From: Lauer, Michael (NIH/OD) [E] (b) (6)
Sent: 4/15/2020 11:08:42 AM
To: Tabak, Lawrence (NIH/OD) [E] (b) (6); Erbelding, Emily (NIH/NIAID) [E] (b) (6)
CC: Marston, Hilary (NIH/NIAID) [E] (b) (6); Lauer, Michael (NIH/OD) [E] (b) (6)
Subject: Re: Draft response for review -- FW: Request for information: Senate Qs - Wuhan Institute of Virology
Attachments: Re: Wuhan lab research

Thanks – just sent you budget details.

Mike

From: "Tabak, Lawrence (NIH/OD) [E]" (b) (6)
Date: Tuesday, April 14, 2020 at 10:12 PM
To: "Erbelding, Emily (NIH/NIAID) [E]" (b) (6)
Cc: "Marston, Hilary (NIH/NIAID) [E]" (b) (6), "Lauer, Michael (NIH/OD) [E]" (b) (6)
Subject: Re: Draft response for review -- FW: Request for information: Senate Qs - Wuhan Institute of Virology

Thanks Emily.
Looping in Mike Lauer,
Larry

From: "Erbelding, Emily (NIH/NIAID) [E]" (b) (6)
Date: Tuesday, April 14, 2020 at 10:11 PM
To: "Tabak, Lawrence (NIH/OD) [E]" (b) (6)
Cc: "Marston, Hilary (NIH/NIAID) [E]" (b) (6)
Subject: Fwd: Draft response for review -- FW: Request for information: Senate Qs - Wuhan Institute of Virology

I am forwarding draft response below to inquiry from Rubio et al earlier.

PI is Peter Dazsak, Eco Health alliance in NYC. Wuhan subcontract is approximately 74k per year. I will try to find more accurate subcontract numbers.

Sent from my iPad

Begin forwarded message:

> **From:** "Abbey, Lillian (NIH/NIAID) [E]" (b) (6)
> **Date:** April 14, 2020 at 4:24:34 PM EDT
> **To:** "Cassetti, Cristina (NIH/NIAID) [E]" (b) (6), "Erbelding, Emily (NIH/NIAID) [E]" (b) (6)
> **Cc:** "Ford, Andrew (NIH/NIAID) [E]" (b) (6), "Bateman, Karen (NIH/NIAID) [E]" (b) (6), "Werner, Alyssa (NIH/NIAID) [E]" (b) (6), "Mulach, Barbara (NIH/NIAID) [E]" (b) (6)
> **Subject: Draft response for review -- FW: Request for information: Senate Qs - Wuhan Institute of Virology**

Dear Cristina and Emily,
Incorporated below in red font is a draft response Andrew developed based on his discussion with Erik. [redacted] (b) (5) Also, Andrew provided the attached publication from mid-March, noting that we may want to share it with the OD.

DRAFT RESPONSE:

Project Number:	2R01AI110964-06	**Contact PI / Project Leader:**	DASZAK, PETER
Title:	UNDERSTANDING THE RISK OF BAT CORONAVIRUS EMERGENCE	**Awardee Organization:**	ECOHEALTH ALLIANCE, INC.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9819304&icde=49588715&ddparam=&ddvalue=&ddsub=&cr=1&csb=default&cs=ASC&pball=

1) What are the goals of the main grant:
[redacted] (b) (5)
2) What are the specific activities supported by the sub to the Wuhan lab and the total costs associated with these activities. Please verify if the creation of recombinant bat in Wuhan is included in their research activities.
[redacted] (b) (5)

Total award information is available in Reporter at link above but budget information about subcontracts is not publicly available as these awards are administered by the grantee institution.

From: Crawford, Chase (NIH/NIAID) [E] [redacted] (b) (6)
Sent: Monday, April 13, 2020 5:41 PM
To: NIAID BUGS <BUGS@niaid.nih.gov>
Cc: Auchincloss, Hugh (NIH/NIAID) [E] [redacted] (b) (6); Harper, Jill (NIH/NIAID) [E] [redacted] (b) (6); NIAID OCGR Leg <NIAIDOCGRLeg@mail.nih.gov>
Subject: Request for information: Senate Qs - Wuhan Institute of Virology

Hi BUGS,

Staff to Senator Marco Rubio (R-FL) has forwarded an email to Building 1 from the White Coat Waste Project (see bottom of email chain). The forwarded message links to recent articles in The Daily Mail and the Washington Examiner on NIH support for previous coronavirus studies involving the Wuhan

Institute of Virology. Building 1 has asked if NIAID has any information related to this research that we can share with staff to Senators Rubio and Mike Braun (R-IN).

To help us better understand this congressional request, is there any background information that you can provide on the activities discussed in the articles referenced below?

Thanks,
Chase
(b) (6)

From: LaMontagne, Karen (NIH/OD) [E] (b) (6)
Sent: Monday, April 13, 2020 4:23 PM
To: NIAID OCGR Leg <NIAIDOCGRLeg@mail.nih.gov>
Subject: Senate Qs - Wuhan Institute of Virology

Hi, NIAID,

Separately, we have heard from the offices of Senators Rubio and Braun about these linked articles:

White Coat Waste
Daily Mail
Washington Examiner

Both offices have asked if there's any information we can share with them related to this matter. Thanks in advance for anything you can provide.

Karen

From: Michelle Mitchell (b) (6)
Date: Monday, April 13, 2020 at 3:42 PM
To: Karen LaMontagne (b) (6)
Subject: Sen. Rubio question - NIH funding Wuhan virus lab

Hey Karen,

Sen. Rubio's staff, Ansley Rhyne, forwarded the email below that she received regarding NIH funding for the Wuhan Institute of Virology. Her boss, along with Rep. Gaetz are working on a letter to ensure no taxpayer dollars are sent to that Institute.

Ansley requested our input. Would you ask NIAID for any information on this issue that we could be shared with Ansley?

Thank you.

MM

From: Justin Goodman <justin@whitecoatwaste.org>
Sent: Monday, April 13, 2020 2:36 PM

To:
Subject: Laura- NIH funding Wuhan virus lab

I hope you had a nice weekend and are staying safe and healthy. I wanted to make sure you saw that our taxpayer watchdog group just exposed that **the National Institutes of Health (NIH) has been sending tax dollars to the controversial Wuhan Institute of Virology for years, including for dangerous lab experiments on coronavirus-infected bats captured from caves.** The Daily Mail, Washington Examiner, Drudge and others ran stories about the troubling find over the weekend.

We're working with Rep. Matt Gaetz (R-FL) and others on a sign-on letter about this and would love to work with you and Senator Rubio as well to ensure no more tax dollars are shipped to the Wuhan Institute of Virology.

I'd be happy to send over more info if you're interested and answer any questions you may have.

Thanks for looking,

Justin

Justin Goodman, M.A.
Vice President, Advocacy and Public Policy
White Coat Waste Project

*Taxpayers shouldn't be forced to pay $20 billion+ for **wasteful** government animal experiments.*

PO Box 26029
Washington, DC 20001
Phone: 860.882.2492
Donate | Blog | Web | Twitter | Facebook

From: Lauer, Michael (NIH/OD) [E] (b) (6)
Sent: 4/15/2020 11:03:46 AM
To: Tabak, Lawrence (NIH/OD) [E] (b) (6)
CC: Schwetz, Tara (NIH/OD) [E] (b) (6); Wolinetz, Carrie (NIH/OD) [E] (b) (6); Lauer, Michael (NIH/OD) [E] (b) (6)
Subject: Re: Wuhan lab research
Attachments: FACTS Snapshot for 2-R01-AI110964-06 DASZAK, PETER QVR.pdf; NoA R01AI110964-06.pdf; NoA R01AI110964-01.pdf

Good morning – see Section IV of the NoAs:

- Type 1: Wuhan gets 134K to 159K per year.
- Type 2: Wuhan gets $76,301.

Thanks, Mike

From: "Tabak, Lawrence (NIH/OD) [E]" (b) (6)
Date: Tuesday, April 14, 2020 at 10:05 PM
To: "Lauer, Michael (NIH/OD) [E]" (b) (6)
Cc: "Schwetz, Tara (NIH/OD) [E]" (b) (6), "Wolinetz, Carrie (NIH/OD) [E]" (b) (6)
Subject: Re: Wuhan lab research

https://projectreporter.nih.gov/project_info_description.cfm?aid=9819304&icde=49593891&ddparam=&ddvalue=&ddsub=&cr=1&csb=default&cs=ASC&pball=

can we get subproject info – costs to Wuhan?

From: "Tabak, Lawrence (NIH/OD) [E]" (b) (6)
Date: Tuesday, April 14, 2020 at 10:00 PM
To: "Lauer, Michael (NIH/OD) [E]" (b) (6)
Cc: "Schwetz, Tara (NIH/OD) [E]" (b) (6), "Wolinetz, Carrie (NIH/OD) [E]" (b) (6)
Subject: Re: Wuhan lab research

Is this what they are referring to: https://worldreport.nih.gov/app/#!/

From: "Tabak, Lawrence (NIH/OD) [E]" (b) (6)
Date: Tuesday, April 14, 2020 at 9:50 PM
To: "Lauer, Michael (NIH/OD) [E]" (b) (6)
Cc: "Schwetz, Tara (NIH/OD) [E]" (b) (6), "Wolinetz, Carrie (NIH/OD) [E]" (b) (6)
Subject: FW: Wuhan lab research

Can I get this information asap please?

From: "Pence, Laura (HHS/ASL)" (b) (6)
Date: Tuesday, April 14, 2020 at 9:47 PM
To: "Tabak, Lawrence (NIH/OD) [E]" (b) (6), "Wolinetz, Carrie (NIH/OD) [E]"

(b) (6), "Schwetz, Tara (NIH/OD) [E]" (b) (6)
Subject: Wuhan lab research

Hi! Can we get info on this ASAP? Need for the morning. Sorry for the fire drill.

Begin forwarded message:

> **From:** "Arbes, Sarah (HHS/ASL)" (b) (6)
> **Date:** April 14, 2020 at 9:30:23 PM EDT
> **To:** "Hallett, Adrienne (NIH/OD) [E]" (b) (6), "Pence, Laura (HHS/ASL)" (b) (6)
> **Cc:** "Morse, Sara (HHS/ASL)" (b) (6)
> **Subject: For AMA in the morning**
>
> Adrienne and Laura –
>
> Can you please help me run ground truth to this article?:
> https://www.soundhealthandlastingwealth.com/health-news/u-s-government-gave-3-7million-grant-to-wuhan-lab-that-experimented-on-coronavirus-source-bats/
>
> Congressman Gaetz is publicly criticizing HHS/NIH for funding the Wuhan laboratory's bat research. Here's this quote from another article: "I'm disgusted to learn that for years the US government has been funding dangerous and cruel animal experiments at the Wuhan Institute, which may have contributed to the global spread of coronavirus, and research at other labs in China that have virtually no oversight from US authorities."

- How long have we been giving research dollars to this lab?
- How much have we given?
- For what purpose?
- If asked to defend our research dollars going to this lab for this purpose, what do you recommend we say?
- Anything else we should know?

> Thanks much!
> Sarah

QVR FACTS

FACTS Data Snapshot for: 2-R01-AI110964-06 (DASZAK, PETER)

Understanding the Risk of Bat Coronavirus Emergence

PRINT CLOSE

Appl Id: 981930

Launch the FACTS System: FACTS

Hop to Country: Project Information CHINA SINGAPORE

Project Info

Project Number	2-R01-AI110964-06 (as reflected under competing project number 2-R01-AI110964-06 in FACTS)
PI Name	DASZAK, PETER
Org Name	ECOHEALTH ALLIANCE, INC.
Project Title	Understanding the Risk of Bat Coronavirus Emergence
FY/Project Dates	2019 (Project Period from 2014-06-01 to 2024-06-30)
Project Status	Awarded (05)
Foreign Appl Flag	Domestic Application with Foreign Collaboration (2)

CHINA

State Department Clearance Request (SDCR ID 219890)

Click the - to hide the Research Objective listed on State Department Clearance.

This work is an extension and renewal of a previous award, approved under clearances 202191 and 211200. The aims of this research project are to examine the mechanism through which coronaviruses (CoVs) jump from animal hosts/reservoirs to humans (spillover events). To accomplish this work the PI and his team will conduct detailed surveillance for coronaviruses in four provinces: Yunnan Guizhou, Guangxi, and Guangdong. The exact sites have not yet been identified; as in the previous award, sites will be selected from the four provinces as work progresses. Surveillance will include sampling of wild bat populations. Samples will be collected from animals from each of these sites, and will be analyzed to determine what coronaviruses are present, and whether the viruses are able to infect humans. The investigators plan to collect samples from bats, approximately 5,000 samples total from 15-20 species across all four provinces. Animals will be captured and lightly anesthetized if necessary. They will be swabbed (mouth/nose, urogenital tract, and rectum), and a small amount of blood will be collected. If available, feces and urine will also be collected. Nearly all wild bats will be released unharmed after sampling. A small number of bats (maximum of 2 per species) may be euthanized in order to collect lung and intestinal tissue required for characterizing viral receptors. In order to understand whether select strains of bat-borne CoVs utilize receptors found in bats have the potential to infect people, the investigators will use mice that have been genetically modified to express the human receptor for SARS-CoV. The investigators anticipate identifying 5-6 SARS-related-CoVs that will be tested in mice, using approximately 15-20 mice per virus strain. A maximum of 120 mice will be used for this work over the project. All work involving samples and viral isolates from bats will be performed at the Wuhan Institute of Virology. All animal work will be performed by trained individuals in accordance with the American Veterinary Medical Association guidelines, and the project is overseen by veterinarians. This work has also been reviewed and approved by the investigator's Institutional Animal Care and Use Committee. This project will also study human exposure to animal coronaviruses across the same four provinces in southern China. Samples will be collected from each of these sites from individuals who 1) who are highly exposed to bats in community settings, including through hunting, butchering, or general handling within the context of their living or working environment (18+ years old); and 2) patients admitted to hospitals and clinics presenting with disease symptoms of clinically-defined severe/acute respiratory illness (SARI/ARI) or influenza-like illness (ILI) of unknown origin (12+ years old). Subjects will be enrolled on a voluntary basis and informed consent will be obtained from all participants. Consenting participants will provide biological samples and complete a questionnaire at the time of acute illness and 35 days after resolution of illness. There will be no follow-up among community participants after initial sample collection. The study population will be selected from the Yunnan, Guangxi, Guangdong, and Guizhou provinces of China. They plan to enroll: 1) in 12 clinic sites across the four provinces, 2,750 individuals (accounting for an estimated 40% loss from follow-up); and 2) in 8 community sites, 1,650 individuals per each of the four provinces, pooled across two sites for each province for a total of 6,660 participants. Enrollment is anticipated to be 100% Asian, with a 50/50 split between males and females. All human subject work will be managed by the team at the Institute for Pathogen Biology.

NIAID Contact	SDCR ACTIONS	ACTION DATES
Bernabe, Gayle Phone: 301-451-1018	Approved	2019-05-30
	Approve	2019-05-30
	Submit to State Department	2019-05-29
	Send to Agency	2019-05-28
	IC Update	2019-05-24
	IC Save	2019-05-10

Collaborator/Site (Site ID: 262256)	Site Flags	Budget Period	Budget Amt	Verified By	Verified Date
ZHU, GUANGJIAN EAST CHINA NORMAL UNIVERSITY School of Life Science, 8327 Science building, 3663 Zhongshan Beilu Shanghai 200062	Animals: Y FWA: Humans: N				

Collaborator/Site (Site ID: 262253)	Site Flags	Budget Period	Budget Amt	Verified By	Verified Date
GUO, LI INSTITUTE OF PATHOGEN BIOLOGY Dong Dan San Tiao, No. 9 Dongcheng District Beijing 100730	Animals: N FWA: Y Humans: Y				

Collaborator/Site (Site ID: 262252)	Site Flags	Budget Period	Budget Amt	Verified By	Verified Date
REN, LEI INSTITUTE OF PATHOGEN BIOLOGY Dong Dan San Tiao, No. 9 Dongcheng District Beijing 100730	Animals: N FWA: Y Humans: Y				

Collaborator/Site (Site ID: 262251)	Site Flags	Budget Period	Budget Amt	Verified By	Verified Date
HU, BEN WUHAN INSTITUTE OF VIROLOGY Xiao Hong SHan, No. 44 Wuchang District Wuhan 430071	Animals: Y FWA: Humans: N				

Collaborator/Site (Site ID: 261948)	Site Flags	Budget Period	Budget Amt	Verified By	Verified Date
SHI, ZHENG LI WUHAN INSTITUTE OF VIROLOGY Xiao Hong SHan, No. 44 Wuchang District Wuhan 430071	Animals: Y FWA: Humans: N				

Collaborator/Site (Site ID: 262250)	Site Flags	Budget Period	Budget Amt	Verified By	Verified Date
ZHOU, PENG WUHAN INSTITUTE OF VIROLOGY Xiao Hong SHan, No. 44 Wuchang District Wuhan 430071	Animals: Y FWA: Humans: N				

SINGAPORE

State Department Clearance Request (SDCR ID 219753)	NIAID Contact	SDCR ACTIONS	ACTION DATES
Click the + to show the Research Objective listed on State Department Clearance.	Bernabe, Gayle Phone: 301-451-1018	Approved Auto Approval Send to Agency Submit to State Department IC Save	2019-05-20 2019-05-20 2019-05-06 2019-05-06 2019-05-01

Collaborator/Site (Site ID: 262258)	Site Flags	Budget Period	Budget Amt	Verified By	Verified Date
WANG, LINFA DUKE-NUS MEDICAL SCHOOL 8 College Road Singapore 169857	Animals: N FWA: Humans: N				

Notice of Award

RESEARCH
Department of Health and Human Services
National Institutes of Health

Federal Award Date: 08/05/2019

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Grant Number: 2R01AI110964-06 REVISED
FAIN: R01AI110964

Principal Investigator(s):
PETER DASZAK, PHD

Project Title: Understanding the Risk of Bat Coronavirus Emergence

Dr. Daszak, Peter
PD/PI
460 West 34th Street
Suite 1701
New York, NY 100012320

Award e-mailed to: (b) (6)

Period Of Performance:
Budget Period: 07/24/2019 – 06/30/2020
Project Period: 06/01/2014 – 06/30/2024

Dear Business Official:

The National Institutes of Health hereby revises this award to reflect a decrease in the amount of $71,770 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to ECOHEALTH ALLIANCE, INC. in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Allergy And Infectious Diseases of the National Institutes of Health under Award Number R01AI110964. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

Tseday G Girma
Grants Management Officer
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Additional information follows

SECTION I – AWARD DATA – 2R01AI110964-06 REVISED

Award Calculation (U.S. Dollars)

Salaries and Wages	$170,123
Fringe Benefits	$53,590
Personnel Costs (Subtotal)	$223,713
Consultant Services	$49,750
Materials & Supplies	$20,850
Travel	$15,027
Subawards/Consortium/Contractual Costs	$229,651
Federal Direct Costs	$538,991
Federal F&A Costs	$122,989
Approved Budget	$661,980
Total Amount of Federal Funds Obligated (Federal Share)	$661,980
TOTAL FEDERAL AWARD AMOUNT	$661,980
AMOUNT OF THIS ACTION (FEDERAL SHARE)	($-71,770)

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
6	$661,980	$661,980
7	$637,980	$637,980
8	$637,980	$637,980
9	$637,980	$637,980
10	$637,980	$637,980

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Name:	Allergy and Infectious Diseases Research
CFDA Number:	93.855
EIN:	1311726494A1
Document Number:	RAI110964B
PMS Account Type:	P (Subaccount)
Fiscal Year:	2019

IC	CAN	2019	2020	2021	2022	2023
AI	8472364	$661,980	$637,980	$637,980	$637,980	$637,980

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: M51C B / **OC**: 414B / **Released**: (b) (6) 08/02/2019
Award Processed: 08/05/2019 12:01:51 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 2R01AI110964-06 REVISED

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – TERMS AND CONDITIONS – 2R01AI110964-06 REVISED

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.

c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2. As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

An unobligated balance may be carried over into the next budget period without Grants Management Officer prior approval.

