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: East China Normal University

*** Start Date:** 10-01-2016 *** End Date:** 09-30-2017 **Budget Period: 4**

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	* Funds Requested ($)
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name: Mime Type:

D. Travel	Funds Requested ($)
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,700.00
2. Foreign Travel Costs	
Total Travel Cost	**2,700.00**

E. Participant/Trainee Support Costs	Funds Requested ($)
1. Tuition/Fees/Health Insurance	
2. Stipends	
3. Travel	
4. Subsistence	
5. Other:	

Number of Participants/Trainees **Total Participant/Trainee Support Costs**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4

*** ORGANIZATIONAL DUNS:** 4209454950000

*** Budget Type:** ○ Project ● Subaward/Consortium

Enter name of Organization: East China Normal University

*** Start Date:** 10-01-2016 *** End Date:** 09-30-2017 **Budget Period: 4**

F. Other Direct Costs	Funds Requested ($)
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Field Work Support Costs	19,800.00
Total Other Direct Costs	**19,800.00**

G. Direct Costs	Funds Requested ($)
Total Direct Costs (A thru F)	**39,167.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1. East China Normal University F&A Rate	8.00	39,167.00	3,133.00
		Total Indirect Costs	**3,133.00**

Cognizant Federal Agency

(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)
Total Direct and Indirect Institutional Costs (G + H)	**42,300.00**

J. Fee	Funds Requested ($)

K. * Budget Justification	File Name: 1243-ECNU NIAID COV BUDGET JUSTIFICATION.pdf (Only attach one file.)	Mime Type: application/pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5

*** ORGANIZATIONAL DUNS:** 4209454950000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: East China Normal University

*** Start Date:** 10-01-2017 *** End Date:** 09-30-2018 **Budget Period: 5**

A. Senior/Key Person

	Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary ($)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
1.	Dr.	Shuyi		Zhang		Co-Investigator							(b) (4), (b) (6)
2.	Dr.	Guangjian		Zhu		Reasearch Technician							

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name: Mime Type: **Total Senior/Key Person** (b) (4), (b) (6)

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits	* Funds Requested ($)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	**Total Number Other Personnel**					**Total Other Personnel**	

Total Salary, Wages and Fringe Benefits (A+B) (b) (4), (b) (6)

RESEARCH & RELATED Budget (A-B) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5

*** ORGANIZATIONAL DUNS:** 4209454950000

*** Budget Type:** ❍ Project ● Subaward/Consortium

Enter name of Organization: East China Normal University

*** Start Date:** 10-01-2017 *** End Date:** 09-30-2018 **Budget Period: 5**

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	* Funds Requested ($)
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name: Mime Type:

D. Travel	Funds Requested ($)
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,700.00
2. Foreign Travel Costs	
Total Travel Cost	**2,700.00**

E. Participant/Trainee Support Costs	Funds Requested ($)
1. Tuition/Fees/Health Insurance	
2. Stipends	
3. Travel	
4. Subsistence	
5. Other:	
Number of Participants/Trainees	**Total Participant/Trainee Support Costs**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5

*** ORGANIZATIONAL DUNS:** 4209454950000

*** Budget Type:** ○ Project ● Subaward/Consortium

Enter name of Organization: East China Normal University

*** Start Date:** 10-01-2017 *** End Date:** 09-30-2018 **Budget Period: 5**

F. Other Direct Costs	Funds Requested ($)
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Field Work Support Costs	14,850.00
Total Other Direct Costs	**14,850.00**

G. Direct Costs	Funds Requested ($)
Total Direct Costs (A thru F)	**30,050.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1. East China Normal University F&A Rate	8.00	30,050.00	2,404.00
		Total Indirect Costs	**2,404.00**

Cognizant Federal Agency

(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)
Total Direct and Indirect Institutional Costs (G + H)	**32,454.00**

J. Fee	Funds Requested ($)

K. * Budget Justification	File Name: 1243-ECNU NIAID COV BUDGET JUSTIFICATION.pdf (Only attach one file.)	Mime Type: application/pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals ($)	
Section A, Senior/Key Person		**96,875.00**
Section B, Other Personnel		
Total Number Other Personnel		
Total Salary, Wages and Fringe Benefits (A+B)		**96,875.00**
Section C, Equipment		
Section D, Travel		**13,500.00**
1. Domestic	13,500.00	
2. Foreign		
Section E, Participant/Trainee Support Costs		
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other		
6. Number of Participants/Trainees		
Section F, Other Direct Costs		**163,350.00**
1. Materials and Supplies		
2. Publication Costs		
3. Consultant Services		
4. ADP/Computer Services		
5. Subawards/Consortium/Contractual Costs		
6. Equipment or Facility Rental/User Fees		
7. Alterations and Renovations		
8. Other 1	163,350.00	
9. Other 2		
10. Other 3		
Section G, Direct Costs (A thru F)		**273,725.00**
Section H, Indirect Costs		**21,898.00**
Section I, Total Direct and Indirect Costs (G + H)		**295,623.00**
Section J, Fee		

EAST CHINA NORMAL UNIVERSITY BUDGET JUSTIFICATION, SUBAWARD

A. Senior/Key Personnel:

Co-Investigator Dr. Shu-Yi Zhang will commit (b) (4), (b) (6) per year to this project to refine field work design, coordinate research, oversee implementation of all activities, analyze data, lead regular meetings with other PD/PI and Other Senior/Key Personnel as well as draft papers. To keep costs low, Dr. Zhang will not take any salary. Research Technician, Dr. Zhu Guangjian, will commit (b) (4), (b) (6) in Years 1 and 2; 34 weeks or (b) (4), (b) (6) in Year 3; (b) (4), (b) (6) in Year 4 and only (b) (4), (b) (6) in Year 5 to directly coordinate field work, liaise with local CDCs, ensure shipment of samples to Wuhan Institute of Virology, and participate in some meetings as well as assist with drafting papers.

B. Other Personnel

There are no additional personnel.

All East China Normal University salaries include the US "overhead" or "fringe", so this is not calculated separately.

C. Equipment

No equipment over $5,000 will be purchased.

D. Travel

We are requesting $2,700 per year for all five years of this award to cover 3-per-year round-trip flights each from Shanghai, China, to Yunnan, Guangdong, and Guangxi for Dr. Zhu Guangjian to meet with collaborating institutions, train field teams, and ensure sample collection, storage, and shipments. Each flight is estimated at $300.

F. Other Direct Costs

Fieldwork Support Costs

In year 1, we are requesting $59,400 to support 12-months of fieldwork costs. This we estimate as follows: $7,200 for driver ($600 per month) and car rental ($600 per month); $2,700 for gas ($450 per month); $10,800 to support a field team of three ($600 per month); and $9,000 for meals and lodging at a rate of $50 per day ($1,500 per month).

In year 2, we are requesting $39,600 to support 8-months of fieldwork costs. This we estimate as follows: $7,200 for driver ($600 per month) and car rental ($600 per month); $2,700 for gas ($450 per month); $10,800 to support a field team of three ($600 per month); and $9,000 for meals and lodging at a rate of $50 per day ($1,500 per month).

In year 3, we are requesting $29,700 to support 24-weeks or 6-months of fieldwork costs. This we estimate as follows: $7,200 for driver ($600 per month) and car rental ($600 per month); $2,700 for gas ($450 per month); $10,800 to support a field team of three ($600 per month); and $9,000 for meals and lodging at a rate of $50 per day ($1,500 per month).

In year 4, we are requesting $19,800 to support 16-weeks or 4-months of fieldwork costs. This we estimate as follows: $7,200 for driver ($600 per month) and car rental ($600 per month); $2,700 for gas ($450 per month); $10,800 to support a field team of three ($600 per month); and $9,000 for meals and lodging at a rate of $50 per day ($1,500 per month).

In year 5, we are requesting $14,850 to support 12-weeks or 3-months of fieldwork costs. This we estimate as follows: $7,200 for driver ($600 per month) and car rental ($600 per month); $2,700 for gas ($450 per month); $10,800 to support a field team of three ($600 per month); and $9,000 for meals and lodging at a rate of $50 per day ($1,500 per month).

H. Indirect Costs

We are requesting an extremely indirect cost of 8% on all direct costs.

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:	Dr.
* First Name:	Peter
Middle Name:	
* Last Name:	Daszak
Suffix:	

2. Human Subjects

Clinical Trial? ☒ No ☐ Yes

* Agency-Defined Phase III Clinical Trial? ☐ No ☐ Yes

3. Applicant Organization Contact

Person to be contacted on matters involving this application

Prefix:	Dr.
* First Name:	Peter
Middle Name:	
* Last Name:	Daszak
Suffix:	
* Phone Number:	(b) (6)
Fax Number:	+1.212.380.4465
Email:	(b) (6)
* Title:	President
* Street1:	460 West 34th Street
Street2:	17th Floor
* City:	New York
County/Parish:	
* State:	NY: New York
Province:	
* Country:	USA: UNITED STATES
* Zip / Postal Code:	10001-2317

PHS 398 Cover Page Supplement

4. Human Embryonic Stem Cells

* Does the proposed project involve human embryonic stem cells? ☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://stemcells.nih.gov/research/registry/. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

OMB Number: 0925-0001

PHS 398 Research Plan

1. Application Type:

From SF 424 (R&R) Cover Page. The response provided on that page, regarding the type of application being submitted, is repeated for your reference, as you attach the appropriate sections of the Research Plan.

*Type of Application:

☒ New ☐ Resubmission ☐ Renewal ☐ Continuation ☐ Revision

2. Research Plan Attachments:

Please attach applicable sections of the research plan, below.

1. Introduction to Application (for RESUBMISSION or REVISION only)		Add Attachment	Delete Attachment	View Attachment
2. Specific Aims	1240-NIH_COv_Specific_Aims.p	Add Attachment	Delete Attachment	View Attachment
3. *Research Strategy	1241-Understanding_the_risk_	Add Attachment	Delete Attachment	View Attachment
4. Inclusion Enrollment Report		Add Attachment	Delete Attachment	View Attachment
5. Progress Report Publication List		Add Attachment	Delete Attachment	View Attachment

Human Subjects Sections

6. Protection of Human Subjects	1254-NIH_COv_Protection_Hum	Add Attachment	Delete Attachment	View Attachment
7. Inclusion of Women and Minorities	1255-NIH_COv_Inclusion_of_W	Add Attachment	Delete Attachment	View Attachment
8. Targeted/Planned Enrollment Table	1256-China_CoV_Planned_enro	Add Attachment	Delete Attachment	View Attachment
9. Inclusion of Children	1257-NIH_COv_Inclusion_of_Ch	Add Attachment	Delete Attachment	View Attachment

Other Research Plan Sections

10. Vertebrate Animals	1258-NIH_COv_Vertebrate_Anim	Add Attachment	Delete Attachment	View Attachment
11. Select Agent Research	1259-NIH_COv_Select_Agent_R	Add Attachment	Delete Attachment	View Attachment
12. Multiple PD/PI Leadership Plan		Add Attachment	Delete Attachment	View Attachment
13. Consortium/Contractual Arrangements	1260-NIH_COv_Consortium_Cont	Add Attachment	Delete Attachment	View Attachment
14. Letters of Support	1261-NIAID_COV_2013_AllSuppo	Add Attachment	Delete Attachment	View Attachment
15. Resource Sharing Plan(s)	1262-NIH_COv_Resource_Sharin	Add Attachment	Delete Attachment	View Attachment

16. Appendix Add Attachments | Remove Attachments | View Attachments

SPECIFIC AIMS:

Zoonotic coronaviruses are a significant threat to global health, as demonstrated with the emergence of severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002, and the recent emergence Middle East Respiratory Syndrome (MERS-CoV). The wildlife reservoirs of SARS-CoV were identified by our group as bat species, and since then hundreds of novel bat-CoVs have been discovered (including >260 by our group). These, and other wildlife species, are hunted, traded, butchered and consumed across Asia, creating a largescale human-wildlife interface, and high risk of future emergence of novel CoVs.

To understand the risk of zoonotic CoV emergence, we propose to examine **1)** the transmission dynamics of bat-CoVs across the human-wildlife interface, and **2)** how this process is affected by CoV evolutionary potential, and how it might force CoV evolution. We will assess the nature and frequency of contact among animals and people in two critical human-animal interfaces: live animal markets in China and people who are highly exposed to bats in rural China. In the markets we hypothesize that viral emergence may be accelerated by heightened mixing of host species leading to viral evolution, and high potential for contact with humans. In this study, we propose three specific aims and will screen free ranging and captive bats in China for known and novel coronaviruses; screen people who have high occupational exposure to bats and other wildlife; and examine the genetics and receptor binding properties of novel bat-CoVs we have already identified and those we will discover. We will then use ecological and evolutionary analyses and predictive mathematical models to examine the risk of future bat-CoV spillover to humans. This work will follow 3 specific aims:

Specific Aim 1: Assessment of CoV spillover potential at high risk human-wildlife interfaces. We will examine if: **1)** wildlife markets in China provide enhanced capacity for bat-CoVs to infect other hosts, either via evolutionary adaptation or recombination; **2)** the import of animals from throughout Southeast Asia introduces a higher genetic diversity of mammalian CoVs in market systems compared to within intact ecosystems of China and Southeast Asia; **We will interview people about the nature and frequency of contact with bats** and other wildlife**; collect blood samples from people highly exposed to wildlife;** and **collect a full range of clinical samples from bats and other mammals in the wild and in wetmarkets;** and screen these for CoVs using serological and molecular assays.