This grant is subject to Streamlined Noncompeting Award Procedures (SNAP).

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) R01AI110964. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Apperdix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:
Additional Costs

SECTION IV – AI Special Terms and Conditions – 2R01AI110964-06 REVISED

Clinical Trial Indicator: No
This award does not support any NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

REVISED AWARD: This award is revised to adjust the budget in accordance with the letter from Aleksei Chmura/ECOHealth Alliance.

Supersedes previous Notice of Award dated **07/24/2019**.

****

This Notice of Award (NoA) includes funds for activity with **The University of North Carolina at Chapel Hill** in the amount of **$77,750** (**$50,000** direct costs **+ $27,750**F&A costs).

This Notice of Award (NoA) includes funds for activity with **Wuhan Institute of Virology** in the amount of **$76,301** (**$70,649** direct costs **+ $5,652** F&A costs).

This Notice of Award (NoA) includes funds for activity with **Institute of Pathogen Biology** in the amount of **$75,600** (**$70,000** direct costs **+ $5,600** F&A costs).

****

The Research Performance Progress Report (RPPR), Section G.9 (Foreign component), includes reporting requirements for all research performed outside of the United States. Research conducted at the following site(s) must be reported in your RPPR:

Wuhan Institute of Virology, CHINA

Institute of Pathogen Biology, CHINA

East China Normal University, CHINA

Duke-NUS Medical School, SINGAPORE

****

This award reflects current Federal policies regarding Facilities & Administrative (F&A) Costs for foreign grantees including foreign sub-awardees, and domestic awards with foreign sub-awardees. Please see: Chapter 16 Grants to Foreign Organizations, International Organizations, and Domestic Grants with Foreign Components, Section 16.6 "Allowable and Unallowable Cost" of the NIH Grants Policy.

****

This award may include collaborations with and/or between foreign organizations. Please be advised that short term travel visa expenses are an allowable expense on this grant, if justified as critical and necessary for the conduct of the project.

****

The budget period anniversary start date for future year(s) will be **July** 1.

****

Dissemination of study data will be in accord with the Recipient's accepted genomic data sharing plan as stated in the page(s) **203** of the application. Failure to adhere to the sharing plan as mutually agreed upon by the Recipient and the NIAID may result in Enforcement Actions as described in the NIH Grants Policy Statement.

****

This award is subject to the Clinical Terms of Award referenced in the NIH Guide for Grants and Contracts, July 8, 2002, NOT AI-02-032. These terms and conditions are hereby incorporated by

reference, and can be accessed via the following World Wide Web address: https://www.niaid.nih.gov/grants-contracts/niaid-clinical-terms-award All submissions required by the NIAID Clinical Terms of Award must be forwarded electronically or by mail to the responsible NIAID Program Official identified on this Notice of Award.

****

Awardees who conduct research involving Select Agents (see 42 CFR 73 for the Select Agent list; and 7 CFR 331 and 9 CFR 121 for the relevant animal and plant pathogens at http://www.selectagents.gov/Regulations.html) must complete registration with CDC (or APHIS, depending on the agent) before using NIH funds. No funds can be used for research involving Select Agents if the final registration certificate is denied.

Prior to conducting a restricted experiment with a Select Agent or Toxin, awardees must notify the NIAID and must request and receive approval from CDC or APHIS.

****

Select Agents:
Awardee of a project that at any time involves a restricted experiment with a select agent, is responsible for notifying and receiving prior approval from the NIAID. Please be advised that changes in the use of a Select Agent will be considered a change in scope and require NIH awarding office prior approval. The approval is necessary for new select agent experiments as well as changes in on-going experiments that would require change in the biosafety plan and/or biosafety containment level. An approval to conduct a restricted experiment granted to an individual cannot be assumed an approval to other individuals who conduct the same restricted experiment as defined in the Select Agents Regulation 42 CFR Part 73, Section 13.b (http://www.selectagents.gov/Regulations.html).

Highly Pathogenic Agent:
NIAID defines a Highly Pathogenic Agent as an infectious Agent or Toxin that may warrant a biocontainment safety level of BSL3 or higher according to the current edition of the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL) (http://www.cdc.gov/OD/ohs/biosfty/bmbl5/bmbl5toc.htm). Research funded under this grant must adhere to the BMBL, including using the BMBL-recommended biocontainment level at a minimum. If your Institutional Biosafety Committee (or equivalent body) or designated institutional biosafety official recommend a higher biocontainment level, the highest recommended containment level must be used.
When submitting future Progress Reports indicate at the beginning of the report:

If no research with a Highly Pathogenic Agent or Select Agent has been performed or is planned to be performed under this grant.

If your IBC or equivalent body or official has determined, for example, by conducting a risk assessment, that the work being planned or performed under this grant may be conducted at a biocontainment safety level that is lower than BSL3.

If the work involves Select Agents and/or Highly Pathogenic Agents, also address the following points:

Any changes in the use of the Agent(s) or Toxin(s) including its restricted experiments that have resulted in a change in the required biocontainment level, and any resultant change in location, if applicable, as determined by your IBC or equivalent body or official.

If work with a new or additional Agent(s)/Toxin(s) is proposed in the upcoming project period, provide:

- A list of the new and/or additional Agent(s) that will be studied;
- A description of the work that will be done with the Agent(s), and whether or not the work is a restricted experiment;
- The title and location for each biocontainment resource/facility, including the name of the organization that operates the facility, and the biocontainment level at which the work will be conducted, with documentation of approval by your IBC or equivalent body or official. It is important to note if the work is being done in a new location.

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: Tseday G Girma
Email: (b) (6) **Phone**: (b) (6) **Fax**: 301-493-0597

Program Official: Erik J. Stemmy
Email: (b) (6) **Phone**: (b) (6)

SPREADSHEET SUMMARY
GRANT NUMBER: 2R01AI110964-06 REVISED

INSTITUTION: ECOHEALTH ALLIANCE, INC.

Budget	Year 6	Year 7	Year 8	Year 9	Year 10
Salaries and Wages	$170,123	$170,123	$170,123	$170,123	$170,123
Fringe Benefits	$53,590	$53,590	$53,590	$53,590	$53,590
Personnel Costs (Subtotal)	$223,713	$223,713	$223,713	$223,713	$223,713
Consultant Services	$49,750	$49,750	$49,750	$49,750	$49,750
Materials & Supplies	$20,850	$14,850	$14,850	$14,850	$14,850
Travel	$15,027	$15,027	$15,027	$15,027	$15,027
Subawards/Consortium/Contractual Costs	$229,651	$229,651	$229,651	$229,651	$229,651
Publication Costs		$6,000	$6,000	$6,000	$6,000
TOTAL FEDERAL DC	$538,991	$538,991	$538,991	$538,991	$538,991
TOTAL FEDERAL F&A	$122,989	$98,989	$98,989	$98,989	$98,989
TOTAL COST	$661,980	$637,980	$637,980	$637,980	$637,980

Facilities and Administrative Costs	Year 6	Year 7	Year 8	Year 9	Year 10
F&A Cost Rate 1	32%	32%	32%	32%	32%
F&A Cost Base 1	$384,340	$309,340	$309,340	$309,340	$309,340
F&A Costs 1	$122,989	$98,989	$98,989	$98,989	$98,989

RESEARCH **Issue Date:** 05/27/2014

Department of Health and Human Services
National Institutes of Health
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Grant Number: 1R01AI110964-01
FAIN: R01AI110964

Principal Investigator(s):
PETER DASZAK, PHD

Project Title: Understanding the Risk of Bat Coronavirus Emergence

Aleksei
President
460 West 34th Street
17th Floor
New York, NY 100012317

Award e-mailed to: (b) (6)

Budget Period: 06/01/2014 – 05/31/2015
Project Period: 06/01/2014 – 05/31/2019

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $666,442 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to ECOHEALTH ALLIANCE, INC. in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Allergy And Infectious Diseases of the National Institutes of Health under Award Number R01AI110964. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

Laura A. Pone
Grants Management Officer
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Additional information follows

SECTION I – AWARD DATA – 1R01AI110964-01

Award Calculation (U.S. Dollars)

Salaries and Wages	$167,708
Fringe Benefits	$54,168
Supplies	$21,400
Travel Costs	$35,918
Other Costs	$10,000
Consortium/Contractual Cost	$227,663
Federal Direct Costs	$516,857
Federal F&A Costs	$149,585
Approved Budget	$666,442
Federal Share	$666,442
TOTAL FEDERAL AWARD AMOUNT	$666,442
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$666,442

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
1	$666,442	$666,442
2	$630,445	$630,445
3	$611,090	$611,090
4	$597,112	$597,112
5	$581,646	$581,646

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Number:	93.855
EIN:	1311726494A1
Document Number:	RAI110964A

PMS Account Type:	P (Subaccount)
Fiscal Year:	2014

IC	CAN	2014	2015	2016	2017	2018
AI	8472350	$666,442	$630,445	$611,090	$597,112	$581,646

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: M51C / **OC**: 414A / **Released**: (b) (6) 05/20/2014
Award Processed: 05/08/2014 01:52:21 PM

SECTION II – PAYMENT/HOTLINE INFORMATION – 1R01AI110964-01

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – TERMS AND CONDITIONS – 1R01AI110964-01

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.

b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 74 or 45 CFR Part 92 as applicable.
d. The NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

An unobligated balance may be carried over into the next budget period without Grants Management Officer prior approval.

This grant is subject to Streamlined Noncompeting Award Procedures (SNAP).

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the Central Contractor Registration. Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) R01AI110964. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

Treatment of Program Income:
Additional Costs

SECTION IV – AI Special Terms and Conditions – 1R01AI110964-01

THIS AWARD CONTAINS GRANT SPECIFIC RESTRICTIONS. THESE RESTRICTIONS MAY ONLY BE LIFTED BY A REVISED NOTICE OF AWARD.

RESTRICTION: This award is issued with the knowledge that subjects may be involved within the period of support, but definite plans were not set forth in the application as per 45 CFR 46.118. No human subjects may be involved in any project supported by this award until all requirements for Human Subjects research as identified in the PHS398/SF424 Instructions have been provided to and approved by NIH.

RESTRICTION: The present award is being made without a currently valid certification of IRB approval for this project with the following restriction: Only activities that are clearly severable and independent from activities that involve human subjects may be conducted pending the NIAID's acceptance of the certification of IRB review and approval.

No funds may be drawn down from the payment system and no obligations may be made against Federal funds for any research involving human subjects prior to the NIAID's notification to the grantee that the identified issues have been resolved and this restriction removed.

~~~~~~~~~
This award includes funds for subcontract/consortium activity with Wuhan Institute of Virology, CHINA and is budgeted as follows:

	-Yr 1	-Yr 2	-Yr 3	-Yr 4	-Yr 5
Total Direct Costs	$123,699	$128,718	$147,335	$147,335	$147,335
F&A Costs @ 8%(MTDC)	$9,896	$10,297	$11,787	$11,787	$11,787
TOTAL COSTS	$133,595	$139,015	$159,122	$159,122	$159,122

Consortiums are to be established and administered as described in the NIH Grants Policy Statement. This written agreement with the consortium must address the negotiated arrangements for meeting the scientific, administrative, financial, and reporting requirements for this grant.
~~~~~~~~~
This award includes funds for subcontract/consortium activity with East China Normal University, CHINA and is budgeted as follows:

	-Yr 1	-Yr 2	-Yr 3	-Yr 4	-Yr 5
Total Direct Costs	$87,100	$67,300	$50,108	$39,167	$14,850
F&A Costs @ 8%(MTDC)	$6,968	$5,384	$4,009	$3,133	$2,404
TOTAL COSTS	$94,068	$72,684	$54,117	$42,300	$32,454

Consortiums are to be established and administered as described in the NIH Grants Policy Statement. This written agreement with the consortium must address the negotiated arrangements for meeting the scientific, administrative, financial, and reporting requirements for this grant.
~~~~~~~~~
Select Agents:
Awardee of a project that at any time involves a restricted experiment with a select agent, is responsible for notifying and receiving prior approval from the NIAID. Please be advised that changes in the use of a Select Agent will be considered a change in scope and require NIH awarding office prior approval. The approval is necessary for new select agent experiments as well as changes in on-going experiments that would require change in the biosafety plan and/or biosafety containment level. An approval to conduct a restricted experiment granted to an individual cannot be assumed an approval to other individuals who conduct the same restricted experiment as defined in the Select Agents Regulation 42 CFR Part 73, Section 13.b (http://www.selectagents.gov/Regulations.html).

Highly Pathogenic Agent:
NIAID defines a Highly Pathogenic Agent as an infectious Agent or Toxin that may warrant a biocontainment safety level of BSL3 or higher according to the current edition of the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL) (http://www.cdc.gov/OD/ohs/biosfty/bmbl5/bmbl5toc.htm). Research funded under this grant must adhere to the BMBL, including using the BMBL-recommended biocontainment level at a minimum. If your Institutional Biosafety Committee (or equivalent body) or designated institutional biosafety official recommend a higher biocontainment level, the highest recommended containment level must be used.
When submitting future Progress Reports indicate at the beginning of the report:

If no research with a Highly Pathogenic Agent or Select Agent has been performed or is planned to be performed under this grant.

If your IBC or equivalent body or official has determined, for example, by conducting a risk assessment, that the work being planned or performed under this grant may be conducted at a biocontainment safety level that is lower than BSL3.

If the work involves Select Agents and/or Highly Pathogenic Agents, also address the following points:

Any changes in the use of the Agent(s) or Toxin(s) including its restricted experiments that have resulted in a change in the required biocontainment level, and any resultant change in location, if applicable, as determined by your IBC or equivalent body or official.
~~~~~~~~~

If work with a new or additional Agent(s)/Toxin(s) is proposed in the upcoming project period, provide:

o A list of the new and/or additional Agent(s) that will be studied;
o A description of the work that will be done with the Agent(s), and whether or not the work is a restricted experiment;
o The title and location for each biocontainment resource/facility, including the name of the organization that operates the facility, and the biocontainment level at which the work will be conducted, with documentation of approval by your IBC or equivalent body or official. It is important to note if the work is being done in a new location.

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Grants Management Specialist: Laura A. Pone
Email: (b) (6) **Phone**: (b) (6) **Fax**: 301-493-0597

Program Official: Erik J. Stemmy
Email: (b) (6) **Phone**: (b) (6)

SPREADSHEET SUMMARY
GRANT NUMBER: 1R01AI110964-01

INSTITUTION: ECOHEALTH ALLIANCE, INC.

Budget	Year 1	Year 2	Year 3	Year 4	Year 5
Salaries and Wages	$167,708	$167,708	$167,708	$167,708	$167,708
Fringe Benefits	$54,168	$54,168	$54,168	$54,168	$54,168
Supplies	$21,400	$19,250	$7,250	$7,000	$3,500
Travel Costs	$35,918	$35,918	$35,918	$35,918	$35,918
Other Costs	$10,000	$13,550	$11,050	$9,800	$9,400
Consortium/Contractual Cost	$227,663	$211,699	$213,239	$201,422	$191,576
TOTAL FEDERAL DC	$516,857	$502,293	$489,333	$476,016	$462,270
TOTAL FEDERAL F&A	$149,585	$128,152	$121,757	$121,096	$119,376
TOTAL COST	$666,442	$630,445	$611,090	$597,112	$581,646

Facilities and Administrative Costs	Year 1	Year 2	Year 3	Year 4	Year 5
F&A Cost Rate 1	44.1%	44.1%	44.1%	44.1%	44.1%
F&A Cost Base 1	$339,194	$290,594	$276,094	$274,594	$270,694
F&A Costs 1	$149,585	$128,152	$121,757	$121,096	$119,376

Subject: Re: Regarding 2R01AI110964-06
Date: Friday, March 5, 2021 at 7:13:02 AM Eastern Standard Time
From: Lauer, Michael (NIH/OD) [E]
To: Fenton, Matthew (NIH/NIAID) [E]
CC: Lauer, Michael (NIH/OD) [E]

OK – you and I need to talk. Just the two of us. Please work with Melanie to find a time (30 minutes, Zoom) that works.

Mike

From: "Fenton, Matthew (NIH/NIAID) [E]" (b) (6)
Date: Friday, March 5, 2021 at 6:45 AM
To: "Lauer, Michael (NIH/OD) [E]" (b) (6)
Subject: Re: Regarding 2R01AI110964-06

Mike - NIAID want to see this non-compliance matter come to a successful resolution so that important research continues and any future grants to EcoHealth Alliance don't get held up. (b) (5)

Matthew

> On Mar 4, 2021, at 10:06 PM, Lauer, Michael (NIH/OD) [E] (b) (6) wrote:
>
> ?
>
> ---
>
> **From:** Peter Daszak (b) (6)
> **Date:** Thursday, March 4, 2021 at 10:02 PM
> **To:** "Lauer, Michael (NIH/OD) [E]" (b) (6)
> **Cc:** Aleksei Chmura (b) (6), Alison Andre (b) (6)
> **Subject:** Regarding 2R01AI110964-06
>
> Dear Dr. Lauer,
>
> I spoke yesterday with my program officer and other NIAID staff regarding our grant on the risk of coronavirus emergence (2R01AI110964-06) that includes collaboration with scientists at the Wuhan Institute of Virology, China. Dr. Matthew Fenton joined the

meeting and told me about his conversation with you about the conditions currently in place on our grant and my efforts to address some of them via my recent work in Wuhan with the WHO. He also commented that you would be willing to talk with me, as PI of this award, about a pathway to reinstate this grant. I would very much value this and am emailing to see if we can arrange a time that's suitable for you, perhaps next week if possible?

I'm cc'ing my assistant Alison Andre, who can help arrange a suitable time, and also our Chief of Staff Aleksei Chmura, who I would hope could join us, as someone who can access any relevant information on this award, and gained his own Ph.D as part of our original R01 work in China. I want to reassure you that I would not request to talk with legal counsel or bring them into a conversation, and that this would be a discussion with scientists focused on the goals of the grant, focused on research to protect us all against further coronavirus spillover.