Specific Aim 2: Receptor evolution, host range and predictive modeling of bat-CoV emergence risk. We propose two competing hypotheses: **1)** CoV host-range in bats and other mammals is limited by the phylogenetic relatedness of bats and evolutionary conservation of CoV receptors; **2)** CoV host-range is limited by geographic and ecological opportunity for contact between species so that the wildlife trade disrupts the 'natural' co-phylogeny, facilitates spillover and promotes viral evolution. We will develop CoV phylogenies from sequence data collected previously by our group, and in the proposed study, as well as from Genbank. We will examine co-evolutionary congruence of bat-CoVs and their hosts using both functional (receptor) and neutral genes. We will predict host-range in unsampled species using a generalizable model of host and viral ecological and phylogenetic traits to explain patterns of viral sharing between species. We will test for positive selection in market vs. wild-sampled viruses, and use data to parameterize mathematical models that predict CoV evolutionary and transmission dynamics. We will then examine scenarios of how CoVs with different transmissibility would likely emerge in wildlife markets.

Specific Aim 3: Testing predictions of CoV inter-species transmission. We will test our models of host range (i.e. emergence potential) experimentally using reverse genetics, pseudovirus and receptor binding assays, and virus infection experiments in cell culture and humanized mice. With bat-CoVs that we've isolated or sequenced, and using live virus or pseudovirus infection in cells of different origin or expressing different receptor molecules, we will assess potential for each isolated virus and those with receptor binding site sequence, to spill over. We will do this by sequencing the spike (or other receptor binding/fusion) protein genes from all our bat-CoVs, creating mutants to identify how significantly each would need to evolve to use ACE2, CD26/DPP4 (MERS-CoV receptor) or other potential CoV receptors. We will then use receptor-mutant pseudovirus binding assays, *in vitro* studies in bat, primate, human and other species' cell lines, and with humanized mice where particularly interesting viruses are identified phylogenetically, or isolated. These tests will provide public health-relevant data, and also iteratively improve our predictive model to better target bat species and CoVs during our field studies to obtain bat-CoV strains of the greatest interest for understanding the mechanisms of cross-species transmission.

RESEARCH STRATEGY

A. SIGNIFICANCE:

General: Severe Acute Respiratory Syndrome, like many other emerging human pathogens (*1*), originated in a wildlife reservoir host, initially thought to be terrestrial mammals (*2*), and later shown by our group to be bats (*3*). Bats harbor the most closely-related viruses to SARS-CoV, and are traded widely for food in the wildlife markets of China (*4*). The diversity of bat-CoVs is very high, and some studies even suggest that the *Coronaviridae* originated within bats (*3, 5-9*). Recently a novel CoV emerged in the Middle East (MERS-CoV) (*10*) and available data (including from our group) suggest that MERS-CoV also has bat origins (*11-13*). Given that hunting and eating of bats continues across Asia, future spillover of bat-CoVs is likely. Yet *salient questions remain: How diverse are bat-CoVs? Can the conditions in these markets enhance bat-CoV evolution and spillover of bat-CoVs?* **The proposed work** addresses these issues and examines viral diversity in a critical zoonotic reservoir (bats), at sites of high risk for emergence (wildlife markets) in an EID hotspot (China) (*14*).

SARS and bat-CoVs: Coronaviruses are found in a wide range of animal species (*15*). Before the SARS epidemic, only two human coronaviruses (HCoVs) had been characterized (HCoV-229E and HCoV-OC43) (*16, 17*). Since then three more human coronaviruses (HCoV-NL63, HCoV HKU-1, and MERS-CoV), in addition to SARS-CoV, have been identified in individuals with respiratory infections (*16, 18, 19*). One of these, HCoV-NL63, is thought to be zoonotic and of bat origin (*6*). Our group recently identified a CoV from bats in Bangladesh closely-related and likely ancestral to HCoV-OC43 (*20*) and is currently characterizing CoVs from bats in Saudi Arabia. The animal origins of SARS-CoV were first suspected due to the association among index cases and the trade in wildlife for food (*21*). Initially, civets and other mammals consumed in restaurants in southern China were implicated (*2*), however these species did not exhibit the high seroprevalence and low viral (PCR) prevalence expected from a natural wildlife reservoir of a zoonotic virus (*21*). **In 2004, our group discovered SARS-like (SL) CoVs in free-living wild bat species in China and demonstrated that human SARS-CoV nestled phylogenetically within this group (*4*)**. However, SARS-CoV uses the angiotensin-converting enzyme 2 (ACE2) receptor to gain entry to human cells (*22*), and bat SL-CoVs appeared unable to bind to ACE2. A large number of novel *Alpha-* and *Betacoronaviruses* have since been discovered in Old and New World bats, but few have been isolated (*8, 11-13, 23-27*). In 2012, we isolated and characterized two bat SL-CoVs from *Rhinolophus sinicus* from Yunnan Province, China that use the ACE2 receptor and are closely related to SARS-CoV (**Fig. 1**) (*28*). We found a seasonal shedding pattern for this SL-CoV, with peak prevalence of 30-50%. Bats from this population are hunted for human consumption, posing two crucial questions: **1) What is the risk of these CoVs emerging in humans? 2) Will the conditions that exist in live animal markets in Asia promote further emergence of bat-CoVs in human populations?**

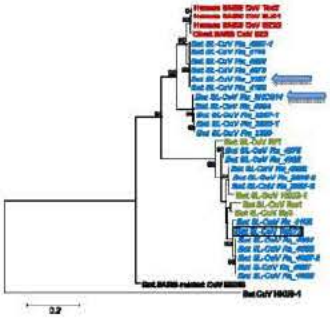


Figure 1. Phylogenetic tree of receptor binding domain sequences of SARS-CoVs (Red), bat SARS-like CoVs discovered by our group in the last 2 years (Blue), and bat SL-CoVs that we published previously in our paper proposing a bat-origin for SARS in 2005 (Green) (*3*). In 2012, we isolated two novel SL-CoVs (SL-CoV-SHC014 and 3367, blue arrows) and have shown for the first time that a bat SL-CoV use the ACE2 receptor which SARS-CoV uses to infect human cells. Unpublished data from Ge *et al.* (in review) (*28*).

Evolution, host-virus co-phylogeny and risk of CoV emergence: There is wide variation in the propensity of viruses for cross-species transmission, within and among viral genera and families (*29*). Coronaviruses undergo genetic recombination by a genomic template-switching mechanism and generate point mutations at a rate similar to that of other RNA viruses, perhaps explaining their capacity for host switching and zoonotic transmission (*15, 30*). This capacity is heightened by the ecology of host species, opportunity for contact, characteristics of the pathogen, and evolutionary (phylogenetic) relationships between hosts (*31-33*). Bats (Order Chiroptera) are the second most diverse group of mammals (~1,200 species) with a wide range ecological and life-history traits that affect their ability to share viruses (*34, 35*) and may explain variation in viral diversity (*36, 37*). Phylogenetic relationships may determine limits to viral binding at receptor sites and to cross-species transmission (*31, 33*), and these factors could be used to predict the risk of spillover (see **Specific Aim 2**). Apart from our own work (see **Section C2b, Fig. 7**), bat and CoV co-evolutionary patterns haven't been rigorously examined. Recent work suggests that most bat-CoV clades correspond to specific bat species or genera (*38, 39*), with little evidence of bat-CoV spillover among species roosting together in the same cave (*40*). There is also evidence for geographically distributed, but related, bat taxa sharing related CoV strains (*8, 38*). In contrast, other studies of wild-caught bats did not find strict co-evolutionary congruence in bat-CoVs for host

species, genera or families (*41-43*). Thus, the same CoV strains may circulate in different bat genera (*41*), and multiple diverse CoV lineages can be found in the same bat species and even individuals (*7, 40, 44, 45*). This, and density of some bat species populations, suggests that viral recombination may be possible in these hosts (*6*). Forced contact in wildlife markets could also facilitate recombination, and may explain divergent Gammacoronavirus strains ancestral to those in birds, in two mammals species in Southern Chinese wetmarkets (*46*). **In this proposal**, we will look for generalizable patterns among bat species and the CoV genotypes they harbor, and use this to examine how phylogeny and contact affect CoV spillover risk.

Host-CoV interactions: an evolutionary approach: The interaction between CoV receptor binding domains (RBDs) and host receptors, e.g. ACE2 for SARS-CoV; dipeptidyl peptidase 4 (DPP4) for MERS-CoV; carcinoembryonic antigen-related cell adhesion molecules (CEACAM) for mouse hepatitis virus; and aminopeptidase N (APN) for hCoV-229E, is critical to understanding limits to host species range (*47-52*). Bats have highly diverse ACE2 receptors at a nucleotide and especially protein level (**Fig. 2**). This is in contrast to other viral receptors in bats, e.g. Ephrin-B2 receptors for henipaviruses (*53, 54*), and DPP4 for MERS-CoV appear to be highly conserved (*51*). Several different genera of bats (e.g. *Myotis*, *Rhinolophus*, and *Rousettus*) have receptors that support viral mediated entry by the SARS-CoV Spike protein (*52, 55*).

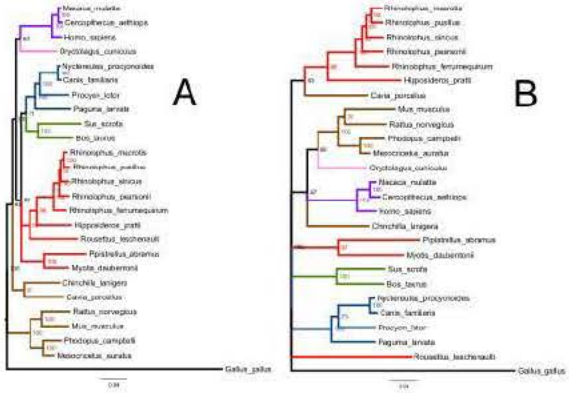


Figure 2. Mammal ACE2 phylogeny using: A) nucleotide data (~2400bp) of ACE2 gene; B) translated protein sequences of same ACE2 genes. All mammal species with available data, including primates (purple), lagomorphs (pink); carnivores (blue); ungulates (green), rodents (brown), and bats (red). Bats are monophyletic and species group with expected taxonomic relationships using nucleotide sequence data (A); but they are paraphyletic a when analyzing protein-level differences (B). This shows functional ACE2 diversity may differ from nucleotide data, and a need to better characterize receptor diversity in a wider range of hosts.

While our preliminary results suggest interesting patterns in bats (**Fig. 2**), the limited number of bat ACE2 sequences precludes robust comparison of co-phylogenetic patterns. **In this study**, we propose to sample dozens of species more than 5 bat families in China, and compare sequence with bats we've sampled globally. This will allow us to build a testable, phylogenetically informed models to examine the extent of, and limits to, batCoV host-range; and will allow us to analyze other receptors like DPP4 for MERS-CoV.

Modeling risk of human infection: The use of mathematical, computational models of viral dynamics has become a standard tool to understand risk of pathogen emergence and spread (*56-60*). However, models that characterize the risk of wildlife-to-human infection require data on contact among populations (*61*), evolutionary constraints of pathogens (*29, 62*), and diversity of novel pathogens (*63*). Because these datasets are usually unavailable, mathematical models can often be theoretical, and of reduced value in predicting risk of pathogen spillover and spread. Building on our group's experience in modeling disease emergence (*64-67*), we will develop a mathematical model that explicitly describes the transmission dynamics and evolutionary dynamics of CoVs in wildlife markets and in bat caves. These models will be parameterized with data we have already collected, and new data from this study, to predict whether novel CoV strains we discover are likely to emerge.

Tests of host range *in vitro*: Receptor usage in different animals is a primary determinant of viral host range. However, while the receptor and receptor binding domains (RBDs) of human-infecting CoVs have been studied intensively, bat-CoVs have not (*22, 47*). In this study, we will determine the RBD of bat-CoVs, develop pseudovirus assays (*68*), and work with a humanized mouse model expressing ACE2 receptor. This provides a way to experimentally test hypotheses on the host-range of novel coronaviruses, even from sequence data. However, despite a plethora of novel CoVs in the recent literature (*38, 39, 44, 45*), there has been little work towards this goal. Furthermore, the recent discovery of MERS-CoV, which uses DPP4, and the use of other receptors for other CoVs (*69*) suggest that this work will be highly significant for other CoVs.