Sincerely,

Peter

Peter Daszak
President

EcoHealth Alliance
460 West 34th Street
New York, NY 10001
USA

Tel.: (b) (6)
Website: www.ecohealthalliance.org

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation

EcoHealth Alliance

Dr. Michael Lauer
Deputy Director for Extramural Research,
NIH, Bethesda, MD.

Re: R01AI110964 and 2R01AI110964
"Understanding the Risk of Bat Coronavirus Emergence"

April 23rd 2021

Dear Dr. Lauer,

I am responding your letter of 4/13/21 regarding our response to conditions placed on the suspended NIH grant 2R01AI110964 "*Understanding the Risk of Bat Coronavirus Emergence*". In particular, this letter addresses your request for documentation on our assessment of WIV's compliance with terms of our subcontracts from the initial (now expired) 5-year award:

"*...copies of all EcoHealth Alliance – WIV subrecipient agreements as well as any and all other documents and information describing how EcoHealth Alliance monitored WIV's compliance with the terms and conditions of award .... NIH must have the right of access to any documents, papers, or other records of the non-Federal entity which are pertinent to the Federal award, in order to make audits, examinations, excerpts, and transcripts" (45 C.F.R. § 75.364); and must have "timely and reasonable access to the non-Federal entity's personnel for the purpose of interview and discussion related to such documents" (id.). These requirements flow down to subawards to subrecipients. 45 C.F.R. § 75.101. "Non-Federal entities must comply with requirements in [45 C.F.R. Part 75] regardless of whether the non-Federal entity is a recipient or subrecipient of a Federal award." 45 C.F.R. 75.101. As the grantee, EcoHealth was required to have in place, "A requirement that the subrecipient permit the pass-through entity and auditors to have access to the subrecipient's records and financial statements as necessary for the pass-through entity to meet the requirements of this part." 45 C.F.R. § 75.352(a)(5)...*"

As requested, we have supplied all EcoHealth Alliance-WIV subrecipient agreements, as well as documents pertaining to EHA's monitoring of WIV's compliance with the terms and conditions of award. The attached documents demonstrate that we have fulfilled all requirements in the CFR codes listed in your letter excerpted above. These documents include:

1. EcoHealth Alliance 2016-2019 Subrecipient Monitoring Forms for WIV. EcoHealth Alliance began this formal subrecipient monitoring policy in 2016 as per OMB Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards (2 CFR 200) ("Uniform Guidance"), specifically §200.331.
2. 2006-2018 WIV Annual Reports. In addition, NIH has full reports on the programmatic results that we filed annually.
3. Wuhan Institute of Virology contracts and invoices for all 5 Years of Grant R01AI110964: 2014-2019
4. Federal Funding Accountability & Transparency Act Reports for WIV. From 2015 – 2019
5. Annual Independent Audit Reports from 2014-2019
6. Inter-Institutional Agreements from DHHS for WIV 2014 & 2019

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018
212.380.4460
EcoHealthAlliance.org

We hope these documents satisfy your request by demonstrating that EcoHealth Alliance maintained detailed records of our appropriate monitoring of WIV's performance against the conditions of our initial (now expired) R01 grant and our contracts with them.

We also would like draw your attention to our letter dated 4.11.2021 regarding plans for biosafety monitoring for the renewal R01, under which we had not yet set up a subcontract with WIV, specifically:

"8. Provide copies of all EcoHealth Alliance – WIV subrecipient agreements as well as any other documents and information describing how EcoHealth Alliance monitored WIV's compliance with the terms and conditions of award, including with respect to biosafety.
As we related in response to your letter of 4/19/2020 that asked us to suspend work with WIV, we had not yet set up a subcontract with WIV for the period of this award, therefore no such subrecipient agreements exist. Our plan was to monitor WIV's compliance as we had in the 5 years prior, by means of semi-annual meetings with the lead investigator and assessments of compliance against all conditions of the award. Additionally, following the NIH's termination, then reinstatement and suspension of our funding, we have contracted with a leading lab biosafety contractor based in Southeast Asia (Dr. Paul Selleck) who has extensive experience commissioning, accrediting and auditing BSL-2, -3, and -4 labs, and has worked for over a decade at the BSL-4 Australian Animal Health Lab. We will be using their services where appropriate for foreign lab subcontractees to assess lab biosafety procedures and conduct audits, including following the full reinstatement of 2R01AI110964. Finally, we have appointed a Senior Field Veterinarian who will oversee all EcoHealth Alliance fieldwork in the region and ensure continued compliance with biosafety when conducting animal capture, sampling and sample handling. We have done this at EcoHealth Alliance's own expense, despite our unblemished record on biosafety, to pre-empt calls for further sanctions against our work given the continued attacks against EcoHealth Alliance in the press after the termination of our NIH grant."

We believe the attached documents lay out details of how we had previously monitored compliance according to the federal codes you cite, and the above response lays out an appropriate plan for biosafety monitoring. Together, we believe they appropriately and fully addresses your condition #8 for full reinstatement with access to funding for the renewal phase of the R01.

Yours sincerely,

(b) (6)

Dr. Peter Daszak, President
(t) (b) (6); (e) (b) (6)

EcoHealth Alliance
520 Eighth Avenue, Suite 1200
New York, NY 10018
212.380.4460
EcoHealthAlliance.org

UNCLASSIFIED
SBU

MRN:	18 BEIJING 138
Date/DTG:	Jan 19, 2018 / 190739Z JAN 18
From:	AMEMBASSY BEIJING
Action:	WASHDC, SECSTATE *ROUTINE*
E.O.:	13526
TAGS:	SHLH, ETRD, ECON, PGOV, CN
Captions:	SENSITIVE
Reference:	17 WUHAN 48
Subject:	China Opens First Bio Safety Level 4 Laboratory

1. (SBU) **Summary and Comment:** The Chinese Academy of Sciences (CAS) has recently established what is reportedly China's first Biosafety Level 4 (BSL-4) laboratory in Wuhan. This state-of-the-art facility is designed for prevention and control research on diseases that require the highest level of biosafety and biosecurity containment. Ultimately, scientists hope the lab will contribute to the development of new antiviral drugs and vaccines, but its current productivity is limited by a shortage of the highly trained technicians and investigators required to safely operate a BSL-4 laboratory and a lack of clarity in related Chinese government policies and guidelines. (b)(5)

(b)(5)

(b)(5) **End Summary and Comment.**

China Investing in Infectious Disease Control

2. (U) Between November 2002 and July 2003, China faced an outbreak of Severe Acute Respiratory Syndrome (SARS), which, according to the World Health Organization, resulting in 8,098 cases and leading to 774 deaths reported in 37 countries. A majority of cases occurred in China, where the fatality rate was 9.6%. This incident convinced China to prioritize international cooperation for infectious disease control. An aspect of this prioritization was China's work with the Jean Merieux BSL-4 Laboratory in Lyon, France, to build China's first high containment laboratory at Wuhan's Institute of Virology (WIV), an institute under the auspices of the Chinese Academy of Sciences (CAS). Construction took 11 years and $44 million USD, and construction on the facility was completed on January 31, 2015. Following

two years of effort, which is not unusual for such facilities, the WIV lab was accredited in February 2017 by the China National Accreditation Service for Conformity Assessment. It occupies four floors and consists of over 32,000 square feet. WIV leadership now considers the lab operational and ready for research on class-four pathogens (P4), among which are the most virulent viruses that pose a high risk of aerosolized person-to-person transmission.

Unclear Guidelines on Virus Access and a Lack of Trained Talent Impede Research

3. (SBU) In addition to accreditation, the lab must also receive permission from the National Health and Family Planning Commission (NHFPC) to initiate research on specific highly contagious pathogens. According to some WIV scientists, it is unclear how NHFPC determines what viruses can or cannot be studied in the new laboratory. To date, WIV has obtained permission for research on three viruses: Ebola virus, Nipah virus, and Xinjiang hemorrhagic fever virus (a strain of Crimean Congo hemorrhagic fever found in China's Xinjiang Province). Despite this permission, however, the Chinese government has not allowed the WIV to import Ebola viruses for study in the BSL-4 lab. Therefore, WIV scientists are frustrated and have pointed out that they won't be able to conduct research project with Ebola viruses at the new BSL-4 lab despite of the permission.

(b)(6)

(b)(6) Thus, while the BSL-4 lab is ostensibly fully accredited, its utilization is limited by lack of access to specific organisms and by opaque government review and approval processes. As long as this situation continues, Beijing's commitment to prioritizing infectious disease control - on the regional and international level, especially in relation to highly pathogenic viruses, remains in doubt.

(b)(6) noted that the new lab has a serious shortage of appropriately trained technicians and investigators needed to safely operate this high-containment laboratory. University of Texas Medical Branch in Galveston (UTMB), which has one of several well-established BSL-4 labs in the United States (supported by the National Institute of Allergy and Infectious Diseases (NIAID of NIH)), has scientific collaborations with WIV, which may help alleviate this talent gap over time. Reportedly, researchers from GTMB are helping train technicians who work in the WIV BSL-4 lab. Despite this, (b)(6) they would welcome more help from U.S. and international organizations as they establish "gold standard" operating procedures and training courses for the first time in China. As China is building more BSL-4 labs, including one in Harbin Veterinary Research Institute subordinated to the Chinese Academy of Agricultural Sciences (CAAS) for veterinary research use, (b)(6) the training for technicians and investigators working on dangerous pathogens will certainly be in demand.

Despite Limitations, WIV Researchers Produce SARS Discoveries

6. (SBU) The ability of WIV scientists to undertake productive research despite limitations on the use of the new BSL-4 facility is demonstrated by a recent publication on the origins of SARS. Over a five-year study, (b)(6) (and their research team) widely sampled bats in Yunnan province with funding support from NIAID/NIH, USAID, and several Chinese funding agencies. The study results were published in PLoS Pathogens online on Nov. 30, 2017 (1), and it demonstrated that a SARS-like coronaviruses isolated from horseshoe bats in a single cave contain all the building blocks of the pandemic SARS-coronavirus genome that caused the human outbreak. These results strongly suggest that the highly pathogenic SARS-coronavirus originated in this bat population. Most importantly, the researchers also showed that various SARS-like coronaviruses can interact with ACE2, the human receptor identified for SARS-coronavirus. This finding strongly suggests that SARS-like coronaviruses from bats can be transmitted to humans to cause SARS-like disease. From a public health perspective, this makes the continued surveillance of SARS-like coronaviruses in bats and study of the animal-human interface critical to future emerging coronavirus outbreak prediction and prevention. (b)(5) (b)(5) WIV scientists are allowed to study the SARS-like coronaviruses isolated from bats while they are precluded from studying human-disease causing SARS coronavirus in their new BSL-4 lab until permission for such work is granted by the NHFCP.

1. Hu B, Zeng L-P, Yang X-L, Ge X-Y, Zhang W, Li B, et al. (2017) Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insights into the origin of SARS coronavirus. PLoS Pathog 13(11): e1006698. https://doi.org/10.1371/journal.ppat.1006698

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MRN:	18 WUHAN 38
Date/DTG:	Apr 19, 2018 / 190551Z APR 18
From:	AMCONSUL WUHAN
Action:	WASHDC, SECSTATE *ROUTINE*
E.O.:	13526
TAGS:	SHLH, PGOV, CN, PREL, TBIO, KGHI, CDC, EAID, KHIV, IN, JP, TW, TSPL, PINS, SENV
Captions:	SENSITIVE
Reference:	A) 18 BEIJING 138 B) 17 BEIJING 2458 C) 11 MUMBAI 630 D) 17 TOKYO 716 E) 13 SEOUL 790
Subject:	China Virus Institute Welcomes More U.S. Cooperation on Global Health Security

1. (SBU) **Summary with Comment:** China's Wuhan Institute of Virology, a global leader in virus research, is a key partner for the United States in protecting global health security. Its role as operator of the just-launched Biosafety Level 4 (or "P4") lab -- the first such lab in China -- opens up even more opportunities for expert exchange, especially in light of the lab's shortage of trained staff (Ref A). (b)(5)

(b)(5)

(b)(5) **End Summary with Comment.**

2. (U) Wuhan Institute of Virology researchers and staff gave an overview of the lab and current cooperation with the United States to visiting Environment, Science, Technology and Health Counsellor Rick Switzer and Consulate Wuhan Consul General Jamie Fouss in late March. In the last year, the institute has also hosted visits from the National Institutes of Health (NIH), National Science Foundation, and experts from the University of Texas Medical Branch in Galveston. The institute reports to the Chinese Academy of Sciences in Beijing.

P4 Lab is Open and Transparent, Officials Emphasize

3. (SBU) The Wuhan P4 lab, referring to labs with the highest level of safety precautions, became fully operational and began working with live viruses early this year. Institute officials said they believed it is the only operational P4 lab in Asia aside from a U.S. Centers for Disease

Control (CDC)-supported facility in Pune, India (Ref C). China plans to stand up a second P4 lab in Harbin. Institute officials said Japan's biosafety labs are "old" and lack cutting-edge equipment, so they consider Japan's labs to be "P3 Plus" (*Note*: the Japanese government says it has one P4-level lab in the Tokyo suburbs, though its activities are limited, and Japan is building a new P4 lab in Nagasaki, see Ref D. Taiwan operates at least one P4 lab. South Korea was close to opening a P4 lab as of last year, see Ref E. *End.Note.*) Wuhan's lab is located about 20 miles from the city center in Zhengdian district, and the institute plans to gradually consolidate its other training, classroom and lab facilities at that location.

4. (U) Officials described the lab as a "regional node" in the global biosafety system and said it would play an emergency response role in an epidemic or pandemic. The lab's English brochure highlighted a national security role, saying that it "is an effective measure to improve China's availability in safeguarding national bio-safety if [a] possible biological warfare or terrorist attack happens."

5. (SBU) Institute officials said there would be "limited availability" for international and domestic scientists who had gone through the necessary approval process to do research at the lab. They stressed that the lab aimed to be a "worldwide, open platform" for virology. They said they welcomed U.S. Centers for Disease Control (CDC) experts, noting that the Chinese Academy of Sciences was not strong on human disease expertise, having only focused on it in the last 15 years, after the SARS outbreak. A Wuhan-based French consulate official who works on science and technology cooperation with China also emphasized that the lab, which was initiated in 2004 as a France-China joint project, was meant to be "open and transparent" to the global scientific community. "The intent was to set up a lab to international standards, and open to international research," he said. French experts have provided guidance and biosafety training to the lab, which will continue, the French official said. Institute officials said that France provided the lab's design and much of its technology, but that it is entirely China-funded and has been completely China-run since a "handover" ceremony in 2016.

6. (U) In addition to French assistance, experts from the NIH-supported P4 lab at the University of Texas Medical Branch in Galveston have trained Wuhan lab technicians in lab management and maintenance, institute officials said. The Wuhan institute plans to invite scientists from the Galveston lab to do research in Wuhan's lab. One Wuhan Institute of Virology researcher trained for two years at the Galveston lab, and the institute also sent one scientist to U.S. CDC headquarters in Atlanta for six months' work on influenza.

NIH-Supported Research Revises SARS Origin Story

7. (U) NIH was a major funder, along with the Natural Science Foundation of China (NSFC), of SARS research by the Wuhan Institute of Virology's [redacted] This lends weight to the theory that SARS originated in bat populations before jumping first to civet cats (likely via bat feces) and then to humans. [redacted]

(b)(6)
(b)(6) team has provided support in statistical modeling to assess the risk of more coronaaviruses like SARS crossing over to human populations.

Ready to Help with the Global Virome Project

8. (U) Institute officials expressed strong interest in the Global Virome Project (GVP), and said Chinese funding for the project would likely come from Chinese Academy of Sciences funding already earmarked for One Belt, One Road-related initiatives. The GVP aims to launch this year as an international collaborative effort to identify within ten years virtually all of the planet's viruses that have pandemic or epidemic potential and the ability to jump to humans. "We hope China will be one of the leading countries to initiate the Global Virome Project," one Wuhan Institute of Virology official said. China attended a GVP unveiling meeting in January in Thailand and is waiting for more details on the initiative. The officials said that the Chinese government funds projects similar to GVP to investigate the background of viruses and bacteria. This essentially constituted China's own Virome Project, officials said, but they noted the program currently has no official name.

9. (SBU) The Wuhan Institute of Virology's (b)(6) is the (b)(6) (b)(6) (b)(6) which is designed to show "proof of concept" and be a forerunner to the Global Virome Project. (b)(6) with the EcoHealth Alliance (a New York City-based NGO that is working with the University of California, Davis to manage the (b)(6) recently planned to visit Wuhan to meet with (b)(6) (b)(6) noted that China has expressed interest in building the GVP database, which would put China in a leadership position. Other countries have confidence in China's ability to build such a database, but are skeptical on whether China could remain transparent as a "gatekeeper" for this information. (b)(6) said (b)(6) expressed frustration with the slow progress so far in launching GVP, noting that the effort lacked funding sources, needed to hire a CEO, and would have to boost its profile at G7, G20 and other high-level international meetings.

U.S.-China Workshop Explores Research Partnerships

10. (U) The Institute also has ongoing collaboration with the U.S. National Science Foundation, including a just-concluded workshop in Shenzhen, involving about 40 scientists from the United States and China, on the topic of the "Ecology and Evolution of Infectious Diseases." Co-sponsored by the Natural Science Foundation of China (NSFC), (b)(6) (b)(6) (b)(6) The workshop explored opportunities for U.S.-China research cooperation in areas like using "big data" to predict emerging infectious diseases, climate change's effect on vector-borne diseases, and pathogen transmission between wildlife, domestic animals and humans.

11. (SBU) Some workshop participants also expressed skepticism about the Global Virome Project's (GVP) approach, saying that gaining a predictive understanding of viruses with pandemic potential would require going beyond the GVP's strategy of sample collection, to take an "ecological" approach that considers the virome beyond vertebrate systems to identify

mechanisms driving pathogen evolution. A follow-on workshop will be held in June at the University of Berkeley. NSF and NSFC hope to jointly announce a funding call for collaborative projects later this year.