B. INNOVATION:

This project is an innovative fusion of virology, ecology, and mathematical modeling. The analysis of CoV genetic diversity in bats and other mammals in southern China, combined with characterization of and co-phylogenetic analysis with CoV functional genes (e. g. ACE2, receptor of SARS-CoV and DPP4 for MERS-CoV) has not yet been attempted, and **will allow us to better understand the patterns of host-switching**. Previous studies using molecular clock analysis have found that the bat SARS-like-CoV to civet/human SARS-CoV divergence

ranged from 7-17 years (mean 4.9) before the 2003 outbreak (*7, 70*). We will use a novel **phylogenetic and mathematical modeling approach to examine how dynamics of contact and pathogen transmission among hosts in markets drives viral evolution and emergence**. We will determine **how many years it takes for a coronavirus to evolve an R_0 >1 and therefore have epidemic potential** using a modeling framework that combines evolutionary changes and multi-host dynamics (Specific Aim 3), expanding on published approaches (*71-73*). We will then **simulate coronavirus emergence under different market conditions to identify most likely scenarios that can inform strategies to prevent future outbreaks.** Finally, we will use pseudovirus binding assays, *in vitro* infections and humanized mice expressing ACE2 to test our analyses on the novel viruses we have, and will, identify.

We will use our multidisciplinary approach to examine fundamental questions on how the wildlife trade, wetmarkets and other target interfaces promote the emergence of coronaviruses, and **assess the risk of future spillover of CoVs from bats or other mammals and humans**. In particular, despite 10 years since the emergence of SARS and the discovery of 60+ novel bat-CoVs, three significant issues remain unanswered: **1) What are the natural limits to CoV host range, and can this be predicted by the host-receptor-virus relationship; 2)** Are the conditions in wildlife markets sufficient to allow enough interspecies transmission that coronaviruses **can evolve the ability to infect new hosts, including humans**, either by accumulation of point mutations, or by recombination events; or **3)** Is the expansion of the wildlife trade **bringing expanded diversity of CoVs into the enhanced human-animal interface present in wet markets**?

C. APPROACH

C1: Specific Aim 1. Assessment of CoV spillover potential at high risk human-wildlife interfaces:

C1a) General strategy and supporting studies: SARS-CoV emerged in live animal markets in Guangdong, with unrelated spillover events in at least five of seven municipalities, suggesting widespread introduction into wildlife markets within this city (*21*). We propose to characterize the species composition of bats and small mammals in wildlife markets where there is a high degree of contact between animals and people. We will identify additional high risk interfaces that may occur in southern China such as guano collection, which we have recently identified as a potential CoV exposure risk in Thailand (*12*). We will interview people at high-risk interfaces and who are enrolled in acute respiratory or influenza-like illness surveillance programs conducted by our colleagues at CDCs in Shanghai, Guangdong, Yunnan, and Guangxi. These data will be used to parameterize the contact process (χ) in our mathematical model of CoV emergence (**see Aim 3**).

We will assess **1)** whether market conditions provide enhanced capacity (increased **evolutionary opportunity**) for bat-CoVs to evolve the ability to infect other hosts, either via repeated inter-species transmission, positive selection or recombination events; and **2)** whether the intake of wildlife from Southeast Asia by China introduces a greater diversity of hosts and a correspondingly diverse group of CoVs (increased **ecological opportunity**). We will conduct CoV pathogen discovery in samples from humans and wildlife at these sites and examine their receptor binding domains to identify their ability to bind to ACE2, DPP4, or CEACAM receptors in humans. We will compare CoV diversity in China with that in wildlife across Southeast Asia (from our current work on other funded programs, and published data) that may potentially enter China's wildlife trade. Data from this aim will be used to assess the likelihood of inter-species bat-CoV transmission (see also **Specific Aim 2**).

Working in high-contact human-wildlife interfaces can be challenging. However, we have already collected significant preliminary data to accomplish Aim 1. We have located and surveyed wildlife markets in Yunnan, Guangdong, GuangXi and Fujian provinces, and have identified populations that hunt and consume bats in Yunnan province. We have begun to characterize the species composition of free-ranging bat populations and have collected samples **from over 1000 bat individuals (28 spp.) from 35 localities in over 15 (two-thirds of all) Chinese Provinces**. We will also utilize archived wild bat, rodent, and civet samples collected by our team in Malaysia, Thailand and Indonesia on another large federally-funded project to provide samples of species regularly imported into China (**section C1b**) (*21, 74*).

Wildlife Markets: Ten years following the SARS-CoV outbreaks, there is little information available on the *current* diversity of bats and other mammals available in the wet markets in southern China. One study found that 91 species of vertebrates, including 40 mammal species, were being traded in Guangxi, China (*75*). Further, little data is available on the origin of wild animals brought into the market system. In some cases, animals may be locally collected, while in other cases animals may be imported from Southeast Asia, including adjacent Vietnam (*74-76*) – factors which will affect the diversity of CoVs. Captive and free-ranging rodents are found in markets and may be an additional host for CoVs (*77*). We have worked with Yunnan Institute of Endemic Diseases Control and Prevention since June 2012 (see **Letters of Support**). We have conducted initial surveillance in Nujiang, Baoshan Denong and Xishuangbanna prefectures and Ruili, which is a major wildlife trade gateway between Myanmar and China **(Fig. 3)**. We have collected 187 small mammals from markets in Yunnan and tested them for coronaviruses using a 1-step PCR assay (*78*), finding 2/21 shrews (*Crocidura attentuata*) are CoV-positive.

Figure 3: Map of wildlife trade routes from Southeast Asia into China. Modified from (*79*).

Other animal samples available for this project: To date, our group has collected more than 90,000 high quality specimens from 15,000 animals representing key wildlife reservoirs for zoonoses such as bats, rodents and primates under our USAID-EPT PREDICT project. Clinical samples include blood, throat swabs, feces and urogenital swabs and represent animals from 10 different countries including Bangladesh, India, Malaysia, Thailand, Indonesia, China, Brazil, Bolivia, Colombia, Peru, and Mexico. 50,000 of these samples originate from Asia, and are currently being screened for novel coronaviruses (**See Section C2a, Fig. 6**). **We have also collected more than 500 bat specimens representing seven species from the Kingdom of Saudi Arabia in collaboration with Saudi Arabia's Ministry of Health and Columbia University.** Nearly 20,000 of our samples come from bats, and will be used to analyze CoV diversity along with novel CoVs we identify.

Identifying novel CoVs in wild bats in China: We have already conducted significant CoV surveillance in China for bats, other wildlife and humans. For this, we use pan-coronavirus PCR protocols based on conserved RNA-dependent RNA polymerase (RdRp) motifs A and C to screen samples at Wuhan Institute of Virology (*80*). Besides a large number of SL-CoVs, we have detected several novel bat-CoVs including strains closely related to CoV HKU4/5, CoV 1A &1B, CoV HKU 2, 6, & 8. For the first time, we have also isolated and characterized a bat-CoV from China that uses ACE2 receptors (see **Section C3a preliminary data**) (*28*). **In all, we have identified sequences from 268 novel bat-CoVs (140 from China alone) from bat species collected in Bangladesh, Thailand, Mexico, Brazil and China (See Section C2a, Fig. 6).** We have an additional 5,000+ clinical samples from free-ranging bats and rodents from Guangdong province, from an ongoing study which are being screened for viral pathogens, including CoVs at Guangdong Entomological Institute.

Survey of people highly exposed to wildlife in Guangdong, China: We have worked with Guangdong CDC since 2008, under a currently active IRB protocol, to interview and sample people working in live animal markets, hunters and restaurant workers with a high level of exposure to animals. We have interviewed volunteer participants about the nature and frequency of animal interactions; collected biological samples (blood, feces, sputum), and trained participants to collect animal blood samples (dried blood spots on filter paper) from animals they butchered or hunted. We enrolled 1300 participants across 12 sites within Guangdong Province (**Fig. 4**).

Figure 4: Sites of current human sample collection by Guangdong CDC for zoonotic pathogen surveillance in Guangdong Province, Southern China. Each star represents a large wildlife market where we have enrolled market and restaurant workers (total = 1,300) for our zoonotic pathogen spillover study. Seventeen people had IgG antibodies to SARS-CoV and a follow-up study is underway.

Samples have been tested for antibodies to animal pathogens, including SARS-CoV. **Of the 1300 serum samples screened using a SARS-CoV ELISA, 17 were positive for IgG antibodies to SARS-CoV.** These patients were not acutely ill at the time of sample collection, and this finding suggests one of three possibilities: 1) that SARS-CoV is still circulating in Guangdong markets; 2) that these people may have been exposed during the time of the 2002-3 outbreak; or 3) that the ELISA used is cross-reacting to another CoV. Review of their history of wildlife exposure is currently underway. In Shanghai, the Shanghai Municipal Center for Disease Control and Prevention (see **Letters of Support**) currently conducts surveillance on people with influenza-like illness in rural communities surrounding Shanghai. We will develop a similar study of people in

these communities who have exposure to wildlife. We will review and re-screen archived blood samples at Guangdong CDC for other bat coronaviruses once we determine candidates that could likely infect humans. to see whether there is exposure to CoVs other than SARS. We will re-screen these samples with specific serological assays based on bat-CoVs that will help differentiate between SARS-CoV IgG and other bat-CoV IgG to see whether there is exposure to CoVs other than SARS (*3, 81*). We will expand our survey to Guangxi, Fujian, Shanghai and Yunnan provinces to survey regions where SARS-CoV was not reported, but where wildlife trade, hunting, and bat guano collection is common.

C1b) Market characterization, wildlife sampling and human surveys: We have conducted surveillance at the wildlife markets of Guangdong where early cases of SARS-CoV were identified. From 2011-2013 we interviewed and sampled animal vendors, hunters and restaurant workers who butcher wildlife (**See Section C1a, Fig. 4**). For this proposed study, we will identify 10 markets in Guangxi, Yunnan, and Fujian Provinces (**Fig. 5**). We will characterize the physical size, number of vendors, diversity and abundance of mammalian species in each market. A questionnaire will be developed based on the one we used in Guangdong, to collect data on the nature and frequency of animal exposure of people who work in markets or hunt wildlife. We will conduct interviews to determine which bat species are sold, typical numbers, and source locations. We will collect information about recent acute respiratory illness and include those who have had undiagnosed acute respiratory symptoms within 3 months of the survey. We will then screen volunteers from this cohort for bat-CoV antibodies using existing and newly developed assays. We will compare exposure rates between people who are highly exposed to wildlife and a control group from the same regions.

Figure 5: Proposed sampling sites in Southern China (Guangdong, Guangxi, and Fujian Provinces) for the current study. Arrows indicate wildlife trade routes. Letters indicate wild animal markets in Guangdong (A-R), Guangxi (S-W), Hunan (X) and Fujian (Y).

In Shanghai, where wildlife markets are less common than southern provinces, we will interview voluntary participants under surveillance by Shanghai CDC for influenza-like illness. We will compare CoV exposure rates in people with acute respiratory illness to a control group from the same region (**see letter of support**).

Wildlife sampling: We will locate wild bat populations used to supply local markets in Yunnan, Guangdong, Guangxi, and Fujian. We will sample a minimum of 30 individuals from 30 different bat species representing but not limited to the following families: *Rhinolophidae, Hipposideridae, Vespertillionidae, Mollossidae,* and *Pteropodidae*, all of which are known to carry *alpha-* or *betacoronaviruses* and are consumed by people (*4, 7, 82*). Bat SL-CoV PCR prevalence is 10%-38% (*4, 24*). Given 10% prevalence in bat populations, sampling 30 individuals would ensure a CoV detection probability of 95%. In all wildlife markets, we will opportunistically sample a variety of insectivorous and frugivorous bats, and other mammals if available, taking fresh feces or rectal swabs, saliva (oropharyngeal swab), and blood. A small number of bats will be sacrificed as vouchers and to collect intestinal tissue for CoV receptor analyses if required. We will use cyt-b to identify host species.

Human exposure to CoVs study: Expanding on our work in Guangdong, we will develop a voluntary study of animal vendors and hunters in Guangxi, Yunnan, and Fujian provinces in cooperation with local Bureaus of Public Health and CDCs. We will develop a survey to identify people with high exposure to wildlife, particularly bats, and will recruit volunteers, collect blood, sputum, and stool sample from each enrolled participant. We will screen sera for antibodies to SARS-CoV, other alpha & beta coronaviruses including MERS-CoV, and novel bat-CoVs. We will screen stool from CoV seropositive participants for CoV nucleic acid. We will also develop specific bat-CoV serological assays and share these with our Chinese collaborators. In each province in southern China we will aim to include 10 markets and survey 20 vendors per market; 20 additional wildlife hunters per province (220 case subjects); 400 control subjects from the general population near the markets in each province (total of 620 people per province). For Shanghai, we will enroll 200 acute respiratory illness cases and 400 non-respiratory controls (600 total), The total number of human subjects will be 2460. The study will be conducted in Guangxi, Yunnan, Fujian and Shanghai provinces (see **Section E, Human Subjects**).