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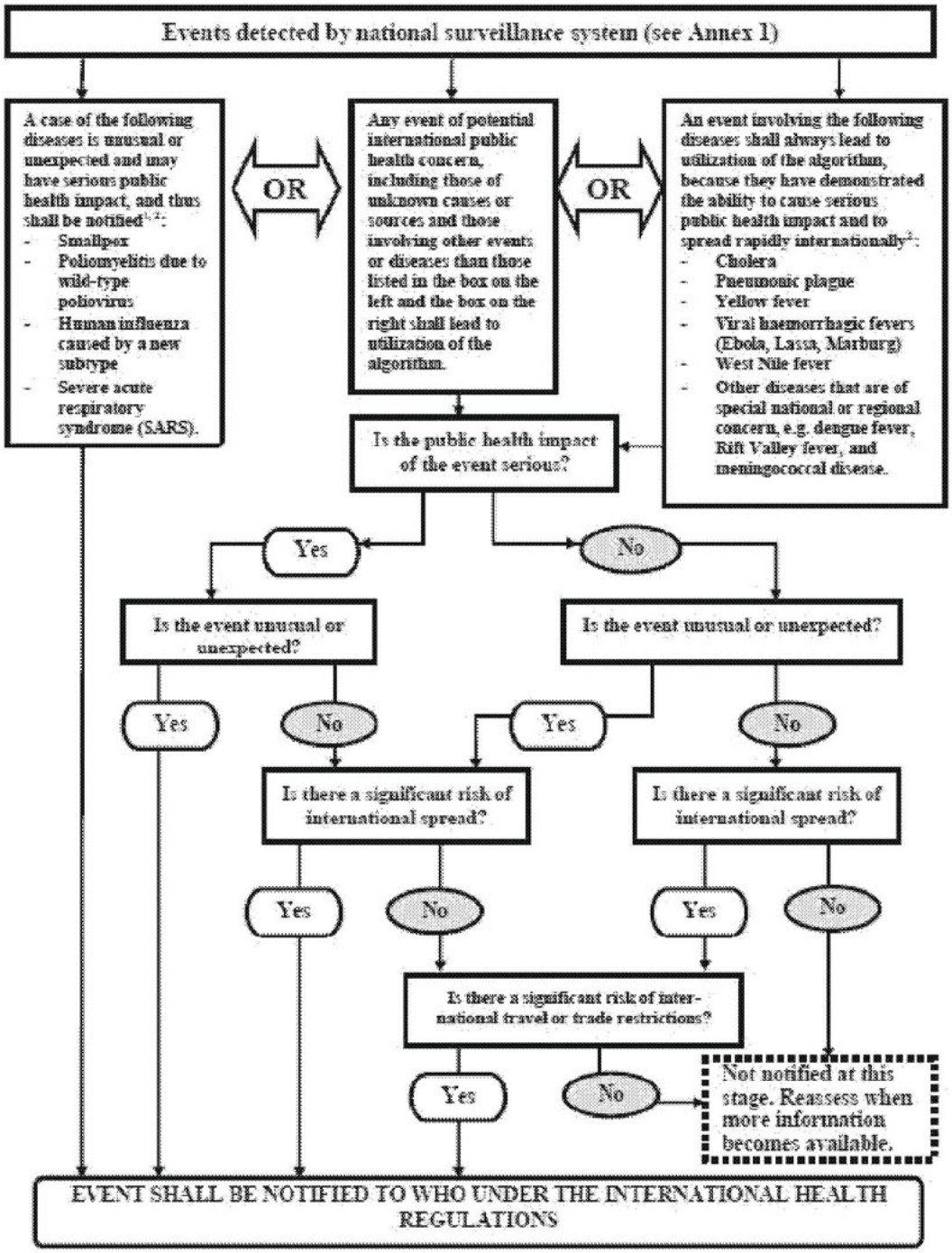
Annex 2 of the 2005 International Health Regulations

ANNEX 2

DECISION INSTRUMENT FOR THE ASSESSMENT AND NOTIFICATION OF EVENTS THAT MAY CONSTITUTE A PUBLIC HEALTH EMERGENCY OF INTERNATIONAL CONCERN



[1] As per WHO case definitions.
[2] The disease list shall be used only for the purposes of these Regulations.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

September 3, 2020

The Honorable Eddie Bernice Johnson
Chairwoman, Committee on Science, Space, and Technology
U.S. House of Representatives
Washington, DC 20515

Dear Madam Chairwoman:

Thank you for your June 26, 2020 letter regarding the National Institutes of Health's (NIH) oversight of the grant awarded to EcoHealth Alliance, Inc. The Department of Health and Human Services has asked NIH to respond, and I am pleased to respond on behalf of NIH

On April 19, 2020, NIH sent a letter to the EcoHealth Alliance, the institutional awardee of the grant, ordering the suspension of funds to the Wuhan Institute of Virology ("WIV"), one of the grant's sub-recipients. On Friday afternoon, April 24, 2020, NIH sent a second letter to EcoHealth Alliance, terminating the grant.

On July 8, 2020, NIH sent a letter to EcoHealth Alliance (enclosed) indicating the grant was reinstated; however, funding and activities were suspended pending complete, accurate, and satisfactory answers, materials, and information regarding a number of specific concerns about biosafety and other practices at its sub-recipient, WIV. Furthermore, EcoHealth Alliance was instructed to correct its repeated noncompliance due to its failure to report all sub-awards in the Federal Subaward Report System. EcoHealth Alliance had been directed in NIH Notices of Award to generate these reports as required by the Transparency Act sub-award and executive compensation reporting requirement of 2 C.F.R. Part 170.

The July 8 letter to EcoHealth Alliance indicated that the suspension of the grant was taken in accordance with 45 C.F.R. § 75.371, which permits suspension of award activities in cases of non-compliance, and the NIH Grants Policy Statement (GPS) Section 8.5.2, which permits NIH to take immediate action to suspend a grant when necessary to protect the public health and welfare. This action is not appealable under 42 C.F.R. § 50.404 and the NIH GPS, Section 8.7.

On August 14, 2020, EcoHealth Alliance responded by letter declining to answer any of the seven specific concerns NIH requested in the July 8 letter. At the time of this writing, the grant has been reinstated with all funding and activities suspended pending EcoHealth Alliance's answers to the government's safety and compliance concerns. As this matter is still pending, no further documentation can be provided at this time.

Thank you for your engagement on this important issue. I have sent an identical copy of this response to each of the co-signers of your letter.

Sincerely,

Michael S. Lauer -S Digitally signed by Michael S. Lauer -S
Date: 2020.09.03 14:23:48 -04'00'

Michael S. Lauer, MD
NIH Deputy Director for Extramural Research

EcoHealth Alliance

Dr. Michael Lauer
Deputy Director for Extramural Research,
NIH, Bethesda, MD.

Response to the Reinstatement and immediate suspension of 2R01AI110964 "Understanding the Risk of Bat Coronavirus Emergence"

April 11th 2021

Dear Dr. Lauer,

I am responding your letters of 7/8/2020 and 10/3/2020 regarding the reinstatement and immediate suspension of NIH grant 2R01AI110964 "*Understanding the Risk of Bat Coronavirus Emergence*", that was terminated "for convenience" on 4/24/2020. In particular, this letter addresses the conditions you state would need to be fulfilled in order for us to have access to the funds to continue this work.

As you know, we had not set up any subcontracts to the Wuhan Institute of Virology under this renewal R01. Immediately following NIH's letter on 4/19/2020 that the WIV was being 'investigated', we suspended all plans for contractual work with WIV. This termination of a funded relationship with the institute makes it extraordinarily difficult and more likely impossible to provide the information requested about an autonomous foreign organization – as would also be the case for a domestic one - that our organization neither works with currently, nor has control over.

Additionally, our collaborative work with the Wuhan Institute of Virology prior to your grant termination letter of 4/24/2020 and that planned in the suspended grant, is wholly unrelated to many of the conditions listed below. These conditions also pertain to certain events and situations that in no way involve EcoHealth Alliance or are not under our control. Thus, most of the conditions below are either unrelated to EcoHealth Alliance's planned research in our highly rated, approved and funded grant application, and/or to the biosafety of our continued research funded by the suspended grant when it is reinstated in full.

Furthermore, in our recent correspondence with NIH regarding the latest in a series of FoIA requests, we were informed (1/26/2021 – see email correspondence at the end of this letter) by an NIH staff member Garcia-Malene Gorka that "any indication from my program that there is an ongoing investigation into WIV can now be disregarded, as we recently confirmed there are no pending investigations into that organization." Because this was the explanation in your initial letter of 4/19/2020 for the decisions from your office regarding restrictions on, termination of, then reinstatement and suspension of our grant, we believe that these decisions should now be reassessed.

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Despite our concerns about the relevance, fairness, or ability to fulfil the conditions as set forth in detail below, I have made extensive efforts to satisfy NIH's broad concerns, and have provided details of how these are relevant to each condition below. This includes serving as an expert on the WHO-China joint Mission on the Animal Origins of COVID-19, which involved 1 month on the ground in China (including 2 weeks locked in quarantine), at great personal burden and risk to me, to our organization, and to my family. I undertook this mission at a time when I have had increasing levels of personal attack and harassment, including a white-powder letter to my home address a few weeks after the details of our grant termination went public, and death threats that begun at the same time and continue to this day. It is clear in the wording of these attacks that many are a direct result of dangerous conspiracy theories inadvertently amplified by NIH's grant termination, and repeated in the conditions listed below. This type of harassment has accelerated to the point that personal security guards are now stationed at my home address, where I have also had to install invasive equipment and set up procedures to protect my family against expected violent attacks. Additionally, I now meet regularly with FBI agents and others at my home to monitor these threats. As I am sure you appreciate, this has a significant toll on my work, my personal life and my family.

Below, I detail our response to each of the conditions placed on our suspended grant, in an effort to provide as much information as possible and to explain the limitations on what we can do to respond. I look forward to your reply and hope that these will allow NIH to lift the suspension on funding so that we can continue our work to help protect our nation, indeed the global population, against future coronavirus pandemics. Should you wish, I feel certain we may discuss these points without legal counsel in a scientist-to-scientist conversation, as you have suggested verbally to others at NIH, and they have conveyed to me.

1. Provide an aliquot of the actual SARS-CoV-2 virus that WIV used to determine the viral sequence.
We believe this condition is effectively impossible for us to fulfil, for the following reasons. Firstly, there is no scientific nor administrative rationale for us to attempt to obtain a SARS-CoV-2 aliquot given that it is not part of our funded collaboration with WIV. Secondly, EcoHealth Alliance scientists do not have any capacity to work on such an aliquot (EHA does not conduct virological laboratory work on SARS-CoV-2) in the USA. This further reduces the validity of a scientific basis for this request to WIV. Thirdly, EcoHealth Alliance scientists were not part of the work that WIV conducted to determine the viral sequence of SARS-CoV-2, and this was not part of our (then active) R01 funded collaboration. This is publicly stated by the lack of EHA authors listed on the paper and the lack of acknowledgement of our grant as a funding source for this work. This publicly discounts any claim of sample ownership or control. Fourthly, the collaborative research laid out in our now-suspended grant does not include the shipping of human viral isolates out of China. Finally, during the last 16 months, there has been a series of vitriolic attacks from the US Government accusing China of bioengineering and releasing SARS-CoV-2 or of otherwise allowing COVID to become pandemic. Given these attacks, and WIV's status as a government entity, it seems to us incredulous that any request, particularly without scientific rationale, from a US non-profit to a Chinese Government laboratory for an active sample of a pathogenic human virus would likely be successful. We note that 1) to our knowledge China has not supplied such an aliquot to any formal request from a government; and 2) that if circumstances were reversed and a Chinese non-

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governmental institution requested a similar pathogenic viral aliquot from a US government BSL-4 laboratory, this would also be unlikely to be fulfilled.

While we understand that it may be of scientific interest to some US-based researchers to analyze this viral sequence, this scientific interest could easily be satisfied without the need for an aliquot. The full genome of this viral sequence was uploaded to a freely accessible database on January 10 2020, and has been used widely by scientists in the USA (included those funded by NIH) and around the world in their work. Furthermore, isolates of the virus from patients in Thailand and Australia during early 2020 are essentially the same, and have been shared extensively.

2. Explain the apparent disappearance of Huang Yanling, a scientist / technician who worked in the WIV lab but whose lab web presence has been deleted.

International experts on the WHO COVID-19 origins mission, including myself, asked direct questions on this issue to staff at WIV, including the Director of the institute, the P4 Lab Director, Dr. Shi and others. The response from all was consistent, as stated in the WHO mission report published 3/30/2020: "This person according the WIV staff was an alumnus who graduated in 2015 and was now working in a different province and did not accept to talk with media. The person had been contacted and tested and ascertained to be healthy."

Given that the WHO team was not given access to this individual, and that China's personal privacy laws are preclude our ability to insist on a meeting, it is difficult to see how a request from a US non-profit would have been approved. It seems at the least to be significantly outside the remit of a US-based non-profit organization to inquire further about the whereabouts of a citizen of a foreign country who has never to our knowledge been involved in our work, and over whom we have no control, influence, nor legal responsibility.

Finally, while many conspiracy theorists have suggested that the lack of a web presence of this person suggests some nefarious activity, there are dozens of unremarkable and routine reasons why a person may be removed from a web listing of employees or students. Not least of these is when a staff member leaves an institution, or a student graduates.

3. Provide the NIH with WIV's responses to the 2018 U.S. Department of State cables regarding safety concerns.

We believe that WIV senior staff comments reported in the WHO COVID origins mission report directly address this request in that they publicly state that no significant safety issues were found in their laboratory prior to, or following, the emergence of COVID. Any questions regarding the safety of the WIV also need to be put into the context of the widely published history of this lab as being built to international safety engineering standards, adhering to international safety practice standards indicated in the BMBL, and with lead WIV staff trained in safety in the United States by a known authority running the BSL-4 lab at the University of Texas Medical Branch in Galveston (as reported in the U.S. Dept of State cables). Furthermore, no verifiable evidence of safety issues have been reported prior to, or following the U.S. Dept of State cables.

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Regarding the U.S. Dept. of State cables, these do not in fact provide evidence of safety concerns at the laboratory. Neither do they convincingly imply safety issues. In fact, they may be simply interpreted as a request for funding from a diplomatic mission set up to further joint US-China research. It is important to note that initially only very limited phrases from these cables were selectively leaked by a Washington Post reporter in an opinion piece that did not verify nor quote direct sources. This opinion piece is demonstrably incomplete in its reporting, however it has been widely cited as providing evidence of safety issues at WIV (https://www.washingtonpost.com/opinions/2020/04/14/state-department-cables-warned-safety-issues-wuhan-lab-studying-bat-coronaviruses/). I have some detailed knowledge of the background to these cables because the diplomatic visit to WIV that they report was a direct result of our NIH-funded work. As part of EcoHealth Alliance's work in China over the past 15 years, including that funded by NIAID, I visited the US Embassy in Beijing regularly and was involved in discussions with US Embassy staff to set up a field visit to the WIV in order to generate goodwill between the US and China at a time when President Trump was planning a state visit. I did this out of a sense of duty to our government, and to the NIH so that our project could help foster goodwill between our countries, as well as provide an indication of the importance of NIH's work. Following the US Embassy staff mission, I was told by people privy to the cable's contents that the articles were positive and supportive of the work we were doing under NIAID funding, and that the trip was a success.

Now that the full text of these cables (embedded at the end of this letter) has been released with minor redactions (https://news.slashdot.org/story/20/07/20/0611205/full-text-of-us-state-department-cables-finally-released-showing-safety-in-chinese-lab), it seems that this more positive interpretation is justified. As you can see in the excerpts below, the request for more laboratory technician support could be reasonably interpreted as simply a request for the funding for more laboratory technician support, rather than a statement that the lab was unsafe, particularly given that the visit was set up as part of an effort to further develop US-China collaborative research opportunities. Furthermore, the cables are extremely positive about the importance of the collaborative work we were conducting with WIV under NIAID funding:

"**REDACTED** noted that the new lab has a serious shortage of appropriately trained technicians and investigators needed to safely operate this high-containment laboratory. University of Texas Medical Branch in Galveston (UTMB), which has one of several well-established BSL-4 labs in the United States (supported by the National Institute of Allergy and Infectious Diseases (NIAID of NIH)), has scientific collaborations with WIV, which may help alleviate this talent gap over time. Reportedly, researchers from GTMB are helping train technicians who work in the WIV BSL-4 lab. Despite this they would welcome more help from U.S. and international organizations as they establish "gold standard" operating procedures and training courses for the first time in China."

"The ability of WIV scientists to undertake productive research despite limitations on the use of the new BSL-4 facility is demonstrated by a recent publication on the origins of SARS. Over a five-year study **REDACTED** (and their research team) widely sampled bats in Yunnan province with funding support from NIAID/NIH, USAID, and several Chinese funding agencies. The study results were published in PLoS

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Pathogens online on Nov. 30, 2017 (1), and it demonstrated that a SARS-like coronaviruses isolated from horseshoe bats in a single cave contain all the building blocks of the pandemic SARS-coronavirus genome that caused the human outbreak. These results strongly suggest that the highly pathogenic SARS-coronavirus originated in this bat population. Most importantly, the researchers also showed that various SARS-like coronaviruses can interact with ACE2, the human receptor identified for SARS coronavirus. This finding strongly suggests that SARS-like coronaviruses from bats can be transmitted to humans to cause SARS-like disease. From a public health perspective, this makes the continued surveillance of SARS-like corona viruses in bats and study of the animal-human interface critical to future emerging coronavirus outbreak prediction and prevention."

4. Disclose and explain out-of-ordinary restrictions on laboratory facilities, as suggested, for example, by diminished cell-phone traffic in October 2019, and the evidence that there may have been roadblocks surrounding the facility from October 14-19, 2019.

The WIV staff categorically stated to the WHO mission that their lab is audited annually and no unusual events have been identified. The reports of diminished cell-phone traffic and roadblocks have not been verified or published by reliable sources. Furthermore, should hard evidence of diminished cell-phone traffic and roadblocks exist, it is not necessarily indicative of any issues related to concerns about the laboratory studies underway or safety or security incidents within the laboratory. These issues could be explained by any one of a series of issues that occur regularly in the US without nefarious connotations. For example, they could be due to roadwork or other infrastructure repair or maintenance, technical problems with cell-phone transmission, or rerouting of traffic as regularly occurs in Washington DC and other cities due to transport of visiting dignitaries or other events. Finally, there is no credible reason to think that any request a US non-profit might make to the Chinese government for an explanation of traffic or cell-phone issues would result in any response.

5. Explain why WIV failed to note that the RaTG13 virus, the bat-derived coronavirus in its collection with the greatest similarity to SARS-CoV-2, was actually isolated from an abandoned mine where three men died in 2012 with an illness remarkably similar to COVID-19, and explain why this was not followed up.

Since your letter of 7/8/2020, it has been widely reported that WIV scientists have published an addendum to their original paper in *Nature* that described SARS-CoV-2 and compared it phylogenetically to RaTG13. In this follow-up publication, they explain the rationale for conducting work in this mine, and any potential connection to the miner's illnesses and deaths. Importantly, they state that serological results in their lab at the time of the incident did not show that these miners were positive for SARSr-CoVs as some media articles have suggested. They then re-tested the miner samples in 2020 using a range of assays, and found no evidence of SARS-related CoV, nor of SARS-CoV-2 specific antibodies or nucleic acid. During the meeting of the WHO mission team with WIV staff, they were asked a series of questions about the miner's illnesses. The responses were that, while symptoms identified were similar to COVID in that they had pneumonia (a common occupational hazard for miners), their symptoms were also similar to other bacterial or fungal pneumonias. This, and the lack of evidence for SARSr-CoV infection, led them to conclude that SARS or COVID infection was not the cause of these miner's illnesses.

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6. Additionally, EcoHealth Alliance must arrange for WIV to submit to an outside inspection team charged to review the lab facilities and lab records, with specific attention to addressing the question of whether WIV staff had SARS-CoV-2 in their possession prior to December 2019. The inspection team should be granted full access to review the processes and safety of procedures of all of the WIV fieldwork (including but not limited to collection of animals and biospecimens in caves, abandoned man-made underground cavities, or outdoor sites). The inspection team could be organized by NIAID, or, if preferred, by the U.S. National Academy of Sciences.