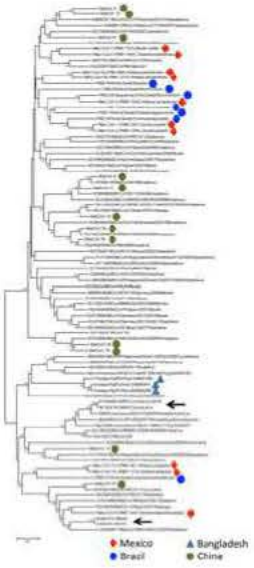
C1c) Data analysis: Human sera and stool samples will be tested at provincial CDC labs (see **letters of support**) and animal samples will be screened at the Wuhan Institute of Virology (Co-I, Shi)**.** Serum or plasma samples will be tested for CoV antibodies using ELISAs specific for SARS-CoV and bat SL-CoVs that we have developed (*4, 68, 83*). Fecal and saliva samples will be tested for CoV viral nucleic acid using a series of pancoronavirus PCR assays that target a region in the RdRp that is highly conserved among coronaviruses and for which we have a positive control, developed by our group under another federally-funded contract (*13, 23,*

84). The RdRp gene will be sequenced from all positive PCR samples and used to build co-phylogenetic trees (see **Specific Aim 2**). We will also test these pathogens for recombination events in markets vs. wild sampled CoVs after viral strains are characterized. Data from **Aim 1** will be used to parameterize mathematical models of viral transmission (**Specific Aim 3**) in markets to estimate relative risk of emergence depending on different diversity of mammals, contact rates, size of markets, and evidence for human exposure to bat-CoVs.

C1d) Potential Pitfalls and Solutions: We may find lower than expected levels of wildlife diversity in markets in Southern China. If this occurs, we have access to tens of thousands of wildlife samples from over 20 countries globally from work on a current NIAID R01 (Daszak PI) to assess diversity of viral pathogens in bats in Asia and Latin America, a large multi-year contract from USAID (Emerging Pandemic Threats: PREDICT program, Daszak PI) to conduct surveillance and pathogen discovery in wildlife in Asia and Latin America and two Nipah virus R01s. We have already discovered >250 novel CoVs from bats in these countries (**Section C2a**) including >100 from China. A second setback would be that access to markets becomes restricted due to political sensitivities. We are working closely with long-term local collaborators at ECNU and the Institute of Virology, Wuhan, both of which institutions are well respected nationally. The Institute of Virology is the National Center of Excellence for viral pathogens, and has Federal authority for viral research. Furthermore, we have shown through our work with Guangdong CDC that we can conduct long-term collaborations in these sites. Finally, we have selected a large number of wildlife market sites, so the closing of one will not affect all sampling activities.

C2: Specific Aim 2. Receptor evolution, host range and predictive modeling of bat-CoV emergence risk:

C2a) General strategy and supporting studies: *Can we use information on CoV sequence, host sequence and behavioral traits and population dynamics at critical human-wildlife interfaces to predict which CoVs are most likely to emerge?* To answer this, we will use data from our characterization of bat-CoVs, host range, receptor genes, serological data, and from field-collected data to build and parameterize three related models. **First**, using phylogenetic reconciliation we will map the co-phylogenetic patterns of bats and their CoVs using neutral and functional markers (RBDs and host receptor genes). We will compare free-ranging and market-sampled species assemblages and test the related hypothesis that wildlife markets disrupt 'natural' bat – CoV host associations and increase recombination and/or accelerated evolution to facilitate emergence. **Second**, we will construct generalized linear models that encompass phylogenetic information to test the two related hypothesis that spillover potential and host-range of bat-CoVs is limited by: 1) opportunity for contact; or 2) phylogenetic relatedness of host species and their receptor genes. **Third**, we will use mathematical matrix modeling to investigate bat-CoV transmission and evolutionary dynamics, and test the potential of novel CoVs to infect humans, bats, and other market animals. This model will be informed by serological data, market surveys, and receptor binding data from bat cell line and humanized mouse inoculation studies.



Phylogenetic studies of known and novel bat-CoVs: Phylogenetic methods can be used to identify recent host shifts and spillover events of CoVs, often these events are due to anthropogenic changes to host ecology, e.g. *Rhinolophus* spp. and human/civet SARS-CoV in the wildlife trade (*4, 7*). It has been proposed that repeated passage between civets and humans in wet markets facilitated SARS-CoV evolution towards greater human and civet ACE2 receptor affinity (*85*), and accelerated evolution and positive selection in CoVs was detected after host spillover (*86*). It is not known if bat-CoVs follow predictable patterns of co-phylogeny between host and virus; many studies found unique CoV strains circulating in different bat lineages, but also multiple CoV strains have been identified in the same bat species and individuals (*7, 40, 44, 45*).

Figure 6 (above): Phylogenetic tree (RdRp) of selected bat-CoVs from Genbank, including as subset of the 268 novel bat-CoVs discovered by our group through our USAID-EPT PREDICT pathogen discovery work in China, Brazil, Bangladesh and Mexico.

Wildlife trade and market dynamics may promote the cross-species transmission of distinct bat-CoV strains and facilitate viral recombination within these hosts (*46*); the extent of this will depend on the role of host phylogeny vs. contact in limiting bat-CoV spillover. Using our extensive database of bat and other wild animal CoVs that we have characterized, isolated, or are available on Genbank, we will examine these constraints for known and novel CoVs we identify. Over the past four years, we have conducted large surveys of bat pathogens globally, including the discovery of sequences from 268 novel bat-CoVs (including 140 from China) (**Fig. 6**).

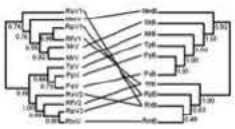


Figure 7 (left): Host-pathogen co-phylogeny of bat-CoVs from China (*43*). Bat genera: R, *Rhinolophus*; Mm *Miniopterus*; Mr, *Myotis*; P, *Pipistrellus*; V= viral sequence, B= bat sequence. This figure suggests rhinolophid CoVs may have a greater ability to jump hosts. Warrants further investigation using functional genetic markers and data from more species.

C2b) Co-phylogenetic analysis of bat-CoVs: We will use coronavirus and host sequence data generated in this project, from archived samples that we collected from bats just after the SARS outbreak, and previously published CoV strains from a diverse range of host species to quantify co-evolutionary patterns and host range in bat-CoVs. Combined analyses of host and viral phylogenies **will allow us better understand if host phylogeny (and receptor gene similiarity) can predict CoV host switching and whether or not market systems have disrupted the "natural" patterns of CoV association** (e.g. **Fig. 7,** from (*43*)). We will reconstruct phylogenetic relationships of CoVs using a combination of the HEL, N, RdRp, and S genes, as each has a different evolutionary rate and will allow us to test patterns of cophylogeny at different taxonomic scales. We will reconstruct host species relationships from tissue collected in our study using both neutral (mitochondrial and nuclear, e.g. cytB and RAG2) and functional (e.g. ACE2 CoV receptor) host genetic markers. Multiple alignments will be performed MAFFT (*87*), and phylogenies estimated using maximum likelihood (*88*) and Bayesian inference (*89*) for each viral and host gene, and concatenated virus datasets when no viral recombination is detected. We will test for statistical significance using ParaFit implemented in CopyCat (*90*) and AxPcoords (*91*), and visualize these using TreeMap v2.02β (*92*). These methods will allow us to identify which particular host-virus associations contribute most to the observed patterns. We will partition our dataset by collection localities and higher-level taxonomic groups to test co-phylogenetic significance at multiple spatial and taxonomic scales. To test the null hypothesis that there is no pattern of co-evolution we will perform permutations to randomized hosts–virus associations and then measure congruence relative to the host tree. By comparing the patterns of host-CoV co-phylogeny in natural bat communities (cave sites) vs. wet markets, we will be able to identify anomalies that may likely signal recent spillover events. To test for genetic recombination in market vs. wild-collected bat-CoVs, we will use sliding window analysis (*7*) and RDP3 v3.44 software (*93*). We will use previous methods to test for positive selection and identify specific virus residues under selective pressure (*94*).

Quantifying CoV strain sharing between host species: We will use viral sequence data from RdRp and S genes to delimit unique CoV "species" or "genotypes" at different taxonomic and sampling levels. We will test for non-random patterns of association of viral community assemblages between species (*95-97*) (*98*). This will involve calculating Jaccard's index of similarity (J) for the viral assemblages between pairs of species and testing for deviations from that expected by random chance using Monte Carlo randomizations (*99*). Deviation from the null model will be calculated as the difference between the mean J observed (J_{obs}) in the data and the mean J expected, such that $J_{dev} = J_{obs} - J_{null}$. Positive values of J_{dev} will thus indicate that CoV community assemblages between host species are more similar than would be expected by random chance, while negative values would indicate greater dissimilarity in the viral assemblages than would be expected by chance.

C2c) Predictive model of CoV host-range and diversity: We will develop a predictive model of host-range for bat-CoVs using data of bat distribution in natural caves and the markets, geographic ranges, ecological and behavioral characteristics of host species from our field studies and the literature, host and viral phylogenies, and associations of host species to particular CoV strains/clades. We will include phylogenetic distance between bat species and other mammal hosts from various neutral and receptor genes generated in this study. We will use CoV similarity indices (Jaccard, above) as our response variables in multiple regression models, i.e. generalized linear models (GLMs) and phylogenetic generalized linear mixed models (PGLMMs) with relevant bat ecological, phylogenetic, morphological, behavioral, and life history traits as our predictor variables, to assess the relative contribution of host phylogeny, viral traits, or species-specific ecological traits in explaining CoV diversification and sharing. We will calculate indices of host specificity that account for host phylogeny (*100, 101*), to further test hypotheses of whether bat-CoVs are more likely shared between host ecological groups or among species with similar life-history traits vs. relatedness. All statistical analyses will be conducted in R with relevant packages for community ecology and species diversity (vegan, fossil), and phylogenetic modeling (ade4, ape).

Extension of this model beyond China will allow us to map **a global spatial and phylogenetic risk gradient for CoV emergence based on host species traits, mammalian phylogeny (including functional CoV receptor genes), and relatedness of CoVs**. Further, we can use the results from our logistic regressions to identify gaps in surveillance, where bat species are found to share a lower than expected number of CoV strains given a threshold level of contact and relatedness with other host species. We will test our predictions of host range from the analytical model for bat-CoVs using synthetic reconstruction of bat-CoVs and *in vitro* studies of ortholog

receptor binding with different mammalian cell lines (**Aim 3**). Specifically, we will evaluate the ability of novel bat-CoVs to recognize and bind to selected receptors (ACE2, CEACAM, APN, receptor for alpha-CoV, or DPP4/CD26, receptor of MERS-CoV) reconstructed from divergent bat taxa. We envision an iterative process over the first few years of this grant whereby initial data are generated from known host-CoV associations, results from the model will be tested experimentally, and then data from experimental studies will be used to refine the models and better inform field sampling in China and globally.

Analyses of literature database: We have built a database of virus-host associations for 131 bat species and all 50 unique ICTV recognized bat viruses. We used a logistic GLM regression approach with host and virus variables, and found that host phylogeny (i.e. phylogenetic distance to other bat host species) was a strong predictor of observed virus sharing across bat species (trend with phylogeny only shown in **Fig 8**). We will adapt this approach by using host genetic distance of functional receptor genes instead of neutral markers, and CoV data collected from our standardized survey efforts.

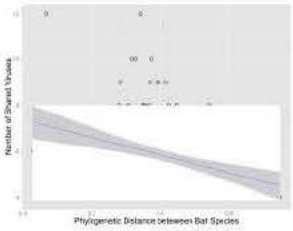


Fig 8. Scatterplot showing a decrease in the number of shared viruses with decreasing phylogenetic relatedness among bat species. Dataset includes all bat species pairs with >3 shared viruses for ~200 bat-virus associations form the literature (Olival, unpublished). Pairwise phylogenetic distance from maximum likelihood tree using cytochrome B mtDNA data.

C2d) Modeling the dynamics of CoV spillover risk: A key question in EID research is the role of viral evolution in enabling pathogen emergence. While some EID pathogens cause epidemic or pandemic disease because they readily transmit among humans ($R_{0,Human} > 1$, e.g., HIV, A/H1N1pdm), or only spillover directly from animals ($R_{0,Human} = 0$, e.g. West Nile Virus). Others, including MERS-CoV, may spillover regularly to humans, and even cause small clusters of human-to-human transmission, but have not yet caused a major epidemic or pandemic ($1 > R_{0,Human} > 0$, e.g., Nipah virus, monkeypox, Influenza H5N1). A looming issue is the likelihood of such a pathogen evolving to become a major epidemic or pandemic (i.e., $R_{0,Human} > 1$). Divergence times between ancestral bat-CoVs and hCoVs can vary widely and provide a timeline of past spillover events, e.g. 560+ years between hCoV-NL63 and its progenitor alpha-CoV (*6*) and ~20 years between bat SARS-like CoVs and human or civet SARS-CoV (*7, 70*).

The limits on SARS emergence are still unclear: Were the bat SL-CoVs unable initially to bind to human receptors, or was it necessary for a precursor CoV to evolve and adapt to humans for SARS-CoV to emerge? Were civets or similar non-bat, non-human hosts a critical intermediate evolutionary step in the transition from bats to humans, or were they incidentally infected along with humans simply by virtue of similar receptors? To examine the timeline for different emergence pathways, we have built a model framework (below) to represent the wildlife market environment and include viral ecology and evolution. We will use a matrix framework (*72, 102*) to determine how the pathogen is transmitted among different host species and between locations. We have already built the framework of this model (below), and have listed the data that we will collect in the current study to parameterize it (**Table 1, below**). To incorporate strain variation and evolution, we will adapt the approach of Antia *et al.* (*71*) by integrating a branching process approach to our matrix framework. **We will use these techniques to develop "What If" scenarios that predict how different strains of CoV would emerge, and potentially evolve, in different market systems within Asia and elsewhere** (e.g. scenarios with different host diversity and different levels of host-host and host-human contact within markets).