The WHO mission was negotiated at the very highest levels as the legitimate way to proceed in an investigation of COVID-19 origins, particularly with such critical geopolitical ramifications from this pandemic. Given the intensity of political attacks and conspiracy theories around this lab, it is unreasonable to expect that the Chinese government or WIV would respond to a request from a US non-profit for an outside inspection team. The 11 international expert members of the WHO team included authorities on epidemiology, animal-origin viral infections and One Health. Members of this team have extensive experience conducting lab audits (e.g. Dr. Peter Ben Embarek), running laboratories dealing with human clinical samples (e.g. Drs. Dominic Dwyer, Thea Fischer), and commissioning, managing and accrediting laboratories in foreign countries (myself, Dr. Fabian Leendertz). The WHO-China Joint Study report details the field site visits to multiple labs in Wuhan, including the WIV and summarizes our findings. This includes information on the management of the WIV, safety at the labs, audits and training and testing of staff. I acted in good faith to try to conform to the WHO terms of reference while ensuring that as much information on the laboratory was provided in the report. This information specifically addresses one of your questions above, with categorical statements from WIV senior staff that they did not have SARS-CoV-2 in their possession prior to December 2019.

After returning to the USA, and in the weeks prior to the publication of the report, I worked hard to make sure this critical information was shared as rapidly as possible with the US Government and agencies, including by:

- Briefing Drs. Anthony Fauci and Clifford Lane of NIAID on the findings of the mission;
- Presenting a full talk about the work to the NIAID COVID PI group that meets weekly
- Briefing FBI and other US Government intelligence agency staff
- Briefing members of the US NASEM Forum on Microbial Threats
- Briefing staff on the White House National Security Council
- Briefing staff on the House Committee for Science, Space, and Technology

7. Lastly, EcoHealth Alliance must ensure that all of its subawards are fully reported in the Federal Subaward Reporting System

This has been done and all subawards fully reported as soon as we could once you notified us of this requirement in your letter of 7/8/2020.

8. Provide copies of all EcoHealth Alliance – WIV subrecipient agreements as well as any other documents and information describing how EcoHealth Alliance monitored WIV's compliance with the terms and conditions of award, including with respect to biosafety.

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New York, NY 10018
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EcoHealthAlliance.org

As we related in response to your letter of 4/19/2020 that asked us to suspend work with WIV, we had not yet set up a subcontract with WIV for the period of this award, therefore no such subrecipient agreements exist. Our plan was to monitor WIV's compliance as we had in the 5 years prior, by means of semi-annual meetings with the lead investigator and assessments of compliance against all conditions of the award. Additionally, following the NIH's termination, then reinstatement and suspension of our funding, we have contracted with a leading lab biosafety contractor based in Southeast Asia (Dr. Paul Selleck) who has extensive experience commissioning, accrediting and auditing BSL-2, -3, and -4 labs, and has worked for over a decade at the BSL-4 Australian Animal Health Lab. We will be using their services where appropriate for foreign lab subcontractees to assess lab biosafety procedures and conduct audits, including following the full reinstatement of 2R01AI110964. Finally, we have appointed a Senior Field Veterinarian who will oversee all EcoHealth Alliance fieldwork in the region and ensure continued compliance with biosafety when conducting animal capture, sampling and sample handling. We have done this at EcoHealth Alliance's own expense, despite our unblemished record on biosafety, to pre-empt calls for further sanctions against our work given the continued attacks against EcoHealth Alliance in the press after the termination of our NIH grant.

9. Describe EcoHealth's efforts to evaluate WIV's risk of noncompliance with Federal statutes, regulations, and the terms and conditions of the subaward.

Over a 15-year period of collaboration with WIV, we have found no evidence to suggest that there was any element of noncompliance with any of the conditions of the grants or contracts covering our collaboration. Our interactions with all staff at the institute have been professional, respectful, open, and with a focus on the science at a very high level. This has contributed to a relationship built on trust and one that is entirely comparable to our scientific collaborations with laboratories in the US, Europe, Australia, Thailand and over 20 other countries. We continue to believe that this laboratory is highly competent and is an extremely low risk for undisclosed accidental release of virus, and there is no verifiable indication as to why we should not continue to believe so. We would of course consider a change in this assessment if significant and verifiable evidence of lab biosafety issues or breach of other Federal statutes are brought forth, but to date we are aware of none.

10. Provide copies of all WIV biosafety reports from June 1, 2014 through May 31, 2019.

Given the intense geopolitical pressure around the accusations that WIV intentionally or accidentally released SARS-CoV-2 (something which the WHO mission deemed 'extremely unlikely'), obtaining such information is not a plausible option at present.

11. Additional information, re. Lack of ongoing investigation into Wuhan Institute of Virology by NIH:

From: Garcia-Malene, Gorka (NIH/OD) [E] (b) (6)
Sent: Tuesday, January 26, 2021 12:20:51 PM
To: [REDACTED]
Cc: [REDACTED] Bartok, Lauren (NIH/NIAID) [E]; NIH FOIA
Subject: [EXT] FW: FOIA Case No. 55702 re: EcoHealth Alliance & Grant No. R01AI110964-6

Good afternoon, **[REDACTED]** –

I'd like to insert myself into the unfolding FOIA conversation in hopes of providing some helpful context. Our records show that this competing renewal has in fact been funded. In addition, any indication from my program that there is an ongoing investigation into WIV can now be disregarded, as we recently confirmed there are no pending investigations into that organization. If we can agree on the above, all that would remain is to receive your proposed redactions to the records sought under the FOIA request.

Please let me know if there are any questions. I look forward to facilitating the Pre-Disclosure Notification process as efficiently as possible.

Best regards.

Gorka Garcia-Malene | FOIA Officer for the National Institutes of Health

From: [REDACTED]
Sent: Monday, January 25, 2021 5:21 PM
To: Bartok, Lauren (NIH/NIAID) [E] (b) (6)
Cc: [REDACTED]
Subject: FOIA Case No. 55702 re: EcoHealth Alliance & Grant No. R01AI110964-6

Dear Ms. Bartok:

As you may recall, this firm represents EcoHealth Alliance, Inc. ("EcoHealth Alliance"), with respect to certain FOIA requests, including the instant request, FOIA Case No. 55702. The instant request seeks the same documents sought last year in FOIA Case No. 53996, regarding the research project *Understanding the Risk of Bat Coronavirus Emergence*, funded under grant 2R01AI110964. A copy of our prior letter regarding FOIA 53996 is available via the link provided below using the password **[REDACTED]**. On the grounds set forth in the letter, FOIA 53996 was denied in its entirety.

Likewise, FOIA 55702 should be denied and the grant documents should be withheld. First, grant 2R01AI110964-06 remains an unfunded competing renewal grant that is the subject of a pending first-level appeal and, thus, the materials are not subject to disclosure under NIH Grants Policy Statement §2.3.11.2.2. Moreover, in the context of the appeal, NIH has made multiple requests for further information regarding The Wuhan Institute of Virology ("WIV"), which requests indicate that a law enforcement investigation concerning WIV remains ongoing. Second, as demonstrated by the recent attack on the US Capital fueled by disinformation and conspiracy theories, the need to protect the privacy of EcoHealth Alliance's employees and affiliates is more important than ever. Last, while EcoHealth Alliance did not initially identify that the grant proposal contained confidential-commercial and propriety information, this is not dispositive. Moreover, since the

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filing of the renewal application, there has been a global COVID-19 pandemic, which has sparked international and highly competitive research in the area of bat coronaviruses.

At the very least, the responsive documents will require significant redactions. While the grant documents were previously reviewed and redacted in connection with FOIA 53996, we require a further opportunity to review the documents to confirm, *inter alia*, that all personnel information has been removed given the heightened risk of harm in this unprecedented political environment. Accordingly, EcoHealth Alliance respectfully requests a forty-five (45) day extension of time to respond to FOIA 55702, to allow sufficient time for EcoHealth Alliance to conduct a further review of the responsive documents and provide an updated letter response that incorporates recent developments and specific justifications for additional redactions.

Please confirm that NIH will deny FOIA 55702 in its entirety or that NIH is agreeable to EcoHealth Alliance's request for an extension of time to provide a particularized response to FOIA 55702. Please also confirm NIH's receipt of this email.

Thank you.

Best,
[REDACTED]

FOIA Case No. 53996 - EcoHealth Alliance's Letter Response to FOIA Request, dated June 5, 2020 (With Exhibits)
[REDACTED]

[REDACTED]

Tarter Krinsky & Drogin LLP
1350 Broadway | New York | NY | 10018
www.tarterkrinsky.com | LinkedIn
COVID-19 RESOURCE CENTER

12. Publicly released details of U.S. Department of State Cables regarding visit to Wuhan Institute of Virology, as cited in condition #3 above. These are available from a number of sources, including the Washington Post and (https://news.slashdot.org/story/20/07/20/0611205/full-text-of-us-state-department-cables-finally-released-showing-safety-in-chinese-lab).

UNCLASSIFIED
SBU

MRN:	18 BEIJING 138
Date/DTG:	Jan 19, 2018 / 190739Z JAN 18
From:	AMEMBASSY BEIJING
Action:	WASHDC, SECSTATE *ROUTINE*
E.O.:	13526
TAGS:	SHLH, ETRD, ECON, PGOV, CN
Captions:	SENSITIVE
Reference:	17 WUHAN 48
Subject:	China Opens First Bio Safety Level 4 Laboratory

1. (SBU) **Summary and Comment:** The Chinese Academy of Sciences (CAS) has recently established what is reportedly China's first Biosafety Level 4 (BSL-4) laboratory in Wuhan. This state-of-the-art facility is designed for prevention and control research on diseases that require the highest level of biosafety and biosecurity containment. Ultimately, scientists hope the lab will contribute to the development of new antiviral drugs and vaccines, but its current productivity is limited by a shortage of the highly trained technicians and investigators required to safely operate a BSL-4 laboratory and a lack of clarity in related Chinese government policies and guidelines. (b)(5)

(b)(5)

(b)(5) **End Summary and Comment.**

China Investing in Infectious Disease Control

2. (U) Between November 2002 and July 2003, China faced an outbreak of Severe Acute Respiratory Syndrome (SARS), which, according to the World Health Organization, resulting in 8,098 cases and leading to 774 deaths reported in 37 countries. A majority of cases occurred in China, where the fatality rate was 9.6%. This incident convinced China to prioritize international cooperation for infectious disease control. An aspect of this prioritization was China's work with the Jean Merieux BSL-4 Laboratory in Lyon, France, to build China's first high containment laboratory at Wuhan's Institute of Virology (WIV), an institute under the auspices of the Chinese Academy of Sciences (CAS). Construction took 11 years and $44 million USD, and construction on the facility was completed on January 31, 2015. Following

two years of effort, which is not unusual for such facilities, the WIV lab was accredited in February 2017 by the China National Accreditation Service for Conformity Assessment. It occupies four floors and consists of over 32,000 square feet. WIV leadership now considers the lab operational and ready for research on class-four pathogens (P4), among which are the most virulent viruses that pose a high risk of aerosolized person-to-person transmission.

Unclear Guidelines on Virus Access and a Lack of Trained Talent Impede Research

3. (SBU) In addition to accreditation, the lab must also receive permission from the National Health and Family Planning Commission (NHFPC) to initiate research on specific highly contagious pathogens. According to some WIV scientists, it is unclear how NHFPC determines what viruses can or cannot be studied in the new laboratory. To date, WIV has obtained permission for research on three viruses: Ebola virus, Nipah virus, and Xinjiang hemorrhagic fever virus (a strain of Crimean Congo hemorrhagic fever found in China's Xinjiang Province). Despite this permission, however, the Chinese government has not allowed the WIV to import Ebola viruses for study in the BSL-4 lab. Therefore, WIV scientists are frustrated and have pointed out that they won't be able to conduct research project with Ebola viruses at the new BSL-4 lab despite of the permission.

(b)(6)

(b)(6) Thus, while the BSL-4 lab is ostensibly fully accredited, its utilization is limited by lack of access to specific organisms and by opaque government review and approval processes. As long as this situation continues, Beijing's commitment to prioritizing infectious disease control - on the regional and international level, especially in relation to highly pathogenic viruses, remains in doubt.

(b)(6) noted that the new lab has a serious shortage of appropriately trained technicians and investigators needed to safely operate this high-containment laboratory. University of Texas Medical Branch in Galveston (UTMB), which has one of several well-established BSL-4 labs in the United States (supported by the National Institute of Allergy and Infectious Diseases (NIAID of NIH)), has scientific collaborations with WIV, which may help alleviate this talent gap over time. Reportedly, researchers from GTMB are helping train technicians who work in the WIV BSL-4 lab. Despite this, (b)(6) they would welcome more help from U.S. and international organizations as they establish "gold standard" operating procedures and training courses for the first time in China. As China is building more BSL-4 labs, including one in Harbin Veterinary Research Institute subordinated to the Chinese Academy of Agricultural Sciences (CAAS) for veterinary research use (b)(6) the training for technicians and investigators working on dangerous pathogens will certainly be in demand.

Despite Limitations, WIV Researchers Produce SARS Discoveries

6. (SBU) The ability of WIV scientists to undertake productive research despite limitations on the use of the new BSL-4 facility is demonstrated by a recent publication on the origins of SARS. Over a five-year study, (b)(6) (and their research team) widely sampled bats in Yunnan province with funding support from NIAID/NIH, USAID, and several Chinese funding agencies. The study results were published in PLoS Pathogens online on Nov. 30, 2017 (1), and it demonstrated that a SARS-like coronaviruses isolated from horseshoe bats in a single cave contain all the building blocks of the pandemic SARS-coronavirus genome that caused the human outbreak. These results strongly suggest that the highly pathogenic SARS-coronavirus originated in this bat population. Most importantly, the researchers also showed that various SARS-like coronaviruses can interact with ACE2, the human receptor identified for SARS-coronavirus. This finding strongly suggests that SARS-like coronaviruses from bats can be transmitted to humans to cause SARS-like disease. From a public health perspective, this makes the continued surveillance of SARS-like coronaviruses in bats and study of the animal-human interface critical to future emerging coronavirus outbreak prediction and prevention. (b)(5) (b)(5) WIV scientists are allowed to study the SARS-like coronaviruses isolated from bats while they are precluded from studying human-disease causing SARS coronavirus in their new BSL-4 lab until permission for such work is granted by the NHFCP.

1. Hu B, Zeng L-P, Yang X-L, Ge X-Y, Zhang W, Li B, et al. (2017) Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insights into the origin of SARS coronavirus. PLoS Pathog 13(11): e1006698. https://doi.org/10.1371/journal.ppat.1006698

Signature:	BRANSTAD
Drafted By:	(b)(6)
Cleared By:	
Approved By:	
Released By:	
Info:	CHINA POSTS COLLECTIVE *ROUTINE*
Dissemination Rule:	Archive Copy

UNCLASSIFIED
SBU

We await your response at the earliest opportunity.

Yours sincerely,

Dr. Peter Daszak
President

(t) (b) (6); (e) (b) (6)
cc. Dr. Aleksei A. Chmura (Chief-of-Staff)

EcoHealth Alliance
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New York, NY 10018
212.380.4460
EcoHealthAlliance.org

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

September 3, 2020

The Honorable Bill Foster
Chairman, Subcommittee on Investigations and Oversight
Committee on Science, Space, and Technology
U.S. House of Representatives
Washington, DC 20515

Dear Representative Foster:

Thank you for your June 26, 2020 letter regarding the National Institutes of Health's (NIH) oversight of the grant awarded to EcoHealth Alliance, Inc. The Department of Health and Human Services has asked NIH to respond, and I am pleased to respond on behalf of NIH

On April 19, 2020, NIH sent a letter to the EcoHealth Alliance, the institutional awardee of the grant, ordering the suspension of funds to the Wuhan Institute of Virology ("WIV"), one of the grant's sub-recipients. On Friday afternoon, April 24, 2020, NIH sent a second letter to EcoHealth Alliance, terminating the grant.

On July 8, 2020, NIH sent a letter to EcoHealth Alliance (enclosed) indicating the grant was reinstated; however, funding and activities were suspended pending complete, accurate, and satisfactory answers, materials, and information regarding a number of specific concerns about biosafety and other practices at its sub-recipient, WIV. Furthermore, EcoHealth Alliance was instructed to correct its repeated noncompliance due to its failure to report all sub-awards in the Federal Subaward Report System. EcoHealth Alliance had been directed in NIH Notices of Award to generate these reports as required by the Transparency Act sub-award and executive compensation reporting requirement of 2 C.F.R. Part 170.

The July 8 letter to EcoHealth Alliance indicated that the suspension of the grant was taken in accordance with 45 C.F.R. § 75.371, which permits suspension of award activities in cases of non-compliance, and the NIH Grants Policy Statement (GPS) Section 8.5.2, which permits NIH to take immediate action to suspend a grant when necessary to protect the public health and welfare. This action is not appealable under 42 C.F.R. § 50.404 and the NIH GPS, Section 8.7.

On August 14, 2020, EcoHealth Alliance responded by letter declining to answer any of the seven specific concerns NIH requested in the July 8 letter. At the time of this writing, the grant has been reinstated with all funding and activities suspended pending EcoHealth Alliance's answers to the government's safety and compliance concerns. As this matter is still pending, no further documentation can be provided at this time.

Thank you for your engagement on this important issue. I have sent an identical copy of this response to each of the co-signers of your letter.

Sincerely,

Michael S. Lauer -S Digitally signed by Michael S. Lauer -S
Date: 2020.09.03 14:24:38 -04'00'

Michael S. Lauer, MD
NIH Deputy Director for Extramural Research

Date: April 19, 2020

From: Michael S Lauer, MD
NIH Deputy Director for Extramural Research

Lauer, Michael (NIH/OD) [E] Digitally signed by Lauer, Michael (NIH/OD) [E] Date: 2020.04.19 10:47:40 -04'00'

To: Kevin Olival, PhD
Vice-President for Research
EcoHealth Alliance
(b) (6)

Naomi Schrag, JD
Vice-President for Research Compliance, Training, and Policy
Columbia University
(b) (6)

Subject: Project Number 2R01AI110964-06

Dear Dr. Olival and Ms. Schrag:

EcoHealth Alliance, Inc. is the recipient, as grantee, of an NIH grant entitled "Understanding the Risk of Bat Coronavirus Emergence." It is our understanding that one of the sub-recipients of the grant funds is the Wuhan Institute of Virology ("WIV"). It is our understanding that WIV studies the interaction between corona viruses and bats. The scientific community believes that the coronavirus causing COVID-19 jumped from bats to humans likely in Wuhan where the COVID-19 pandemic began. There are now allegations that the current crisis was precipitated by the release from WIV of the coronavirus responsible for COVID-19. Given these concerns, we are pursuing suspension of WIV from participation in Federal programs.

While we review these allegations during the period of suspension, you are instructed to cease providing any funds from the above noted grant to the WIV. This temporary action is authorized by 45 C.F.R. § 75.371(d) ("Initiate suspension or debarment proceedings as authorized under 2 C.F.R. part 180"). The incorporated OMB provision provides that the funding agency may, through suspension, immediately and temporarily exclude from Federal programs persons who are not presently responsible where "immediate action is necessary to protect the public interest." 2 C.F.R. § 180.700(c). It is in the public interest that NIH ensure that a sub-recipient has taken all appropriate precautions to prevent the release of pathogens that it is studying. This suspension of the sub-recipient does not affect the remainder of your grant assuming that no grant funds are provided to WIV following receipt of this email during the period of suspension.