To examine strain evolution, we will model ***n*** possible strains, where strain 1 is the initial variant, and strain ***n*** is the variant that has a human $\mathbf{R_0}$ >1, with ***n-2*** variants in between, which may each have their own $\mathbf{R_0}$ that depends on the host community using 'Who-Acquires-Infection-From-Whom' (WAIFW) matrix framework (below). Following Antia *et al.* (*71*), we assume the mutation rate, μ, is the same for all variants, that only single mutations can occur, and we ignore back-mutation. However, we will reconsider these assumptions if changes in these can alter the expected outcomes of the mathematical results. We also assume that the total number of secondary infections generated by an individual with variant ***i*** is Poisson distributed with mean $\mathbf{R_0^{(i)}}$. A proportion μ of the variants will have mutated or recombined into type ***i+1***, while the proportion (1- μ) remains the same, as type ***i***. We will separate out the cases of mutation and recombination by placing different restrictions on the changes that could occur in the strains as they move from type ***i*** to type ***i+1***. These assumptions result in the probability generating functions:

$$f_i(s_1, s_2, \ldots, s_m) = \exp\left(-(1-\mu)R_0^{(i)}(1-s_i)\right)\exp\left(-\mu R_0^{(i)}(1-s_{i+1})\right) \quad \text{for} \quad i < m$$

(5) $$\text{otherwise} \quad f_m(s_1, s_2, \ldots, s_m) = \exp\left(-R_0^{(m)}(1-s_m)\right)$$

Through this branching process approach we can gain insight into the limitations and possibilities that stochastic processes may impose on the evolution of strain diversity in both limited diversity settings (e.g., only bats and humans), and highly diverse environments (e.g., markets with other hosts such as civets and bamboo rats). We can also adapt this methodology to compare mutation, which we expect to take small incremental movements in a fitness landscape that may have low fitness valleys between a wild-host adapted strain and a human or other host adapted strain, and recombination which may be able to take larger leaps across a given fitness landscape. Using this framework we can vary the $\mathbf{R_0}^{(i)}$ depending on the fitness of the mutants in various hosts, and the host diversity and abundance, simulating the complex fitness landscapes of real CoV systems. We can calculate the number of secondary hosts infected as $\mathbf{R_0} = \chi\phi\tau$, where τ is the duration of infectiousness, and χ is the rate of contact. Our receptor binding studies and predictive GLM models of host range will be used to inform ϕ, the joint probability that a susceptible host becomes infected when exposed. We will model our system both mathematically from a simple $\mathbf{R_0}$ perspective for insight, as well as using a spatial stochastic-birth-death simulation implementation to understand the implications of multiple scales of variation, including mutation and recombination and the implications for stochasticity for CoV emergence. To do this we will expand our basic equation, $\mathbf{R_0} = \chi\phi\tau$, into a matrix formulation to incorporate the multiple hosts within this system. Each strain and spatial location (e.g., market), can be represented by a different matrix. Thus we have:

$$X_k = \begin{bmatrix} \chi_{1,1,k} & \cdot & \cdot \\ \cdot & \cdot & \cdot \\ \cdot & \cdot & \chi_{i,j,k} \end{bmatrix} \quad \Phi_k = \begin{bmatrix} \phi_{1,1,k} & \cdot & \cdot \\ \cdot & \cdot & \cdot \\ \cdot & \cdot & \phi_{i,j,k} \end{bmatrix} \quad T_k = \begin{bmatrix} \tau_{1,1,k} & \cdot & \cdot \\ \cdot & \cdot & \cdot \\ \cdot & \cdot & \tau_{i,j,k} \end{bmatrix} \tag{1}$$

which we can use to define a 'WAIFW' $\mathbf{\Omega_k}$ matrix (*73, 103*) of which the eigenvalue gives us an estimate of $\mathbf{R_0}$ for the whole system, for a given strain and location. The 'WAIFW' matrix is:

$$\Omega_k = \begin{bmatrix} \chi_{1,1,k}\phi_{1,1,k}\tau_{1,1,k} & \cdot & \cdot \\ \cdot & \cdot & \cdot \\ \cdot & \cdot & \chi_{i,j,k}\phi_{i,j,k}\tau_{i,j,k} \end{bmatrix} \tag{2}$$

Critically, this enables us to analyze certain 'what-if' scenarios. For example, we can examine the role of civets in emergence by assuming that the strain which initially infected civets had to evolve in order to then infect humans. This would give us two strains in a single location, each with its own $\mathbf{R_0}$. Alternatively, we can assume that all three SARS-CoV host species (bats, civets, humans) were in the same market place, and a single CoV strain. In this case we would have a single matrix, with all three species, and values in every cell of the matrix. By keeping the separate pieces of the $\mathbf{R_0} = \chi\phi\tau$ equation, in the matrix form, we can examine potential public health control measures (e.g. quarantine, culling or separating species into different market locations) (*104*), which might also vary depending on the nature of receptor binding and strain evolution. To account for assumptions, we will investigate the implications of mixing in a stochastic environment. We have already built a stochastic-birth death, discrete event simulation of the spread of EIDs for Avian Influenza in multi-species markets and farms. We will adapt these simulations for strain and receptor diversity interactions with multiple species of CoV hosts. **This suite of modeling approaches will allow us to integrate our ecological and molecular approaches to understanding the potential pandemic emergence threat posed by the whole suite of bat-CoVs.**

Table 1: Data Needs for Model:

Parameter	Description	Sources
τ_{Human}, τ_{Bat}, $\tau_{Other?}$	Duration of infectiousness, Humans, Bats, other spp.	Humans (*57, 105-108*), Bats (*7*), other species (*108, 109*)
$\phi_{Human->Human}$	Joint probability an infected Human can transmit to susceptible Human	(*57, 105-107*)
$\phi_{Bat->Human}$, $\phi_{Other->Human}$ $\phi_{Bat->Other}$, $\phi_{Bat->Human}$ $\phi_{Other->Other}$	Joint probability an infected host can transmit to susceptible; can use receptor binding in host species for parameterization	*(*109*)
$\phi_{?}$	As above	Generally assume 0 or $\phi_{i,j} = \phi_{j,i}$ *
$\chi_{i,j}$	Contact rates	Market Surveys, using map overlap for non-market areas.
μ	Mutation rate	Literature
ξ	Recombination rate	Literature
N_{Human}, N_{bat}, N_{other}	Population density of bats, humans, other	Market surveys, census & transect data.

* Use knowledge of receptor bindings to appropriately upscale or downscale relative to human-to-human case of SARS and laboratory studies on other animals. We will run sensitivity analyses for these parameters.

We will assume that twice the estimate for SARS $R_{0,Human}$ rounded up to the max of the 95% CI to give 5 or 10 represents a near maximum, and 0 forms a lower boundary. We will assume τ is constant regardless of species and again do sensitivity analysis using SARS-CoV values. We test the following hypotheses: 1) That recombination can either substantially boost (H_A: $\Delta Pr > 0$) or mutation have the same effect (H_A: $\Delta Pr > 0$) on the probability of CoV spillover into humans, or that only recombination and mutation together provide a substantial boost to spillover probability (H_A: $\Delta Pr > 0$); 2) That known (e.g. civets) or unknown intermediate animal hosts or no intermediate hosts are necessary for CoV spillover to humans; 3) That high diversity of intermediate hosts either increases or decreases the probability of CoV spillover into humans. We will use our modeling framework to examine the potential CoV spillover in different markets, using the market data from Specific Aim 1, evolutionary characteristics of the CoVs from Aim 2, and specifically-acquired data to parameterize the model. **Table 1 (above)** lists parameters in the model, and gives available sources for data.

Previous experience of modeling disease emergence: Our group has used mathematical models to test hypotheses on zoonotic disease emergence for over 15 years. We use computational models that are tailored for the specific pathogen type or combination of hosts involved, and parameterize these with extremely detailed datasets specific for the emergence event. We then run simulations to test hypotheses on the spillover of viruses and the emergence of zoonoses. For Nipah virus (NiV), another bat-borne zoonosis, we obtained data from pig production facilities in Malaysia (*110, 111*), from experimental infection of bats and *in vitro* under BSL-4 conditions for viral transmission parameters (*112, 113*). We used this approach to demonstrate the cause of NiV emergence (*111*). We have successfully used similar approaches to demonstrate viable causal mechanisms for the emergence of Hendra virus (*114*), Avian influenza (*115-117*) and West Nile virus (*118-120*).

C2e) Potential pitfalls and solutions: The diversity of coronaviruses that we identify may be inadequate for robust co-phylogenetic analysis. We have already shown proof of concept in preliminary data through USAID and NIAID funded projects that we have detected new coronaviruses in most bat species examined; there has been a large amount of research from several groups showing a broad diversity of coronaviruses; previous studies from us and other groups have provided evidence of a diversity of coronaviruses associated with bats and there is high likelihood that we will identify more. In China specifically, 23% of bat samples we have screened were positive for CoVs, thus we do not anticipate a lack of diverse CoVs (*28*). For modeling studies, not all necessary parameters may be easily obtained. We will use information from the SARS-CoV outbreak, where we have detailed data from the WHO investigations on serology and viral isolation from market wildlife; and from our recent and current work in Guangdong province; and an ongoing study on avian influenza in Shanghai and Guangdong markets (Co-I Zhang). Lastly, for parameters that we cannot actually estimate, we may be able to posit reasonable limits. For example we can constrain the probability of spillover: it must be greater than 0, since SARS did in fact spillover (*106*), but it is very unlikely that this probability is higher than the within species transmission probability. If the rate of transmission within a host species is unestimatable, we can use data from other diseases in similar species, such as bat rabies. Thus we can readily perform a sensitivity analysis for unknown parameters within a range that is biologically plausible, using sensible constraints.

C3: Specific Aim 3. Testing predictions on CoV inter-species transmission:

How can we test predictive strategies to understand which viruses have the capacity to 'jump hosts'? To answer this, we will analyze the interspecies infection or transmission of CoVs we have identified, particularly the SARS-like CoVs and CoV HUK4/5 that is closely related to MERS-CoV (hCoV-EMC) from Saudi Arabia. Our main approach will be: 1) *in vitro* infection experiments using pseudoviruses carrying the spike proteins (wild type or mutants) or live viruses in cell lines of different origins; 2) binding affinity assays between the spike proteins (wild type or mutants) and different cellular receptor molecules; and 3) humanized mouse experiments if viruses are identified of significant human infection potential (see **Ralph Baric, Letter of Support**).

C3a) General strategy and supporting studies: We will sequence the spike (or other receptor binding/fusion) protein genes from all bat-CoVs we identify, creating mutants of these to identify how significantly each would need to evolve to use ACE2 or CD26/DPP4 (receptor for MERS). We will then use receptor-mutant pseudovirus binding assays, *in vitro* studies with a wide range of cell lines from bats, other mammals including primates and human cell lines, and with humanized mice where particularly interesting viruses are identified phylogenetically, or isolated (see **Ralph Baric, Letter of Support**). These tests will provide direct public health-relevant data, and also iteratively improve our predictive model to better target bat species and CoVs during our field studies to obtain bat-CoV strains of the greatest interest for understanding the mechanisms of cross-species transmission.

Experience working with receptor mutants & pseudovirus binding assays: We have established a stable pseudovirus assay for SARS-CoV and SARS-like CoV and tested the infectivity of these spike proteins in cells expressing ACE2 from human, civet and bats (*52, 68*). We have demonstrated that several bat species are susceptible to the SARS-CoV and that some SARS-like CoV strains can use human ACE2 for cellular entry (*52*). Minor mutations in S proteins or ACE2s greatly affected the receptor binding and finally abolish the pseudovirus entry (*68, 121*) (**Fig. 9**). Recently, we have discovered a number of alpha and beta CoVs including HKU4/5 (*122*)(Ge *et al.*, Co-infection of alphacoronaviruses in one bat community, in China. unpublished results). The established approaches will enable us to analyze the receptor usage of these CoV S proteins and understand the host range and potential interspecies transmission ability of these novel CoVs and finally predict the potential spillover probability of these viruses to humans or other hosts at a molecular level.

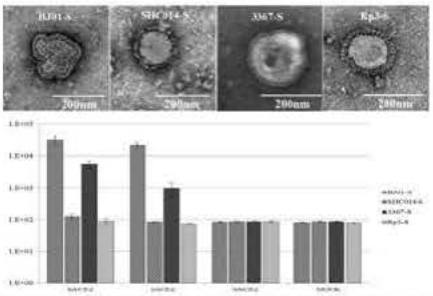


Figure 9: Top panel: HIV pseudovirus carrying spike proteins from human SARS-CoV (BJ01-S) and bat SARS-like CoV (SHC014-S, 3367-S and Rp-S). Bottom panel: Infectivity assay with the above pseudoviruses in HeLa cell lines expressing ACE2 from human, civet and bat.

In vitro cell lines & Humanized mouse model: We have developed primary cell lines and transformed cell lines from 9 bat species using kidney, spleen, heart, brain and intestine. We have used these for virus isolation, infection assays and receptor molecule gene cloning. We also have a large number of cell lines from humans and animals that we will use for virus infectivity assays. We have obtained a letter of support from Dr Ralph Baric, who is keen to collaborate with us initially to infect his humanized mouse model with our bat SL-CoV that uses ACE2, and subsequently to use other CoVs we identify (see **Dr Ralph Baric, Letter of Support**).