77 US Nobel Laureates in Science

May 21, 2020

Secretary Azar and Director Collins:

The 77 signatories of this letter, American Nobel Laureates in Physiology or Medicine, Chemistry, and Physics, are gravely concerned about the recent cancellation of a grant from the National Institutes of Health (NIH) to Dr. Peter Daszak at the EcoHealth Alliance in New York. We believe that this action sets a dangerous precedent by interfering in the conduct of science and jeopardizes public trust in the process of awarding federal funds for research.

For many years, Dr. Daszak and his colleagues have been conducting highly regarded, NIH-supported research on coronaviruses and other infectious agents, focusing on the transmission of these viruses from animal hosts to human beings. Their work depends on productive collaborations with scientists in other countries, including scientists in Wuhan, China, where the current pandemic caused by a novel coronavirus arose. Now is precisely the time when we need to support this kind of research if we aim to control the pandemic and prevent subsequent ones.

As has now been widely reported, the grant to the EcoHealth Alliance was abruptly terminated by NIH on April 24, 2020, just a few days after President Trump responded to a question from a reporter who erroneously claimed that the grant awarded millions of dollars to investigators in Wuhan. Despite the misrepresentation of Dr. Daszak's grant, despite the high relevance of the studies to the current pandemic, and despite the very high priority score that his application for renewal had received during peer review, the NIH informed Dr. Daszak and his colleagues that the grant was being terminated because "NIH does not believe that the current project outcomes align with the program goals and agency priorities." Such explanations are preposterous under the circumstances.

We are scientists who have devoted our careers to research, both in medical and related scientific disciplines that bear on the overall health and well-being of society, as well as fundamental scientific research, much of it supported by NIH and other federal agencies. We take pride in our nation's widely admired system for allocating funds based on expert review and public health needs. The abrupt revoking of the award to Dr. Daszak contravenes these basic tenets and deprives the nation and the world of highly regarded science that could help control one of the greatest health crises in modern history and those that may arise in the future.

We ask that you act urgently to conduct and release a thorough review of the actions that led to the decision to terminate the grant, and that, following this review, you take appropriate steps to rectify the injustices that may have been committed in revoking it.

Peter Agre	Chemistry	2003	James P. Allison	Medicine	2018
Sidney Altman	Chemistry	1989	Frances H. Arnold	Chemistry	2018
David Baltimore	Medicine	1975	Barry Clark Barish	Physics	2017
Paul Berg	Chemistry	1980	J. Michael Bishop	Medicine	1989
Elizabeth H. Blackburn	Medicine	2009	Michael S. Brown	Medicine	1985
William C. Campbell	Medicine	2015	Mario R. Capecchi	Medicine	2007
Thomas R. Cech	Chemistry	1989	Martin Chalfie	Chemistry	2008
Steven Chu	Physics	1997	Elias James Corey	Chemistry	1990
Robert F. Curl Jr.	Chemistry	1996	Johann Deisenhofer	Chemistry	1988
Andrew Z. Fire	Medicine	2006	Edmond H. Fischer	Medicine	1992
Joachim Frank	Chemistry	2017	Jerome I. Friedman	Physics	1990
Walter Gilbert	Chemistry	1980	Sheldon Glashow	Physics	1979
Joseph L. Goldstein	Medicine	1985	Carol W. Greider	Medicine	2009
David J. Gross	Physics	2004	Roger Guillemin	Medicine	1977
Leland H. Hartwell	Medicine	2001	Dudley R. Herschbach	Chemistry	1986
Roald Hoffmann	Chemistry	1981	H. Robert Horvitz	Medicine	2002
Louis J. Ignarro	Medicine	1998	William G. Kaelin Jr.	Medicine	2019
Eric R. Kandel	Medicine	2000	Wolfgang Ketterle	Physics	2001
Brian K. Kobilka	Chemistry	2012	Roger D. Kornberg	Chemistry	2006
Robert J. Lefkowitz	Chemistry	2012	Anthony J. Leggett	Physics	2003
Michael Levitt	Chemistry	2013	Roderick MacKinnon	Chemistry	2003
John C. Mather	Physics	2006	Craig C. Mello	Medicine	2006
William E. Moerner	Chemistry	2014	Mario J. Molina	Chemistry	1995
Ferid Murad	Medicine	1998	Douglas D. Osheroff	Physics	1996

James Peebles	Physics	2019
William D. Phillips	Physics	1997
Sir Richard J. Roberts	Medicine	1993
James E. Rothman	Medicine	2013
Richard R. Schrock	Chemistry	2005
Phillip A. Sharp	Medicine	1993
George P. Smith	Chemistry	2018
Thomas C. Sudhof	Medicine	2013
Joseph H. Taylor Jr.	Physics	1993
Susumu Tonegawa	Medicine	1987
Harold E. Varmus	Medicine	1989
Rainer Weiss	Physics	2017
Eric F. Wieschaus	Medicine	1995
Frank Wilczek	Physics	2004
Michael W. Young	Medicine	2017
Saul Perlmutter	Physics	2011
H. David Politzer	Physics	2004
Michael Rosbash	Medicine	2017
Randy W. Schekman	Medicine	2013
Gregg L. Semenza	Medicine	2019
Hamilton O. Smith	Medicine	1978
Horst L. Stormer	Physics	1998
Jack W. Szostak	Medicine	2009
Kip Stephen Thorne	Physics	2017
Daniel C. Tsui	Physics	1998
Steve Weinberg	Physics	1979
Carl E. Wieman	Physics	2001
Torsten N. Wiesel	Medicine	1981
Robert Woodrow Wilson	Physics	1978

SUMMARY STATEMENT

PROGRAM CONTACT: Erik Stemmy (b) (6)

(Privileged Communication)

Release Date: **01/02/2014**

Application Number: **1 R01 AI110964-01**

Principal Investigator

DASZAK, PETER PHD

Applicant Organization: ECOHEALTH ALLIANCE, INC.

Review Group: **CRFS**
Clinical Research and Field Studies of Infectious Diseases Study Section

Meeting Date: **12/18/2013**
Council: **JAN 2014**
Requested Start: **10/01/2013**

RFA/PA: **PA11-260**
PCC: **M51C**

Project Title: **Understanding the Risk of Bat Coronavirus Emergence**

SRG Action: **Impact Score:** (b) (5) **Percentile:** (b) (5)

Next Steps: **Visit http://grants.nih.gov/grants/next_steps.htm**

Human Subjects: (b) (4), (b) (5)
Animal Subjects:
Gender:
Minority:
Children:

Project Year	Direct Costs Requested	Estimated Total Cost
1	499,993	(b) (4), (b) (5)
2	499,469	
3	499,978	
4	499,953	
5	499,974	
TOTAL	2,499,367	

ADMINISTRATIVE BUDGET NOTE: The budget shown is the requested budget and has not been adjusted to reflect any recommendations made by reviewers. If an award is planned, the costs will be calculated by Institute grants management staff based on the recommendations outlined below in the COMMITTEE BUDGET RECOMMENDATIONS section.

1R01AI110964-01 DASZAK, PETER

BUDGETARY OVERLAP
PROTECTIONS FOR HUMAN SUBJECTS UNACCEPTABLE

RESUME AND SUMMARY OF DISCUSSION: This impressive application proposes studies to determine factors that increase the risk of zoonotic coronavirus (CoV) emergence 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). Given the SARS outbreak and the current emergence of MERS in the Middle East, the significance relates to advancing the knowledge of zoonotic potential of coronaviruses. (b) (5)

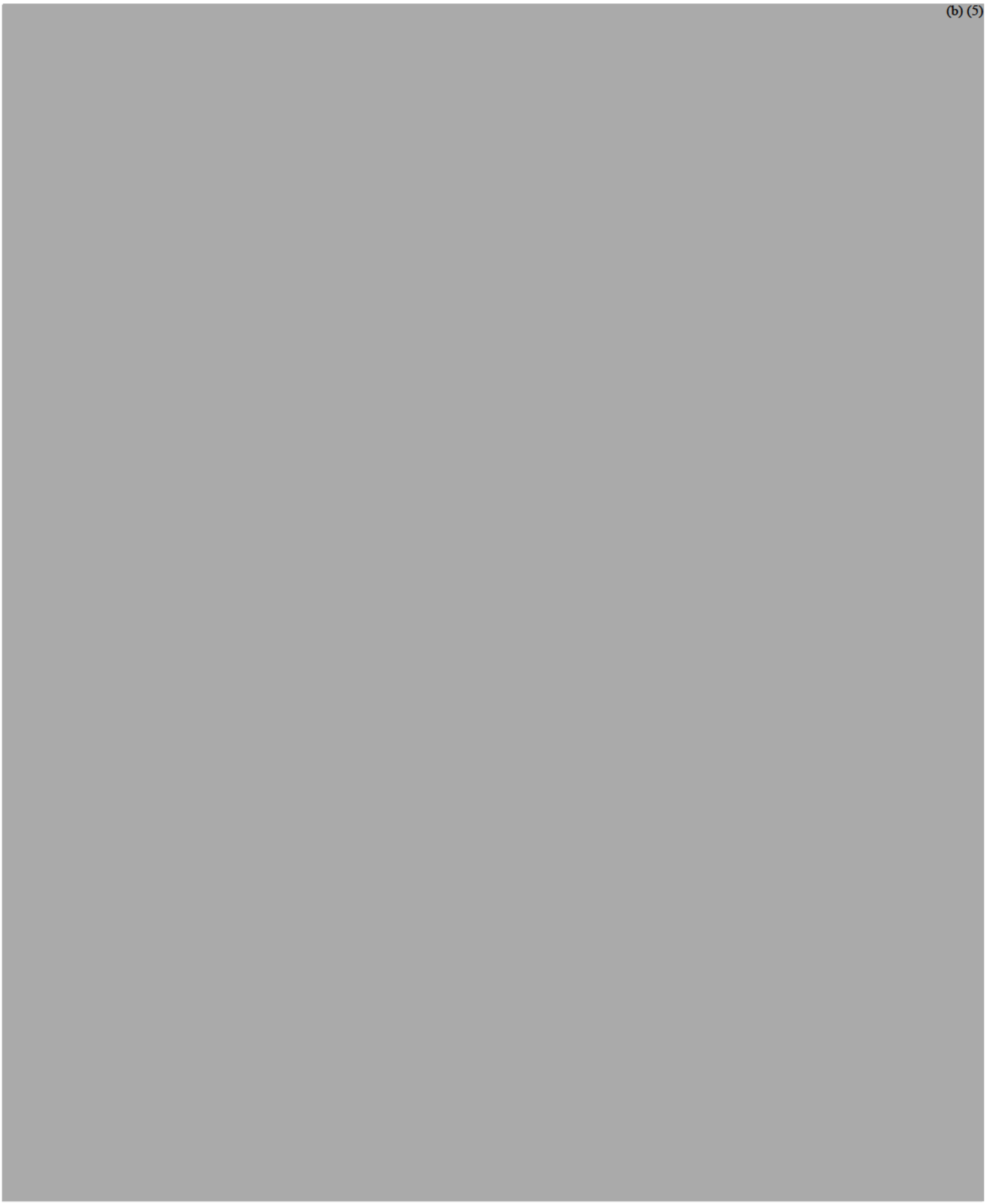
DESCRIPTION (provided by applicant): This project will examine the risk of future coronavirus (CoV) emergence from wildlife using in-depth field investigations across the human-wildlife interface in China, molecular characterization of novel CoVs and host receptor binding domain genes, mathematical models 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 large scale 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.

PUBLIC HEALTH RELEVANCE: 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).

CRITIQUE 1:

(b) (5)

[redacted]


(b) (5)

(b) (5)

Protections for Human Subjects:

(b) (5)

Inclusion of Women, Minorities and Children:

(b) (5)

Vertebrate Animals:

(b) (5)

Biohazards:

(b) (5)

Select Agents:

(b) (5)

Resource Sharing Plans:

(b) (5)

Budget and Period of Support:

(b) (5)

CRITIQUE 2:

(b) (5)

[redacted]

(b) (5)

Protections for Human Subjects:

(b) (5)

Inclusion of Women, Minorities and Children:

(b) (5)

Vertebrate Animals:

(b) (5)

Budget and Period of Support:

(b) (5)

CRITIQUE 3:

(b) (5)

(b) (5)

Protections for Human Subjects:

(b) (5)

Inclusion of Women, Minorities and Children:

(b) (5)

Vertebrate Animals:

(b) (5)

Biohazards:

(b) (5)

Budget and Period of Support:

(b) (5)

(b) (5)

THE FOLLOWING RESUME SECTIONS WERE PREPARED BY THE SCIENTIFIC REVIEW OFFICER TO SUMMARIZE THE OUTCOME OF DISCUSSIONS OF THE REVIEW COMMITTEE ON THE FOLLOWING ISSUES:

PROTECTION OF HUMAN SUBJECTS (Resume): (b) (5)

PROTECTIONS FOR HUMAN SUBJECTS (Resume): (b) (5)

(b) (5)

INCLUSION OF WOMEN PLAN (Resume): (b) (5)

INCLUSION OF MINORITIES PLAN (Resume): (b) (5)

INCLUSION OF CHILDREN PLAN (Resume): (b) (5)

VERTEBRATE ANIMALS (Resume): (b) (5)

BUDGETARY OVERLAP:

(b) (5)

COMMITTEE BUDGET RECOMMENDATIONS: (b) (5)

NIH has modified its policy regarding the receipt of resubmissions (amended applications). See Guide Notice NOT-OD-10-080 at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-10-080.html.

The impact/priority score is calculated after discussion of an application by averaging the overall scores (1-9) given by all voting reviewers on the committee and multiplying by 10. The criterion scores are submitted prior to the meeting by the individual reviewers assigned to an application, and are not discussed specifically at the review meeting or calculated into the overall impact score. Some applications also receive a percentile ranking. For details on the review process, see http://grants.nih.gov/grants/peer_review_process.htm#scoring.

MEETING ROSTER

Clinical Research and Field Studies of Infectious Diseases Study Section
Infectious Diseases and Microbiology Integrated Review Group
CENTER FOR SCIENTIFIC REVIEW
CRFS
December 18, 2013

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* Temporary Member. For grant applications, temporary members may participate in the entire meeting or may review only selected applications as needed.

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SUMMARY STATEMENT

PROGRAM CONTACT: Erik Stemmy (b) (6)

(Privileged Communication)

Release Date: 03/06/2019
Revised Date:

Application Number: 2 R01 AI110964-06

Principal Investigator

DASZAK, PETER

Applicant Organization: ECOHEALTH ALLIANCE, INC.

Review Group: CRFS
Clinical Research and Field Studies of Infectious Diseases Study Section

Meeting Date: 02/14/2019
Council: MAY 2019
Requested Start: 06/01/2019

RFA/PA: PA18-484
PCC: M51C

Project Title: Understanding the Risk of Bat Coronavirus Emergence

SRG Action: Impact Score: (b) (5) Percentile (b) (5)
Next Steps: Visit https://grants.nih.gov/grants/next_steps.htm
Human Subjects: (b) (4), (b) (5)
Animal Subjects:
Gender:
Minority:
Children:

Project Year	Direct Costs Requested	Estimated Total Cost
6	515,358	(b) (4), (b) (5)
7	515,358	
8	515,358	
9	515,358	
10	515,358	
TOTAL	2,576,790	

ADMINISTRATIVE BUDGET NOTE: The budget shown is the requested budget and has not been adjusted to reflect any recommendations made by reviewers. If an award is planned, the costs will be calculated by Institute grants management staff based on the recommendations outlined below in the COMMITTEE BUDGET RECOMMENDATIONS section.

2R01AI110964-06 DASZAK, PETER

RESUME AND SUMMARY OF DISCUSSION: This outstanding application seeks to understand what factors allow coronaviruses, including close relatives to SARS, to evolve and emerge in the human population by studying viral diversity in their animal reservoirs (bats), surveying people that live in high-risk communities in China for evidence of bat-coronavirus infection, and conducting laboratory experiments to analyze and predict which newly-discovered viruses pose the greatest threat to human health. The renewal application follows a [redacted] (b) (5)

DESCRIPTION (provided by applicant): Understanding the Risk of Bat Coronavirus Emergence Novel zoonotic, bat-origin CoVs are a significant threat to global health and food security, as the cause of SARS in China in 2002, the ongoing outbreak of MERS, and of a newly emerged Swine Acute Diarrhea Syndrome in China. In a previous R01 we found that bats in southern China harbor an extraordinary diversity of SARSr-CoVs, some of which can use human ACE2 to enter cells, infect humanized mouse models causing SARS-like illness, and evade available therapies or vaccines. We found that people living close to bat habitats are the primary risk groups for spillover, that at one site diverse SARSr-CoVs exist that contain every genetic element of the SARS-CoV genome, and identified serological evidence of human exposure among people living nearby. These findings have led to 18 published peer-reviewed papers, including two papers in Nature, and a review in Cell. Yet salient questions remain on the origin, diversity, capacity to cause illness, and risk of spillover of these viruses. In this R01 renewal we will address these issues through 3 specific aims: Aim 1. Characterize the diversity and distribution of high spillover-risk SARSr-CoVs in bats in southern China. We will use phylogeographic and viral discovery curve analyses to target additional bat sample collection and molecular CoV screening to fill in gaps in our previous sampling and fully characterize natural SARSr-CoV diversity in southern China. We will sequence receptor binding domains (spike proteins) to identify viruses with the highest potential for spillover which we will include in our experimental investigations (Aim 3). Aim 2. Community, and clinic-based syndromic, surveillance to capture SARSr-CoV spillover, routes of exposure and potential public health consequences. We will conduct biological-behavioral surveillance in high-risk populations, with known bat contact, in community and clinical settings to 1) identify risk factors for serological and PCR evidence of bat SARSr-CoVs; & 2) assess possible health effects of SARSr-CoVs infection in people. We will analyze bat-CoV serology against human-wildlife contact and exposure data to quantify risk factors and health impacts of SARSr-CoV spillover. Aim 3. In vitro and in vivo characterization of SARSr-CoV spillover risk, coupled with spatial and phylogenetic analyses to identify the regions and viruses of public health concern. We will use S protein sequence data, infectious clone technology, in vitro and in vivo infection experiments and analysis of receptor binding to test the hypothesis that % divergence thresholds in S protein sequences predict spillover potential. We will combine these data with bat host distribution, viral diversity and phylogeny, human survey of risk behaviors and illness, and serology to identify SARSr-CoV spillover risk hotspots across southern China. Together these data and analyses will be critical for the future development of public health interventions and enhanced surveillance to prevent the re-emergence of SARS or the emergence of a novel SARSr-CoV.

PUBLIC HEALTH RELEVANCE: Most emerging human viruses come from wildlife, and these represent a significant threat to public health and biosecurity in the US and globally, as was demonstrated by the SARS coronavirus pandemic of 2002-03. This project seeks to understand what factors allow coronaviruses, including close relatives to SARS, to evolve and jump into the human

population by studying viral diversity in their animal reservoirs (bats), surveying people that live in high-risk communities in China for evidence of bat-coronavirus infection, and conducting laboratory experiments to analyze and predict which newly-discovered viruses pose the greatest threat to human health.