C3b) Receptor-mutant pseudovirus binding assays: We will amplify ACE2, DPP4 or other receptor genes of human and bats and clone them into eukaryotic expression vector pcDNA3.1 to construct cells expressing these molecules. We will amplify full length spike genes (S) of bat-CoVs detected from different bat species. The full length S gene, particularly RBDs, will be codon optimized, then cloned into eukaryotic expression vector pcDNA3.1 (*68, 123*). For packaging pseudovirus, S-expressing plasmids (or empty vector control) and pHIV-Luc (pNL4.3.Luc.R$^-$ E$^-$ -Luc) bone plasmid will be co-transfected into 4 x 10^6 293T cells using calcium phosphate transfection system (Promega), after 8 hours, replacing the medium with fresh medium, and supernatants will be harvested at 48 hours post transfection and separated from cell debris by centrifugation at 3,000g, then by passing through a 0.45μm filter (Millipore). The filtered supernatants will be stored at -80°C in aliquots until the use. We will use prepared pseudoviruses bearing different S proteins to infect human and bat ACE2 or DPP4 receptor expressing cells (in Hela cell model), 24 hours post infection, receptor usage by different S proteins will be determined by measuring luciferase activities. We will also induce site mutations in S proteins using site-directed mutation method, then do receptor-mutant pseudovirus binding assays. Pseudovirus infectivity on different human cell lines (A549, 293T, Caco, Huh7, and etc), primary and immortalized bat cell lines (listed below) and other mammalian cell line (mouse, pig, hamster, monkey, and ect) will be also determined by luciferase assay. The results will provide information whether bat-CoVs could use known bat and human ACE2, DPP4 or other known CoV receptors to enter cells, and allow us to determine critical receptor binding sites, viral host range, and to better predict the capacity of our CoVs to infect people.

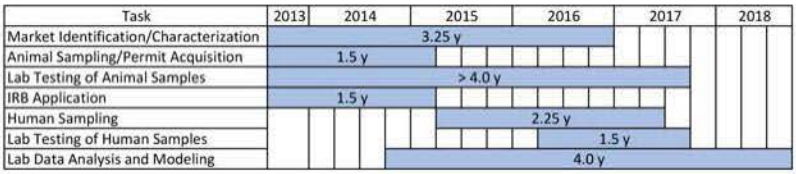
C3c) *In vitro* studies: We will isolate bat-CoVs using Vero E6 cell (susceptible SARS-CoV and MERS-CoV) and primary or transformed bat cell lines that we have developed from *Myotis davidii, Rhinolophus sinicus, Myotis chinensis, Rousettus leschenaultia* and other bats of China (*124, 125*). CoV PCR-positive bat samples (in 200 μl buffer) will be 3,000-12,000 rpm gradient centrifuged, and supernatant will be diluted at 1:10 in DMEM medium, then added to cells, incubated at 37°C for 1 h, the inoculum removed and replaced by fresh DMEM medium with 2% fetal calf serum, and cells checked daily for cytopathic effect (CPE). Double dose triple antibiotics (penicillin 200 IU/ml, streptomycin 0.2 mg/ml, amphotericin 0.5 μg/ml-Gibco) will be included in all culture media. Three blind passages will be carried out for each sample and the culture supernatant and cell pellet examined for presence of virus by RT-PCR using primers targeting the RdRp or S gene after each passage (*28, 126*). Live bat-CoVs will be sequenced to confirm viral receptor and by comparing viral infection in ACE2 or DPP4 expression cells and virus infectivity and replication on different human cell lines (A549, 293T, Caco, Huh7, and etc), bat cells and others (mouse, pig, hamster, monkey) using plaque assay, real time-PCR, and Immunological Fluorescence Assay (IFA). These *in vitro* assays will be used to test viral host species range and transmission possibility of bat-CoVs to human and other mammal, as predicted by our GLM and matrix models.

C3d) Humanized mouse *in vivo* infection experiments: To evaluate pathogenicity of bat-CoVs we will perform *in vivo* infection experiments in humanized mice modified to carry human ACE2 or DPP4 gene in the Wuhan Institute of Virology BSL-3 animal facility. We will passage isolated bat-CoVs in permissive cells twice, administer a specific inoculum (e.g. $1x10^6$ TCID50) to intranasally or intraperitoneally. Mouse body temperature will be monitored with implanted microchips (LifeChip Bio-thermo, Destron Fearing), and mice will be weighed and observed for clinical signs of illness daily. Dead or moribund mice will be euthanized, organs harvested and sectioned. Live animals will be euthanized at three weeks post-inoculation and organs harvested. We will test for neutralizing antibodies against bat-CoVs on days 10, 15 and 21 pi. We will collect nasal washes, oral swabs, and rectal swabs, and urine every two days and quantify virus using qRT-PCR. We will conduct routine histology, immunohistochemistry, qRT-PCR, and virus isolation on tissues. This work will provide information about viral pathogenicity, tissue tropism, transmission route, and infection symptom.

C3e) Binding affinity assay: The recombinant S proteins and receptor molecules (e.g. ACE2 or DPP4) will be expressed in insect cells or eukaryotic cells. Octet RED platform (ForteBio, Menlo Park, CA)) will be used to perform binding affinity kinetics experiments. Streptavidin-coated sensor tips from Fortebio will be used to capture biotinylated S protein onto the surface of the sensor. After reaching baseline, sensors will be moved to the association step containing indicated concentrations of wild or mutant receptor molecules diluted with kinetics buffer for 30 min and then dissociated for 30 min at 25°C. Binding affinity will be determined by collecting the dissociation constants KD, Kon (association-rate), and Koff (dissociation-rate) determined by fitting binding chromatogram data with the Octet®User Software.

C3f) Potential pitfalls and solutions: Through our targeted sampling in China, we may only identify a small portion of the huge diversity of bat-CoVs in bat populations. To resolve this, we plan to expand our sampling locations to include samples from across SE Asia and improve our detection methods targeting more virus sequences. We will also synthesize the S genes based on the published data for viruses we do not obtain. Virus isolation may be a big challenge for this specific aim. In our previous work, we have isolated a number of novel bat viruses including adenovirus, reovirus and SARS-like CoV and have refined and optimized our methods for virus isolation. We will also attempt to construct additional bat cell lines which are lacking interferon response or over expressing the receptor molecules and more susceptible for virus infection to increase isolation success.

D. TIMELINE & MANAGEMENT PLAN:



This project will take 5 years to complete. The initial phase will involve filing the IRB application, identifying sampling sites, and conducting animal sampling and testing. Mid-project efforts will involve initial human sampling, analyses of lab results and production of models. The final phase will involve testing human and wildlife samples and analyses and modeling to maximize results. **Project Management:** Funds will be managed via subcontracts originating with EcoHealth Alliance, which is an A133 (low risk)-audited 501 (c) 3 organization specializing in international research on emerging diseases. PI Daszak will oversee all aspects of the project management. He is an experienced manager, with over 15 years of federally-funded research experience. Prof. Shi, based at the Wuhan Institute of Virology, will oversee all laboratory testing and analyses. Prof. Shuyi Zhang will manage field sampling work. EcoHealth Alliance staff will manage all modeling and analytical approaches (Aims 1 & 2). Communication will be via monthly video-conferences using EHA's NIH ARRA-funded video-conference facility. Travel budget has been requested to enable regular face-to-face meetings for all key staff.

PROTECTION OF HUMAN SUBJECTS:

HUMAN SUBJECTS RESEARCH

1. **Risk to subjects**

This project is a study of human exposure to animal coronaviruses in southern China. Subjects will be enrolled on a voluntary basis and a single interview and sample collection will be conducted. Informed consent will be obtained. People found to be infected with an animal coronavirus will be followed up after 6 months with a secondary interview and collection of biological specimens to determine whether infection is persistent and exposure is ongoing. Primary subjects will be male or female adults who are highly exposed to wildlife through hunting, butchering, or general handling in the context of live animal markets or restaurants that prepare and serve wild animals. The study population will be selected in Shanghai, Yunnan, Fujian, and Guangxi provinces, China, and will be open to people of all ethnicities that fit the subject criteria. We will target human subjects, comprising 220 subjects (market workers and hunters) and 400 controls from the general population in Yunnan, Fujian, and Guangxi provinces plus 600 subjects in Shanghai (total enrolled: 2460). The market types are defined in **Specific Aim 1, Human exposure to CoVs**. There are no data to suggest an ethnic bias for coronavirus exposure or infection, therefore subjects will be enrolled based on exposure criteria, though subjects will not be excluded based on ethnicity or gender. We will endeavor to have an equal number of men and women, if the composition of animal vendors in markets allows.

Sources of Materials: Samples to be collected and screened for coronaviruses include blood, saliva and stool samples. 10 mL of blood will be collected from each subject. Subjects will also be asked to provide saliva and stool in sterile containers. An initial sample collection and interview will be performed by trained medical personnel from the local CDC under the provincial Public Health Bureau. Sample collection will be done once in years 2-4 of the study. Samples will be screened for coronaviruses using PCR and an ELISA at the appropriate CDC microbiology lab or at the Wuhan Institute of Virology. Samples that test positive for coronavirus or antibodies to coronavirus will be followed up after 6 months with a secondary interview designed to determine the current level of exposure to wild animals, and whether exposure at the current level was consistent between the first and subsequent interview. Repeated clinical samples will also be collected and tested for coronaviruses. In all instances, volunteers will be given a medical exam and informed of their test results.

Potential risks: The potential risks to study participants resulting from study participation are minimal. The volume of blood being collected is within normal safety limits. The interview questions will be designed to assess exposure risk, and may ask personal questions, but surveys will be done in private and anonymized to protect privacy. There may be some stress to subjects who are informed that they have been exposed to an animal virus, but counseling will be available and options for medical care will be included in the discussion.

2. Adequacy of protection against risks

Recruitment and informed consent: Prospective study participants will be identified by the research team at each site in partnership with CDC personnel. The team will be thoroughly trained on communicating the research objectives and will be able to address any questions that potential subjects may have. Both written and oral descriptions of the study will be provided in Chinese (in Mandarin or via an interpreter in local dialect if necessary) as part of the informed consent process. Contact details of the collaborators at local CDCs and the study PI will be provided to all subjects, and CDC personnel on the research team will be available on site to answer questions from the study subjects. Test results will be communicated to each subject and counseling offered to minimize stress.

3. Potential benefits to Subjects and Others

There are potential benefits to the study subjects including receiving a physical exam/health check from a medical officer and the potential benefit of identifying an occupational health hazard. At the conclusion of the study, we will deliver an educational workshop for high risk individuals (open to study subjects and non-study subjects) describing the health benefits of using PPE and hand-washing during animal handling activities throughout the day.

4. The importance of knowledge to be gained. There are valuable potential benefits to the general public from the knowledge to be gained by this study, as it may identify sources of zoonotic coronaviruses in the market system or which are commonly hunted. Avoidance of these animals or extra care when handling them may substantially reduce the risk of CoV (and other zoonotic pathogen) transmission.

INCLUSION OF WOMEN AND MINORITIES:

Inclusion of Women: This proposal will enroll men and women as study subjects. Depending on local gender composition of animal vendors, we will make every effort to have men and women equally represented in this study.

Inclusion of Minorities: Subjects will be enrolled in this study without regard to ethnicity. Occupational exposure to wildlife in a market, hunting, or butchering context will be the primary criteria for identifying subjects.

Program Director/Principal Investigator (Last, First, Middle): Daszak, Peter

Targeted/Planned Enrollment Table

This report format should NOT be used for data collection from study participants.

Study Title: The ecology of bat coronaviruses and the risk of future coronavirus emergence.

Total Planned Enrollment: 2460**

TARGETED/PLANNED ENROLLMENT: Number of Subjects			
Ethnic Category	**Females**	**Males**	**Total**
Hispanic or Latino	,0	0	0
Not Hispanic or Latino	1,230	1,230	2,460
Ethnic Category: Total of All Subjects *	1,230	1,230	2,460
Racial Categories			
American Indian/Alaska Native	0	0	0
Asian	1,230	1,230	2,460
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	0	0	0
Racial Categories: Total of All Subjects *	1,230	1,230	2,460

* The "Ethnic Category: Total of All Subjects" must be equal to the "Racial Categories: Total of All Subjects."

(** all study subjects will be enrolled at foreign sites in China)

INCLUSION OF CHILDREN:

Inclusion of Children: Children will not be included in this study. Children do not normally work in wildlife markets, and are not normally involved in the wildlife trade in China.

VERTEBRATE ANIMALS:

1. Detailed description of animal use.
All work with vertebrate animals will be conducted in China.
Capture and sampling techniques for all wild animals described in this study have been previously approved by UC Davis IACUC (Mazet and Epstein; UC Davis 15898; current).

Experimental work using humanized mice will be conducted at the Center for Animal Experiment Biosafety 3 lab of Wuhan University at the School of Medicine in Wuhan, China. The Center is AAALAC accredited and has both an Institutional Biosafety Committee and an Institutional Animal Care and Use Committee. Animals will be housed in a BSL-3 facility and will be under the care of a full-time veterinarian. We will submit our protocols for IACUC approval should this proposal be funded. Conditions for animal use are described below.

Note: The majority of wild animals captured and sampled will be done using non-destructive, techniques. In a small number of instances (~ 2 bats per species), where intestine and lung tissue is required to establish cell lines, animals will be humanely euthanized and a necropsy performed according to accepted protocols (see euthanasia section)

Bat capture. Free-ranging bats will be captured using either a mist net or harp trap. The net system is manned by two people during the entire capture period, and bats are removed from the net as soon as they become entangled to minimize stress and prevent injury. In the Co-PI's (Dr. Epstein) experience, a maximum of 20-30 bats can be safely held and processed by a team of three people per trapping period. Duration of trapping will depend on the capture rate. Bats are placed into a pillowcase or small cloth bag and hung from a branch or post until samples are collected. Bats are held for a maximum of six hours.

Wild rodent capture. Free-ranging rodents will be captured through pit traps and box traps; captive rodents, including resident free-ranging wild rats/rodents in markets, will be manually captured or captured through traps. Traps will be checked a minimum of once daily in the morning. If adverse weather (extreme heat, rain) is expected or researchers are working in areas where predation is common, traps will be checked more frequently, and closed during the adverse weather. Handling of rodents will involve morphometric measurements. Captive and wild rodent sampling procedures (including anesthesia if necessary), will involve manual restraint, venipuncture, mucosal swabs, fecal, urine, and external parasite collection. Following capture, small animals will be restrained with a fine mesh bag to minimize entanglement, taking precautions to ensure the animals are not traumatized by the hoop of the net or through net removal. Larger rodents will be restrained for sampling in specialized squeeze-cages, allowing adjustments appropriate to the size of the animal. Squeeze-cages consist of a wooden frame with a plasticized wire bottom and a Plexiglas shield used to press the animal, while ensuring visible communication between the field veterinarian and the animal. Once squeezed, a rod is inserted to keep the plastic shield in place. The box is then inverted, allowing sampling to be conducted through the open wire bottom and abdomen of the animal when the animal is safely immobilized. Anesthesia for small rodents will be conducted using plastic tubes, with the animals transferred directly from the traps to the tubes containing a cotton swab soaked in ether, isoflurane, or methoxyflurane for anesthetic induction. For larger rodents, chemical restraint and anesthesia (ketamine alone, or ketamine combined with xylazine) will be applied either through the squeeze cages by syringe if applicable.

Laboratory mice. Lab mice will be sourced commercially by the Wuhan Center for Animal Experiment at Wuhan University.

Sample Collection. Bats will be manually restrained during sampling.
Bats: Depending on the species and size of bat, swabs will be taken from the oropharynx, urogenital tract, and rectum. Fresh feces will be collected if available, in which case a rectal swab will not be collected. Blood will be collected from fruit bats either from the cephalic vein or from the radial artery or vein using a 25 gauge needle and 1cc syringe. Blood will be collected from bats weighing less than 100g according to published techniques (*126*).

Principal Investigator/Program Director (Last, first, middle): Daszak, Peter

Rodents: Rodents will be anesthetized prior to sampling.
Once anesthetized a small blood sample will be collected using a capillary tube placed into the retro-orbital sinus. Only trained technicians will perform retro-orbital bleeding and it will only be performed on anesthetized rodents. Femoral or jugular venipuncture may be used for larger rodents (e.g. rats). In all rodents, blood volumes of no more than 1% of body weight will be withdrawn. (example 0.2 ml blood from a 20 gram rodent).

Civets and other small mammals: Anesthesia will be used to restrain small free ranging mammals according to published protocols. Animals will be monitored continuously while recovering from anesthesia. Animals that are sampled in the marketplace, and that may potentially be consumed, will not be anesthetized. Manual restraint will be used and blood will be drawn from the femoral artery or saphenous vein.

Laboratory Mice. Humanized mice will be bred at the University of Wuhan. Mice will be inoculated with a specific dose (e.g. $1x10^6$ TCID50) of virus through different routes (intranasally and intraperitoneally). Mouse body temperature will be monitored with implanted temperature sensing microchips (LifeChip Bio-thermo, Destron Fearing), and mice will be weighed daily. Animals will be observed daily for clinical signs of illness. Moribund mice will be euthanized, according to AVMA recommendations. Live animals will be euthanized at three weeks post-inoculation and organs harvested. We will collect sera on days 10, 15 and 21 to test for neutralizing antibodies against bat CoVs. We will collect nasal washes, oral swabs, and rectal swabs, and urine every two days. These are minimally invasive procedures, and will be performed by experienced lab technicians under the supervision of a full-time veterinarian.

2. Justify use of animals, choice of species, numbers to be used. Species and number used in study:
The purpose of this study is to conduct multi-regional surveillance in large populations of animals to detect coronaviruses that may pose a risk to the health of both humans and animals. The experimental work is designed to understand the ability of bat coronaviruses to bind to human receptors. Because we don't have prevalence estimates for novel strains of coronaviruses, we assume a conservative estimate of 10% prevalence. SARS-like coronaviruses have been found in between 10% and 38% of bats studied (*4, 25*). A 10% in wild populations of bats would require a sample of 30 individuals per species in order to ensure detection of an infected individual with 95% confidence. **Wild bats**: We will sample 30 individuals from 30 different species in each province in China (2 per species euthanized for organ tissue); representing but not limited to the following families: *Rhinolophidae, Hipposideridae, Vespertillionidae, Mollossidae,* and *Pteropodidae*, all of which are present in Southern China and potentially in the wildlife markets. **Bats in wet markets:** We will opportunistically sample a wide variety of insectivorous and frugivorous bats according to what is present in markets. In addition to bats, we will sample civets, raccoon dogs, rats, bandicoots, bamboo rats, and other rodents present in the markets that may act as intermediate hosts. Numbers of animals sampled from markets will be limited to animal availability. In every situation, sampling of wildlife will be conducted in the most humane manner while minimizing the impacts on individual animals and their wild populations. In cases where feces are collected for testing, non-invasive techniques will be used. In all instances, the fewest number of animals will be sampled that will provide valid information and statistical inference for the pathogen and disease of interest and every effort will be made to minimize stress and discomfort for the animal.

A small number of bats (maximum 2 per species) representing each of the species in this study may be euthanized in order to collect lung and intestinal tissue required for characterizing coronavirus receptors. Voucher specimens may also be collected at the discretion of the team leader for the accurate identification of species using molecular methodology.

Humanized mice for experimental infection for Specific Aim 3: In order to understand whether bat coronaviruses that utilize receptors found in people have the potential to infect people, we will use Swiss albino mice (standard breed at Wuhan University) that have been genetically modified to have human receptors. We'll infect them with cultured bat coronaviruses and determine which organs become infected and whether these mice are capable of shedding infectious virus. Humanized mice will be genetically modified to carry human ACE2 or DPP4 gene will be used to evaluate pathogenesis of CoVs. We cannot anticipate exactly how many viruses we will find that are candidates for experimental models, however we estimate that we will use
Principal Investigator/Program Director (Last, first, middle): Daszak, Peter

four adult mice (2 male, 2 female) per virus and that we will identify approximately 20 viruses that will be used for mouse infection experiments. This will require a total of 80 mice over the study period.

3. Provide information on veterinary care. For wild caught animals, **t**here is no specific veterinary care that is appropriate, nor will clinical veterinary facilities be available. Animals that are injured during the capture or sampling process will be assessed by an experienced team leader, and if the animal is determined to be unlikely to survive if released, it shall be euthanized humanely (see euthanasia section). Animals will be released within hours of capture. In the markets, animals will be sampled using manual restraint or anesthesia. Animals will be returned to vendors after sampling, or, if wild caught in the markets (e.g. rodents), they will be released in the area outside the marketplace.

Laboratory mice will be housed in the BSL-3 small animal facility Center for Animal Experiment at Wuhan University. Experimental animals will be regularly monitored by experienced staff and a supervising veterinarian. The animal facility operates 24 hours a day and has full-time veterinarians on staff. All animals will be provided with food and water ad libitum and will otherwise receive standard care.

4. Procedures for ensuring animal comfort, lack of distress, pain, or injury: Animals will not be held longer than 6 hours. Co-PIs, Drs. Epstein and Olival have extensive experience in capture, anesthesia, and sampling wildlife, including bats. In our experience, bats and rodents tolerate the described procedure well. Mist nets will be attended continuously during capture periods, and bats will be extracted from the net as soon as they become entangled. This will minimize stress and injury from entanglement. Bats will be placed individually in cotton bags and hung from tree branches while awaiting processing and during recovery. The bags are sufficiently porous as to allow for ventilation and are designed for bat capture. The enclosed environment seems to calm the bats, as they do not struggle once inside, but they hang quietly. Animals will be monitored by a veterinarian or experienced field team member during all stages of capture, processing, and release. Animals will be kept in a cool place while in the pillowcases. Rodent traps will be set overnight and all traps will be checked in the morning while it still cool outside. Rodents will be kept in a cool, shaded environment during sampling and will be released within 10 hours of capture.

The procedures used in this experiment (blood draw, nasal, oral, and rectal swabs) are minimally invasive, however, mice that show signs of morbidity post-infection will be examined and euthanized according to AVMA standards (see below).

5. Euthanasia: In the event of injury to an animal that results in pain and suffering, and reasonable veterinary care is unavailable, the animal will be euthanized by a veterinarian or trained field team member using ketamine injected intramuscularly 37.5mg/kg and sodium pentobarbital injected intravenously at a dose of 1.0ml per 5kg injected intravenously. This protocol is in accordance with the AVMA euthanasia report (2007). Any animal that is euthanized using a chemical agent will be disposed such that it will not be permitted to enter the food supply either through markets or hunting.

SELECT AGENT RESEARCH/BIOHAZARDS. No select agent research as of 5/25/12

SARS-CoV caused outbreaks with significant case fatality rates, and there are no vaccines available for this agent. SARS-CoV is classified as a BSL-3 agent. The work proposed in this application will involve two aspects: field work and laboratory work. Fieldwork involves the highest risk of exposure to SARS or other CoVs, while working in caves with high bat density overhead and the potential for fecal dust to be inhaled. There is also some risk of exposure to pathogens or physical injury while handling bats, civets, rodents or other animals, their blood samples or their excreta. The Co-PI is a veterinarian with extensive experience working with wildlife species and high-biosecurity pathogens (Nipah virus, ebolavirus, SARS), and great care will be taken in the field to limit the risk of accidental exposure to known or unknown animal pathogens. We have strict procedures for handling bats and working with samples from them as they are secured in the field and transported to the lab. Field team members handling animals will be trained to utilize personal protective equipment and practice proper environmental disinfection techniques. This includes wearing coveralls or dedicated clothing, nitrile gloves, eye protection, and a P95 or P100 respirator. All field clothing and equipment will be disinfected using Virkon disinfectant. All biological waste from field surveys will be disposed of in the appropriate container (sharps box or an autoclave bag) and will be autoclaved at local hospitals or university labs. All personnel will be vaccinated against rabies and have a neutralizing antibody titer, in accordance with WHO and CDC recommendations. Field teams will carry rabies boosters in the field and will receive a booster in the event of a potential rabies exposure.

Field safety protocol: Our procedures to deal with bites, needle-sticks etc. are as follows: The wound is washed thoroughly with soap and water to clean away dirt and debris, then vigorously scrubbed with a sterile gauze bandage and benzalkonium chloride for 5 minutes. If bleeding, pressure is applied with a sterile bandage for until bleeding has stopped. If the wound continues to bleed, medical attention at the nearest hospital is sought. The bat from which the bite or exposure originated is identified, and the samples collected from it labeled on the data sheet that these were involved in an exposure. Our procedures require that the person potentially exposed reports to a major hospital within 24 hours to have wound examined and receive a rabies booster (as per WHO/CDC protocols). The laboratory work is lower risk, as samples placed in lysis buffer will be non-infectious. Samples placed in viral transport medium and frozen will be stored at ultra-low temperatures (-86C) until viral isolation is required. Serum will be heat inactivated (56C for 30 min) prior to testing.

Lab biosafety: Wuhan Institute of Virology and the Wuhan University Center for Animal Experiment BSL-3 lab have an Internal Biosafety Committee and are accredited BSL-2 and BSL 3 laboratories. All experimental work using infectious material will be conducted under appropriate biosafety standards. Disposal of hazardous materials will be conducted according to the institutional biosafety regulations.