CRITIQUE 1

(b) (5)

[redacted]

(b) (5)

(b) (5)

Protections for Human Subjects:

(b) (5)

Inclusion of Women, Minorities and Children:

(b) (5)

Vertebrate Animals:

(b) (5)

Biohazards:

(b) (5)

Renewal:

(b) (5)

Resource Sharing Plans:

(b) (5)

Authentication of Key Biological and/or Chemical Resources:

(b) (5)

Budget and Period of Support:

(b) (5)

CRITIQUE 2

(b) (5)

(b) (5)

(b) (5)

(b) (5)

Protections for Human Subjects:

(b) (5)

Inclusion of Women, Minorities and Children:

(b) (5)

Vertebrate Animals:

(b) (5)

Biohazards:

(b) (5)

Renewal:

(b) (5)

Select Agents:

(b) (5)

Resource Sharing Plans:

(b) (5)

Authentication of Key Biological and/or Chemical Resources:

(b) (5)

Budget and Period of Support:

(b) (5)

CRITIQUE 3

(b) (5)

(b) (5)

Protections for Human Subjects:

(b) (5)

Inclusion of Women, Minorities and Children:

(b) (5)

Vertebrate Animals:

(b) (5)

Biohazards:

(b) (5)

Select Agents:

(b) (5)

Resource Sharing Plans:

(b) (5)

Authentication of Key Biological and/or Chemical Resources:

(b) (5)

Budget and Period of Support:

(b) (5)

THE FOLLOWING SECTIONS WERE PREPARED BY THE SCIENTIFIC REVIEW OFFICER TO SUMMARIZE THE OUTCOME OF DISCUSSIONS OF THE REVIEW COMMITTEE, OR REVIEWERS' WRITTEN CRITIQUES, ON THE FOLLOWING ISSUES:

PROTECTION OF HUMAN SUBJECTS: (b) (5)

INCLUSION OF WOMEN PLAN: (b) (5)

INCLUSION OF MINORITIES PLAN: (b) (5)

INCLUSION OF CHILDREN PLAN: (b) (5)

VERTEBRATE ANIMALS: (b) (5)

COMMITTEE BUDGET RECOMMENDATIONS: (b) (5)

Footnotes for 2 R01 AI110964-06; PI Name: DASZAK, PETER

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MEETING ROSTER

Clinical Research and Field Studies of Infectious Diseases Study Section
Infectious Diseases and Microbiology Integrated Review Group
CENTER FOR SCIENTIFIC REVIEW
CRFS
02/14/2019 - 02/15/2019

Notice of NIH Policy to All Applicants: Meeting rosters are provided for information purposes only. Applicant investigators and institutional officials must not communicate directly with study section members about an application before or after the review. Failure to observe this policy will create a serious breach of integrity in the peer review process, and may lead to actions outlined in NOT-OD-14-073 at https://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-073.html and NOT-OD-15-106 at https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-106.html, including removal of the application from immediate review.

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A. COVER PAGE

Project Title: Understanding the Risk of Bat Coronavirus Emergence	
Grant Number: 5R01AI110964-03	**Project/Grant Period:** 06/01/2014 - 05/31/2019
Reporting Period: 06/01/2015 - 05/31/2016	**Requested Budget Period:** 06/01/2016 - 05/31/2017
Report Term Frequency: Annual	**Date Submitted:** 05/13/2016
Program Director/Principal Investigator Information: PETER DASZAK , BS PHD **Phone number:** **Email:** (b) (6)	**Recipient Organization:** ECOHEALTH ALLIANCE, INC. ECOHEALTH ALLIANCE, INC. 460 W 34TH ST 17TH FLOOR NEW YORK, NY 100012320 **DUNS:** 077090066 **EIN:** 1311726494A1 **RECIPIENT ID:**
Change of Contact PD/PI: N/A	
Administrative Official: ALEKSEI CHMURA 460 W 34th St., 17th Floor New York, NY 10001 **Phone number:** (b) (6) **Email:** (b) (6)	**Signing Official:** ALEKSEI CHMURA 460 W 34th St., 17th Floor New York, NY 10001 **Phone number:** (b) (6) **Email:** (b) (6)
Human Subjects: Yes HS Exempt: No Exemption Number: Phase III Clinical Trial:	**Vertebrate Animals:** Yes
hESC: No	**Inventions/Patents:** No

B. ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

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.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: Year 2 NIAID CoV Report Final.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

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B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

1) Conference and University lectures: PI Daszak, and Co-investigators Shi, Epstein, Olival, Ge, and Zhang gave >100 invited University and Conference lectures including Forum on Microbial Threats (National Academies of Science), Symposium at École du Val-de-Grâce in Paris, Leadership Roundtable at Concordia University Montreal, 1st annual Global Pandemic Policy Summit at Texas A&M Univ., Intl. Conf. of the Wildlife Disease Association in Australia, Intl. Conf. of Conservation Biol in Montpellier France, Michigan State University, Duke University, WDA, ISID conference, Zoological Society of London Symposium, Future Earth meeting, North American Bat Research Symposium, and others that included specific discussion of the current project and results.

2) Agency and other briefings: PI Daszak and Research Technician Dr. Guangjian Zhu introduced this project to potential collaborators within the following agencies: Forestry Dept of Peoples' Republic of China, FAO, TNC, TRAFFIC, China CDC, and TA Foundation in Beijing China in meetings (2015) and also at presentations at the first Wildlife and Public Health Workshop in China (2016) co-hosted by EcoHealth Alliance, the State Forestry Administration of China, and China CDC.

3) Public outreach: PI Daszak presented this work to members of the NIH, NSF, DoD, IUCN, EPA, and the general public, at an EcoHealth Alliance meeting hosted by the Cosmos Club, Washington D.C. (2015); PI Daszak and Co-investigator Zhu reported on this project at a Wildlife Trade and Public Health Seminar, Beijing (2016); PI Daszak introduced this project in a lecture on Pandemics at a New York Academy of Science Panel (2016); Co-PI Y-Z Zhang presented project and results-to-date to department heads and senior researchers at Infectious Disease Departments of four Yunnan Hospitals (2015)

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

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

- Given the reduced amount of wildlife in the local markets within Southern China, and the continued expansion of the Chinese wildlife trade within SE Asia, we would like to conduct short field trips to assess markets, identify wildlife in them, and sample species of bats and other high-risk hosts in countries that neighbor China (Myanmar, Vietnam, Cambodia, Lao PDR) and others that supply wildlife to the international trade to China (Thailand, Malaysia, Indonesia. EcoHealth Alliance has other activities in these countries which would provide leverage to reduce costs of fieldwork, and samples would be tested in Wuhan, China.

- Following the successful collection of ethnographic interviews and focus groups in Year 2, we will be analyzing the qualitative data collection from Years 1 and 2.

- Finalize and conduct survey collection tool for a network study of wildlife farmers using a questionnaire to characterize and map the wildlife value chain.

- After the success of our pilot studies in Year 2, we will continue targeted (at individuals with high risk of exposure to bats), integrated behavioral and biological survey work in Yunnan and expand to Guangxi and Guangdong provinces.

- We will commence our anonymized, surveillance data collection from acutely ill hospital in-patients who satisfy syndromic eligibility criteria; have complete medical records; non-normative laboratory confirmed diagnostic results; and suspected acute viral infection. Eligibility criteria are: (a) suspected acute viral infection; (b) fever > 38°C, and (c) presenting symptoms of at least one of the following:
•Encephalitis of unknown origin
•Hemorrhagic fever of unknown origin
•Respiratory disease
oInfluenza-like illness (ILI)
oSevere Acute Respiratory like Illness (SARI)
•Rash
•Diarrhea
Some patients with particular infections such as with HIV, HCV, and HBV, may be excluded from the study on that basis. Hospital surveillance has the advantage of monitoring an acutely ill population. Anonymized, passive hospital surveillance allows for data collection and viral testing from all eligible hospital patients thereby limiting population sample bias and increasing the likelihood of identifying positive cases. The strengths of this approach are enormous: an unbiased patient population; prospectively collected, anonymized patient data; a low resource effort with a high efficiency design; and impactful research potential for both case series and case control studies. We have already secured approval from the Institutional Review Boards of the Wuhan School of Public Health and Hummingbird IRB.

Specific Aim 2: Receptor evolution, host range and predictive modeling of bat-CoV emergence risk.
Future steps to optimize the model of role of species diversity in CoV emergence risk will include:

- Test and implement our respondent-driven survey to collect specific data on the diversity, abundance, and turnover of species along the wildlife trade network in south China.

- Model viral mixing across the full range parameters found along the wildlife trade network to identify the trade nodes with highest mixing potential. This will include a network analysis of market facility/site connectivity including wild harvest sites, wildlife farming operations, transit holding facilities, and small and large wildlife markets.

- Phylogeographic study of bat-CoV to better understand the geographic distribution and evolution of bat-CoV genetic diversity in south

China.

- Phylogeographic study of bat host (Rhinolophus) species to assess the connectivity of bat populations and infer their historical movements and demographic history to improve our understanding of CoV transmission among bat populations in southern China. Preliminary sequences data has been generated and will be completed and analyzed.

- Cophylogenetic analyses of bat host and CoV phylogenies to assess frequency of cross-species transmission. Comparison of Alpha- and Beta-CoV cophylogenetic patterns building on Year 2 analyses using published sequences and also including Spike gene and additional sequences obtained in Year 2.

- Test and implement our respondent-driven survey to assess diversity, abundance, and turnover of species along the wildlife trade network.

- Examine co-evolutionary congruence of bat-CoVs and their hosts using both functional (receptor) and neutral genes;

- Parameterize mathematical models that predict CoV evolutionary and transmission dynamics
- Continued surveillances of SARS-like CoVs and lineage C betacoronaviruses (MERS-related CoVs) in Southern China;

- Full-length genome sequencing and evolution analysis of SARS-like coronaviruses identified from different bat species and different geographical locations across China;

- Full-length genome sequencing and evolution analysis of Lineage C betacoronaviruses identified from different bat species and different geographical locations across China;

- Full-length genome sequencing and evolution analysis of HKU9-related and HKU10-related bat coronaviruses in China;

Specific Aim 3: Testing predictions of CoV inter-species transmission. The following experiments will be undertaken in Year 2:

- Humanized mice with human ACE2 receptors will be infected with WIV1 and the two rescued chimeric SARS-like coronaviruses to determine the tissue tropism and pathogenicity of bat SL-CoV

- Isolation of novel bat coronaviruses. Live virus or pseudovirus will be used to infect cells of different origin or expressing different receptor molecules. Spillover potential for each isolated virus will be assessed.

- An infectious clone of full-length MERS-CoV will be constructed using reverse genetic method. Using the S sequence of different MERS-related viruses identified from Chinese bats, the chimeric viruses with S gene of bat MERS-related coronaviruses and backbone of the infectious clone of MERS-CoV will be constructed to study the receptor usage and infectivity of bat MERS-related coronavirus.

- Surveillance of infection in human populations by SARS-like CoVs. This work will be performed at locations in Yunnan, Guangxi, and Guangdong provinces, in previously identified areas with human populations of high risk of exposure to bats. PCR and ELISA will be used, respectively, for detection of viral replicase gene and antibodies against the viral nucleocapsid protein.

Year 1 Report: Understanding the Risk of Bat Coronavirus Emergence

Award Number: 1R01AI110964-02

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Section B: Accomplishments

B.1 What are the Major Goals of the Project

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.

B.1a Have the major goals changed since the initial competing award or previous report? No.

B.2 What was accomplished under these goals?

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

In year 2, we continued and expanded the qualitative research begun at the end of Year 1. In addition, a community based integrated biological behavioral surveillance system was developed and pilot tested to identify specific animal exposure risk factors associated with biological evidence of exposure to SARS-like CoV (i.e., seropositive status).

QUALITATIVE RESEARCH

Targeted, in-depth ethnographic interviews were conducted with 47 individuals (18 women; 29 men) in rural Southern China where wildlife trade routes have been documented. Yunnan, Guangxi and Guangdong provinces were specifically selected for study because they have large wildlife populations, a diversity of wildlife species and numerous live animal markets. Individuals who were 18 years of age or older and who were able to provide informed consent were eligible to participate. Twenty-three (49%) in-depth interviews were conducted in Yunnan province at nine different sites, 24 (51%) in Guangxi province at six different sites. In addition, one focus group was conducted in Guangxi. The study was approved by the Institutional Review Boards of the Wuhan School of Public Health and Hummingbird IRB.

Recruitment sites in each province included forested areas or preserves, wildlife farms, hunting areas, wildlife restaurants, live animal markets, caves where people dwell or collect guano and residential areas/farms near known bat caves or roosts. Participants were recruited primarily through local contacts developed as part of wildlife conservation and health research conducted by team members over the past decade. Contacts including wildlife conservationists and researchers, local government health outreach workers and wildlife farmers facilitated introductions and provided referrals. To achieve a sample with sufficient representation of categories of interest, participants were recruited using

purposive sampling, which provides minimum quotas in terms of sex, age and wildlife exposure setting (e.g., live animal market, forest preserve).

The five core themes that guided the in-depth discussions are: 1) human-animal contact, 2) unusual illness experience and response, 3) socioeconomics and daily living, 4) biosafety and 5) human environments and movement/travel. An ethnographic interview guide was developed with examples of questions that could be asked for each theme. In addition, field based participant-observation was ongoing throughout the study and involved observing and talking informally with people in their own natural setting. Field notes were maintained of these ongoing observations and discussions.

Table 1: Species Observed in Wetmarkets in Guangdong Province from 2015 - 2016

Genus species	Common Name
Prionailurus bengalensis	Leopard Cat
Nyctereutes procyonoides	Raccoon Dog
Sus scrofa	Wild Boar
Lepus sinensis	Chinese Hare
Arctonyx collaris	Hog Badger
Hystrix brachyura	Porcupine
Marmota sp.	Marmot
Rhizomes sinensis	Bamboo Rat
Erinaceus sp.	Hedgehog
Mustela putorius	Ferrets
Muridae	Rat (species unknown)
Myocastor coypus	Nutria
Vulpes sp.	Fox
Mustela sibirica	Siberian weasel
Paguma larvata	Masked Palm Civet
Felis catus	Domestic Cat
Canis lupus familiaris	Domestic Dog
Cervinae	Sambar Deer
Ovis aries	Sheep
Capra sp.	Domestic Goat
Ratus norvegicus	Common Rat

Interviews were conducted between March and June 2105 by 10 trained interviewers, none of whom had social science training. Interviewers conducted between one and 22 interviews; three interviewers conducted two thirds of all interviewers. Interviews lasted between 20 and 60 minutes, and were tape-recorded and transcribed verbatim before they were translated into English. All participants received cooking oil valued at US$10 in appreciation of their time.

The data are currently being coded and an analytic database is being constructed. Initial insights include observations by a number of participants, especially those who are older, that there has been a decrease in wildlife in the surrounding environment. This decrease is attributed to many factors including infrastructure development. The government has invested resources to build new roads and renovate local infrastructure with the intention of increasing tourism. This has reduced forested area.

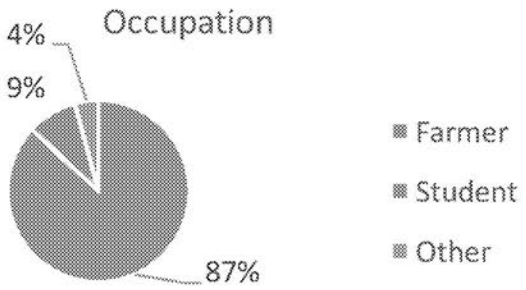
Observations by research staff in live animal markets in Guangzhou found wildlife to be plentiful (see Table 1), although no bats were seen for sale during the observation period. In contrast, wildlife was not found in live animal markets at the sites we visited in either Yunnan or Guangxi. This is a change from previous research visits to the same or similar communities, when bats, rodents and wild boar could be found. Locals in Yunnan and Guangxi attribute the change to conservation law enforcement. The success of conservation enforcement may have moved hunting and trapping underground and made the capture of local wildlife less economically feasible than other income generating activities.

Preliminary analyses are underway. Three specific studies in support of Specific Aim 1 are being developed: the changing wildlife trade in Southern China, the economics of wildlife farming, and zoonotic disease risks resulting from a rapidly changing wildlife trade.

INTEGRATED BIOLOGICAL BEHAVIORAL SURVEILLANCE PILOT STUDY

Currently, mechanisms of zoonotic viral spillover are unknown. In order to evaluate potential risk factors, it is necessary to measure both exposure and outcome data. Therefore, a behavioral risk survey was developed that assessed both animal exposure and experiences of unusual illness both during lifetime and in the past 12 months. In addition, participants were requested to provide serum to test for previous exposure to SARS-like CoV. The integrated surveillance was pilot tested in October 2015 among residents living near bat caves or roosts where SARS-like-CoV has been previously detected in the bat population in Jinning County, Yunnan. Please view the full survey here:

https://www.dropbox.com/s/sv62neywuvl027r/Questionnaire%20Complete.docx?dl=0



Of 218 participants, 139 (64%) were women and 79 (36%) were men, with a mean age of 48 (range: 12-80). Most reported being farmers (87%, and see chart to left); a majority were long term residents (97%). Animal exposures in the past year were extensive, including general (e.g., buying live animals at markets [61%]) and intimate (e.g., being scratched or bitten [9%], slaughter [38%]). In fact, two-thirds of participants reported handling recently killed animal parts and 2 out of 5 reported slaughtering animals. Only 20 (9%) participants reported known exposure to bats.

Standardized syndromic case definitions informed questions concerning unusual illness experience (e.g. severe acute respiratory infections [SARI], influenza-like illness [ILI]). Lifetime, 12 month and unusual illness experience in family for the past 12 months were assessed for all participants. In the past year, SARI was reported by 4 (2%) respondents and for 4 additional family members. Table 2 provides data for all unusual illness experience assessed. None of the participants were found to be seropositive for SARS-like CoV.

Table 2. Unusual Illness Experience

Symptoms	Ever	Past 12 months	Family (12m)
Severe Acute Respiratory Infections (SARI)	15 (6.9%)	4 (1.8%)	4 (1.8%)
Influenza Like Illness (ILI)	54 (24.8%)	16 (7.3%)	26 (11.9%)
Encephalitis	19 (8.7%	4 (1.8%)	3 (1.4%)
Hemorrhagic Fever	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fever with Diarrhea /Vomiting	12 (5.5.%)	2 (0.9%)	3 (1.4%)
Fever with Rash	2 (0.9%)	2 (0.9%)	3 (1.4%)

Although the sample size was small, animal exposures among those who reported unusual illness experiences in the past 12 months were evaluated. Of the four respondents who reported SARI symptoms, 75% reported: raising animals, animals in the home, preparing recently killed animals and buying live animals; 50% reported slaughter. Among the 16 respondents who reported ILI symptoms, 12 (75%) reported handling/preparing recently killed animals, 11 (69%) Handling live animals or having animals in the home, 10 (63%) reported slaughtering/killing animals or buying live animals at wet market, 9 (56%) raised live animals, 7 (44%) reported a pet, and 1 (6%) reported animal feces near food or eating animal touched or damaged food, hunting, or eating raw/undercooked animal products. Finally, among the four respondents who reported encephalitis symptoms, 3 (75%) reported hunting, handling or raising animals, 2 (50%) reported animals in the home, 1 (25%) reported having animals as pets, slaughtering/killing animals, or having bought live animals at wet market.