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CONSORTIUM/CONTRACTUAL ARRANGEMENTS:

Consortium/Contractual Arrangements

This project is a multi-institutional collaboration led by EcoHealth Alliance, New York (Daszak, PI), which will subcontract funds to two institutions: the East China Normal Univerisity (Dr S. Zhang) and the Wuhan Institute of Virology (Dr. Z. Shi), which are both foreign institutions. Dr. Daszak has over 15 years previous experience managing collaborative projects including two R01s on Nipah virus ecology that involved 5 separate foreign institutions, a 5-year NSF/NIH Ecology of Infectious Disease award on West Nile virus which involved multiple subcontractees, an R01 on bat viral discovery that involves multiple international contracts, and a multi-million dollar p.a. contract from USAID that involves 12 international partners. The applicant organization (EcoHealth Alliance) is justified in taking the lead on this project because it specializes in understanding the ecological, and virological processes underlying zoonotic disease emergence. Dr Daszak has conducted significant preliminary work on this issue including 10-years of research on the ecological and related factors of the emergence of SARS and 11-years of work in China. The subcontractees will work on specific issues and areas in which they have proven expertise. These areas are: human and animal field sampling (East China Normal University, Dr. Zhang) and viral discovery, pathogenesis as well as sample storage and shipping (Wuhan Institute of Virology, Dr. Shi). Dr Daszak has launched and co-directed a joint institute in China with Dr Zhang, and has been involved in contractual arrangements with ECNU for 8 years. Drs Shi, Zhang, and Daszak have collaborated together since 2002 and have been involved in running joint conferences, and shipping samples into and out of China.

SCDC
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Shanghai Municipal Center for Disease Control and Prevention
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Dr. Peter Daszak
President
EcoHealth Alliance
460 W 34th St. 17th Floor
New York, NY 10001
USA

Dear Dr. Daszak,

I am writing in response to a request for collaboration on an upcoming NIAID funded R01 entitled "Understanding the risk of bat coronavirus emergence." The Shanghai CDC has a high interest in working with EcoHealth Alliance and its scientists in identifying and preventing the transmission of bat coronaviruses to human populations.

The Shanghai CDC recognizes the mutual benefits to be gained through research cooperation and a successful partnership with EcoHealth Alliance in the field of identification and prevention of zoonotic disease transmission. It is vital to not only identify the diseases themselves, but also identify high-risk human populations and the actions that put them at risk for infection along with evaluating approaches to intervention and disease management.

Understanding and preventing exposure and transmission of zoonotic diseases from wildlife to humans remains a high priority for prevention of pandemics. In our discussion with EcoHealth Alliance, we have agreed to participate in activities that will strengthen the ability of China and other countries in the region to respond to the outbreak of epidemic diseases, particularly those of animal origin. To assist in this study, we will provide participating laboratories in China with human epidemiological information, both new and archived, to support research in bat coronaviruses.

We at the Shanghai CDC look forward to our collaboration with the EcoHealth Alliance team and working further on this worthwhile study.

Sincerely

Fan Wu, M.D.
Director General
Shanghai Municipal Center for Disease Control and Prevention

WUHAN INSTITUTE OF VIROLOGY
The CHINESE ACADEMY OF SCIENCES

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May 23, 2013

To whom it may concern:

On behalf our Institute, I am very pleased to express my strong support for Dr. Zhengli Shi for applying for the R01 entitled "Understanding the Risk of Bat Coronavirus Emergence" under the project managed by Peter Daszak, president of EcoHealth Alliance. Dr. Shi has extensive expertise in viral pathogen discovery. Since 2004, Dr. Shi's laboratory has discovered a variety of genetically diverse bat viruses including bat SARS-like coronavirus, bat adenovirus, and adeno-associated viruses. She has established a worldwide collaborative-group of leading experts on viral pathogens and ecology covering identification of emerging viruses, epidemiology on bat-borne viruses including Hendra and Nipah virus and SARS-coronavirus. Her work with Dr. Peter Daszak led to the discovery of bat SARS-like coronavirus in 2005.

Our Institute would provide all necessary support to Dr. Shi for accomplish the project if it is approved.

Sincerely yours,

Dr. Xinwen Chen
Director, Wuhan Institute of Virology
Chinese Academy of Sciences
Xiao Hong Shan, No. 44
Wuhan 430071 China
(b) (6)

UNC SCHOOL OF PUBLIC HEALTH
DEPARTMENT OF EPIDEMIOLOGY

5/31/2013

Dr. Peter Daszak
President
EcoHealth Alliance
460 W 34th St. 17th Floor
New York, NY 10001
USA

Dear Dr. Daszak,

I am writing in response to a request for collaboration on an upcoming NIAID R01 grant entitled "Understanding the risk of bat coronavirus emergence." I agree that studies are definitely needed to identify the key risk factors and develop strategies that prevent the transmission of bat coronaviruses to human populations. Understanding and preventing exposure and transmission of zoonotic diseases from wildlife to humans remains a high priority for prevention of pandemics.

Our laboratory has developed a variety of animal models for understanding human coronavirus pathogenesis in vivo. We have developed transgenic mouse models in the C57BL/6 mice, expressing hACE2 in ciliated cells from the FOXJ1 promoter. Unlike other epithelial cell promoters (e.g., K18, hACE2 expression from FOXJ1 should be specific to the airway epithelium. FOXJ1 (hepatocyte nuclear factor-3/forkhead homologue 4; HFH-4) is a member of the forkhead/winged helix family of transcription factors whose expression is tightly restricted to cells possessing motile cilia or flagella. Inoculation of these mice with wild type SARS-CoV resulted in lethal respiratory tract infections characterized by high virus titers (>10^8 PFU/day 4), hemorrhage, severe pneumonia and acute respiratory distress syndrome between days 2-7 post infection (Fig 1). We also have aged and immunosenescent models that are highly vulnerable to synthetically reconstructed strains of SARS-CoV from early in the epidemic. This letter states my willingness to collaborate with your group to evaluate the in vivo pathogenesis of interesting bat and animal SARS-like coronaviruses.

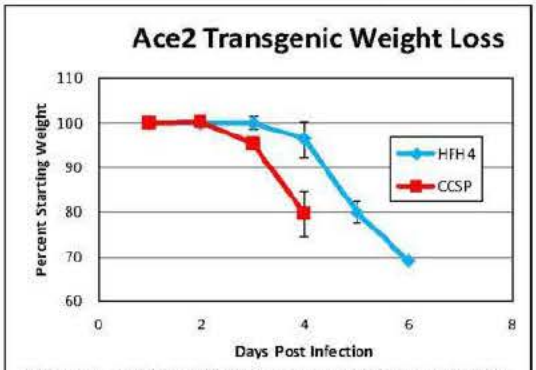

Figure 1. FOXJ1 ACE2 Transgenic Mice are Highly Susceptible to wildtype SARS-CoV Infection. Two different lines were infected with wildtype SARS-virus and clinical disease evaluated at different times postinfection.

It was a pleasure talking with you the other day. I believe your proposal asks fundamentally important questions in the evolution of new human coronaviruses from bats, contributes

dramatically to our understanding of coronavirus variation in natural populations, and provides key insights into the ecology of new emerging infectious diseases. Let me know if I can be of any additional assistance.

Sincerely,

Ralph S. Baric, Professor
Department of Epidemiology
Department of Microbiology and Immunology
Ph: (b) (6)
Email: (b) (6)

云南省地方病防治所
YUNNAN INSTITUTE OF ENDEMIC DISEASES CONTROL AND PREVENTION (YIEDC)

Dr. Peter Daszak
President
EcoHealth Alliance
460 W 34th St. 17th Floor
New York, NY 10001
USA

Dear Dr. Daszak,

I am writing in response to a request for collaboration on an upcoming NIAID funded R01 entitled " Understanding the risk of bat coronavirus emergence." The Yunnan Institute of Endemic Diseases Control and Prevention (EDC) has a high interest in working with EcoHealth Alliance and its scientists in identifying and preventing the transmission of bat coronaviruses to human populations.

The Yunnan EDC recognizes the mutual benefits to be gained through research cooperation and a successful partnership with EcoHealth Alliance, and long term colleague ZhengLi Shi, in the field of identification and prevention of zoonotic disease transmission. It is vital to not only identify the diseases themselves, but also identify high-risk human populations and the actions that put them at risk for infection along with evaluating approaches to intervention and disease management.

Understanding and preventing exposure and transmission of zoonotic diseases from wildlife to humans remains a high priority for prevention of pandemics. In our discussion with EcoHealth Alliance, we have agreed to participate in activities that will strengthen the ability of China and other countries in the region to respond to the outbreak of epidemic diseases, particularly those of animal origin. To assist in this study, we will provide participating laboratories in China with human samples, both new and archived, and support research in bat coronaviruses.

We at the Yunnan EDC look forward to our collaboration with the EcoHealth Alliance team and working further on this worthwhile study.

Sincerely,

Zhang Yunzhi
Yunnan Institute of Endemic Diseases Control and Prevention
Tel: (b) (6) E-mail: (b) (6)

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广东省疾病预防控制中心
Guangdong Provincial Center for Disease Control and Prevention

Dr. Peter Daszak
President
EcoHealth Alliance
460 W 34th St. 17th Floor
New York, NY 10001
USA

Dear Dr. Daszak,

I am writing in response to a request for collaboration on an upcoming NIAID funded R01 entitled " Understanding the risk of bat coronavirus emergence." The Guangdong CDC has a high interest in working with EcoHealth Alliance and its scientists in identifying and preventing the transmission of bat coronaviruses to human populations.

The Guangdong CDC recognizes the mutual benefits to be gained through research cooperation and a successful partnership with EcoHealth Alliance in the field of identification and prevention of zoonotic disease transmission. This partnership will continue a successful five year relationship between the Guangdong CDC and EcoHealth Alliance. It is vital to not only identify the diseases themselves, but also identify high-risk human populations and the actions that put them at risk for infection along with evaluating approaches to intervention and disease management.

Understanding and preventing exposure and transmission of zoonotic diseases from wildlife to humans remains a high priority for prevention of pandemics. In our discussion with EcoHealth Alliance, we have agreed to participate in activities that will strengthen the ability of China and other countries in the region to respond to the outbreak of epidemic diseases, particularly those of animal origin. To assist in this study, we will provide participating laboratories in China with human samples, both new and archived, and support research in bat coronaviruses.

We at the Guangdong CDC look forward to our collaboration with the EcoHealth Alliance team and working further on this worthwhile study.

Sincerely,

Ke Changwen

Ke Changwen

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華東師範大學
科学与技术跨学科高等研究院
Institutes for Advanced Interdisciplinary Research, ECNU

25 May 2013

Dr. Peter Daszak
President
EcoHealth Alliance
460 W 34th St. 17th Floor
New York, NY 10001
USA

Dear Dr. Daszak,

As Dean of Institutes for Advanced Interdisciplinary Research, I am delighted at the prospect of our continued collaboration on the NIAID funded R01 "Understanding the Risk of Bat Coronavirus Emergence."

Since 2005, our organizations have collaborated via our School of Life Science. We have a joint-MOU as well. I have enjoyed our close working relationship with EcoHealth Alliance especially on issues related to emerging infectious diseases and health.

Our collaborations include past and current research projects in Guangzhou, Guangxi, Yunnan, Hainan, and Shanghai as well as capacity building, training, and over 20 joint publications including Science papers, which have led to increased understanding of the ecology of disease dynamics and garnered invaluable data towards predicting and preventing zoonotic disease emergence. My field and laboratory teams based in Beijing, Shanghai, Guangxi, and Guangzhou are ideally positioned to conduct both research and surveillance as we work towards reducing the risk of zoonosis in China.

In our discussion with EcoHealth Alliance, I have agreed to participate in activities that will strengthen the ability of China and other countries in the region to respond to the outbreak of epidemic diseases – particularly those of animal origin.

I look forward to our continued collaboration and the results of this exciting and timely project.

Sincerely,

Zhang shu-yi

Dr. Zhang Shu-Yi
Dean of Institutes for Advanced Interdisciplinary Research
East China Normal University
B319, Science Building, 3663, North Zhongshan Road,
Shanghai 200062 China
(b) (6)

RESOURCE SHARING PLAN:

Data Sharing Plan*:* Sequence data will be made publicly available via GenBank, and shared when requested by other scientists, as soon as a publication is in press. Viral isolates will remain at the Wuhan Institute of Virology initially. Isolates, reagents and any other products, should they be developed, will be made available to other NIH-funded researchers via applicable Wuhan Institute of Virology and EcoHealth Alliance Material Transfer Agreements and/or licensing agreements.

Sharing Model Organisms*:* We do not anticipate the development of any model organisms from this study. Should any be developed, they will be made available to other NIH-funded researchers via applicable Wuhan Institute of Virology and EcoHealth Alliance Material Transfer Agreements and/or licensing agreements.
Genome Wide Association Studies (GWAS): N/A

PHS 398 Checklist

OMB Number: 0925-0001

1. Application Type:

From SF 424 (R&R) Cover Page. The responses provided on the R&R cover page are repeated here for your reference, as you answer the questions that are specific to the PHS398.

* Type of Application:

☒ New ☐ Resubmission ☐ Renewal ☐ Continuation ☐ Revision

Federal Identifier: GRANT11418218

2. Change of Investigator / Change of Institution Questions

☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:
* First Name:
Middle Name:
* Last Name:
Suffix:

☐ Change of Grantee Institution

* Name of former institution:

3. Inventions and Patents (For renewal applications only)

* Inventions and Patents: Yes ☐ No ☐

If the answer is "Yes" then please answer the following:

* Previously Reported: Yes ☐ No ☐

4. * Program Income

Is program income anticipated during the periods for which the grant support is requested?

☐ Yes ☒ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

*Budget Period	*Anticipated Amount ($)	*Source(s)

5. * Disclosure Permission Statement

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☒ Yes ☐ No