Respondents were asked about the source of their unusual illnesses. None reported any kind of animal exposure as a potential source of infection and most stated they had no idea how they had become infected. However, when asked about potential behavior changes made at live animal markets in the last 12 months, participants reported a great deal of change. In particular, respondents reported buying live animals less often (38%), only buying farmed wildlife (54%) or buying meat at the supermarket (23%). (See Table 3).

Table 3: Behavior Change at Wet Market in the last 12 months

Behavior	N	(%)
Wear a mask	4	(3.0)
Wear gloves	5	(3.8)
Wash hands	80	(60.6)
Sometimes shop for meat at supermarket	30	(22.7)
Buy live animals less often	50	(37.9)
Buy only farmed wildlife	71	(53.8)
No longer buy wildlife at wet market	39	(29.5)

The results of this pilot study conducted with a largely female farmer population found high levels of unusual illness, as well as high levels of exposure to animals. There was a notable lack of knowledge of animals' ability to transmit infection. Despite this lack of knowledge, there may be a sense of unease about animal exposures, given the fairly dramatic behavior changes reported at live animal markets. The finding of a reduction in wildlife purchase may be due to sensitivity to the legality of wildlife trade, biasing respondents towards not admitting purchasing wildlife. Although, there were no participants seropositive for SARS-like CoV, serological data may add support to the findings from self-reported syndromic surveillance, once serological assays are optimized.

In preparation for full implementation of the integrated biological behavioral surveillance, the survey has been programmed as an application for use on either a mobile device or computer. Electronic data collection will facilitate survey implementation in the field and quality control of the data being collected. Four field team leads were trained on behavioral survey data collection, data collection technologies (the tablet application) and analysis.

Nucleic acid test results of human biological samples

Testing High-Risk Human Populations for Coronavirus Infection

Surveillance of CoV infections in human populations by SARS-like CoVs was significantly expanded in Year 2, including both custom-built ELISA serology (an assay developed by the Wuhan Institute of Virology to test antibodies against the N protein of SL-CoV) and PCR detection of viral RNA.

Serological test for SL-CoV antibodies in human samples from Jinning, Yunnan Province
In order to assess past exposure to bat CoVs, 223 human sera samples were collected in villages in proximity to the bat habitat from which two SL-CoVs with potential for interspecies infection, WIV1 and WIV16, were discovered in our previous research. An ELISA developed by the Wuhan Institute of Virology was used to test antibodies against the N protein of SL-CoV. A number of human specimens generated high OD values and neutralization test to WIV1 and WIV16 was then performed. These findings are encouraging; however, no neutralization antibodies were detected. In Year 3, we will continue to validate and optimize these ELISA assays and other serological tests to obtain data on past CoV exposure.

PCR test for CoV Nucleic Acid in human samples from several Provinces
We tested 405 individual human samples for CoV RNA to identify evidence of active infection in human populations and to obtain sequence data on strain variation. Individual samples (4 each) were pooled prior to nucleic acid extraction then tested using PCR. When a group tested positive, we then conducted the confirmation test in the individual samples. One single sample (14XN611) from someone who had identified as having had a fever and suffered both a cough and headache in the past 7-days was then identified to be positive for HCoV-HKU1. The low number of PCR detections in human specimens is not unexpected, and will be improved in Year 3-5 by better targeting syndromic individuals for specimen collection and continuing to optimize PCR assays. Refined serological assays (above) will provide sufficient data to assess past exposure to specific CoV lineages, and optimizing of PCR detections will allow for more CoV positive human sequences moving forward.

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

Bat CoV PCR detection and sequencing from live-sampled bat populations
We collected 1,714 anal swab samples, 677 fecal samples, 53 blood samples, and 38 serum samples from 15 bat genera in Guangdong, Yunnan, Sichuan, Hubei, Hunan, Guizhou, Guangxi provinces (Table 4).

Table 4 Bat Samples collected for CoV surveillance in 2015

Sample date	Sample location	Anal	Fecal	Blood	Serum
Mar. 2015	Huidong, Guangdong	69	--	--	--
Jun. 2015	Guangdong	495	--	12	--
Apr. 2015	Menglun, Yunnan	51	--	--	--
May 2015	Jinning, Yunnan	--	193	--	--
May. 2015	Mojiang, Yunnan	93	--	--	--
Oct. 2015	Jinning, Yunnan	30	--	--	--

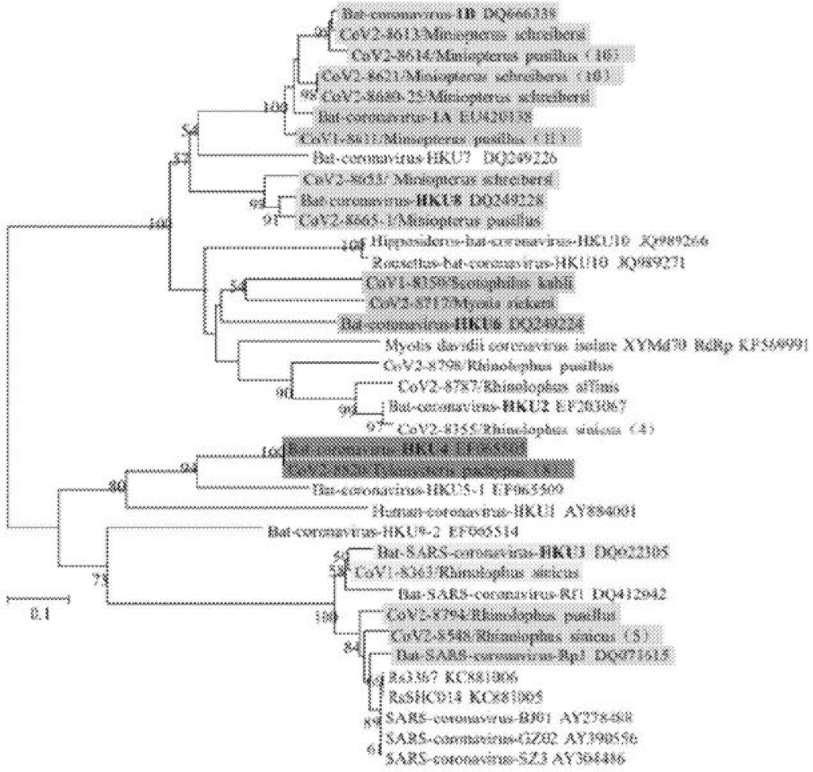
Dec, 2015	Jingna, Yunnan	15	15	13	13
	Miaoxin, Yunnan		42	28	25
Jul, 2015	Zigong, Sichuan	128	--	--	--
Aug, 2015	Hubei		332		
Sep, 2015	Xianning, Hubei		95		
Aug, 2015	Jishou, Hunnan	204			
Aug-Sep, 2015	Tongren, Guizhou	438			
Dec, 2015	Longzhou, Guangxi	191			
	Total	1714	677	53	38

We tested 2,256 samples for CoV RNA and 280 tested positive. The total positive rate is 12.4% (Table 5). Diverse alphacoronaviruses related to Bat CoV 1A, 1B, HKU2, HKU6, HKU7, HKU8 and HKU10 were identified; SARS-like coronaviruses were detected in *Rhinolophus* bats in both Yunnan and Guangdong (Fig 1). Novel lineage B betacoronaviruses more distantly related to SARS-CoV than other SL-CoVs were detected in *Vespertilo superans* in Sichuan. HKU4-related coronaviruses were found in *Tynolycteris pachypus* in Guangdong and Guangxi while HKU5-related coronaviruses were found to be highly prevalent in *Vespertilio superans* in Zigong, Sichuan (41 bats out of 128 tested positive).

Table 5 Test result of bat CoV surveillance in 2015 – 12% positive (280/2,256)

	Yunnan	Guangdong	Hubei	Sichuan	Guangxi	Guizhou	Hunan	Total
Bat species	**No.positive/No.tested**							
Rhinolophus spp.	47/98	12/103				16/225	8/63	83/489
Hipposideros spp.	0/35	0/51	26/152			0/131	0/91	26/460
Ia io						0/3		0/3
Pipistrellus spp.	1/1	0/19				0/2	0/4	1/26
Miniopterus spp.	6/7	34/83				2/6		42/96
Eonycteris spp.	0/3							0/3
Vespertilio superans				41/128				41/128
Myotis spp.		1/38				0/70	0/35	1/143
Taphozous spp.	0/25					0/1		0/26
Tynolycteris pachypus		8/25			27/191			35/216
Scotophilus kuhlii		1/1						1/1
Eptesicus fuscus		0/1						0/1
Tadrida spp.		0/5						0/5
Barbastella							0/1	0/1
Nyclatus velutiaus							0/10	0/10
Fecal samples	28/468		22/180					50/648
Sub-total	82/637	56/326	48/332	41/128	27/191	18/438	8/204	**280/2256**

A



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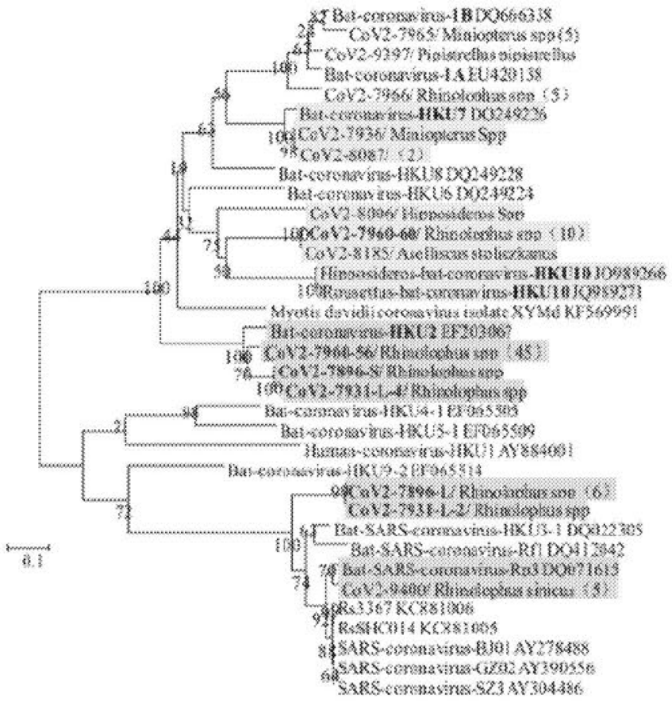


Fig 1 Phylogenetic analysis of partial RdRp gene of CoV (440-nt partial sequence). CoVs identified in 2015 are named by the sample numbers. Sequence amplified from samples co-infected with two CoV strains are indicated in red. (A) CoVs detected in Guangdong. (B) CoVs detected in Yunnan.

Cophylogenetic analysis of CoV host switching

We completed preliminary cophylogenetic analysis of bat host – CoV sequences using data published in the literature and available on Genbank. Two figures from these analyses are highlighted below (Figs 2 and 3) and these methods are currently being extended using partial RdRp CoV and bat mitochondrial DNA sequences from a large number of bat specimens found CoV positive in Year 2 (Table 5, above).

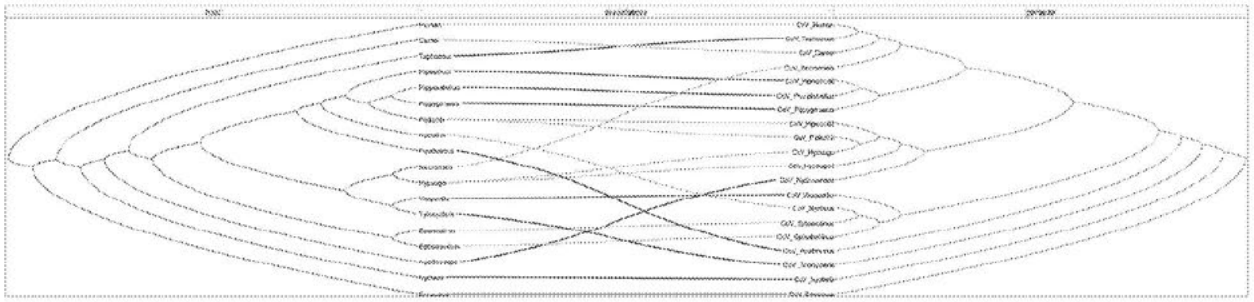


Figure 2: Tanglegram depicting the pattern of infection of bats (and outlier mammalian hosts) by CoVs. The CoV tree was reconstructed from DNA sequences available in GenBank (partial RdRp gene) using Bayesian inference (MrBayes). The topology of host tree was reconstructed using the mammal and bat phylogenies available in Asher & Helgen (2010) and Agnarsson et al. (2011), using methods our group has previously applied to bat parasite cophylogenetic analyses (Lei and Olival 2014). Both ParaFit (ParaFitGlobal = 64957.61, p-value = 0.001) and PACo (m2 = 366.44, p-value = 0.013) provided evidence for significant global congruence between the two topologies, and evidence for coevolution. Lines connecting taxa indicate host-CoV associations. Red lines indicate significant host-CoV associations as indicated by ParaFit ($p \leqslant 0.05$, 999 permutations).

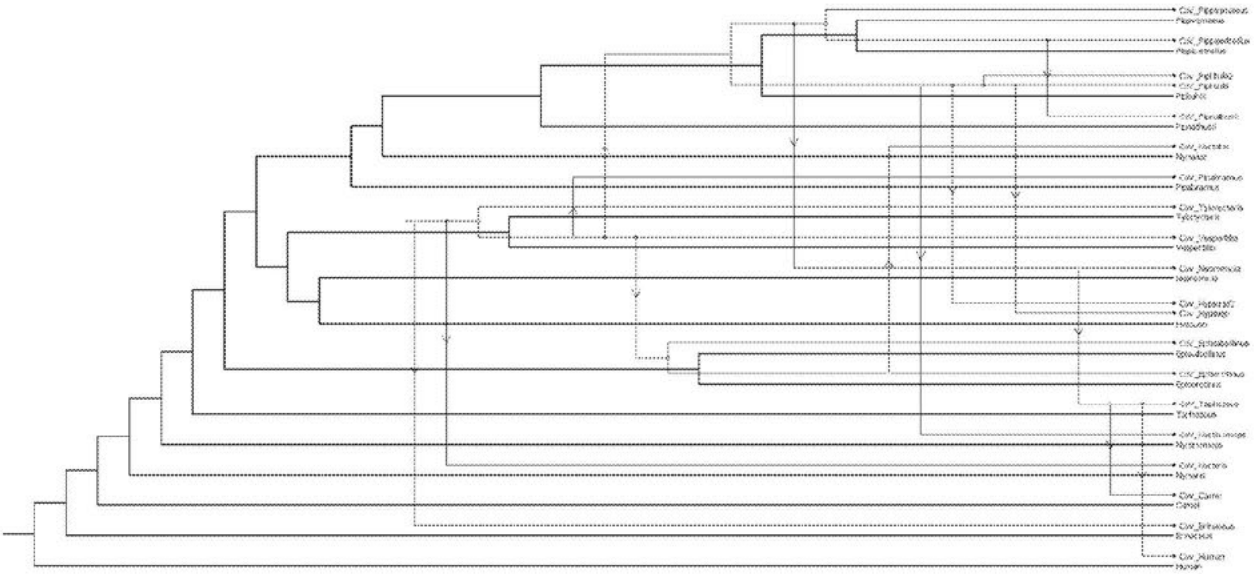


Figure 3: Reconstruction of one of 3 potentially optimal solutions of reconciled host-CoV trees recovered from a Jane analysis. Black and blue lines represent the host and CoV trees, respectively. For each solution, the number of co-speciation events inferred by Jane was always significantly greater than expected by chance. Jane inferred 4 co-speciation events (hollow colored circles), 1 duplication (solid

colored circle), 14 host switches (solid colored circle with arrow), 0 loss and 0 failure to diverge.

Our findings demonstrate co-speciation alone is not sufficient to explain the observed co-phylogenetic pattern and several host switches can be specifically identified. This is the case even if a significant global signal of co-speciation has been detected. This work highlights, the need for these types of detailed cophylgoenetic analyses to best explain the evolutionary history and host-switching of bat-CoVs.

References cited for the above analysis: Agnarsson, I., Zambrana-Torrelio, C.M., Flores-Saldana, N.P. & May-Collado, L.J. (2011) A time-calibrated species-level phylogeny of bats (Chiroptera, Mammalia). *PLOS Currents*, 3:RRN1212. Asher, R.J. & Helgen, K.M. (2010) Nomenclature and placental mammal phylogeny. *BMC Evolutionary Biology*, 10, 1-9. Lei BR, Olival KJ (2014) Contrasting Patterns in Mammal–Bacteria Coevolution: *Bartonella* and *Leptospira* in Bats and Rodents. *PLoS Negl Trop Dis* 8(3): e2738.

Market Characterization Model Parameterization

Our ongoing observational research and mapping of farms and markets suggests that rapid changes in the market and regulatory environment are changing the nature and location of the wildlife market trade. The nexus of the wildlife trade and the potential hotspots of interspecies viral mixing is now in many cases in animal storage facilities and transport between high-volume customers. To define realistic parameters for intermixing wildlife species in areas of high potential mixing, we have developed a preliminary survey and sampling protocol to assess these values as animals move along the value chain – through these storage facilities - using respondent-driven questionnaires to follow and sample along the wildlife trade network and reveal hidden nodes and sites of intermixing of species.

We have expanded our intermixing modeling framework to incorporate the variations along this value chain, where the diversity, abundance, residence time, and contact rates between species change as animals move through the trade network.

Specific Aim 3: Testing predictions of CoV inter-species transmission.

In Year 2, we continued surveillance for novel SARS-like CoVs from bats in Yunnan and Guangdong provinces and obtained full genome sequence for 11 CoV isolates. Full genome analysis of these CoV isolates was completed, including phylogenetic and recombination analyses. Importantly, recombination analysis of the full-length SL-CoV genome sequences from a single bat population revealed that frequent recombination events among different SL-CoV strains occur. Several SL-CoVs that are more genetically similar to SARS-CoV (2003) than any previously discovered were also identified from bat populations in Yunnan province. Full genome analysis suggests that an epicenter of SL-CoV occurs in rhinolophid bats and provides more insight into the evolutionary origin of SARS-CoV.

Full-length genome sequencing of SL-CoVs identified from a single bat colony

To date, including preliminary data submitted for this R01 that we are now analyzing under the current funding, we have conducted 5-years of surveillance of SL-CoV in a single bat colony in Yunnan Province (from 2011 to 2015), leading to the discovery of diverse novel SL-CoVs. Based on genotyping of these SL-CoVs by the region corresponding to the receptor-binding domain (RBD) of SARS-CoVs, 11 isolates were selected and full-length genome sequencing was performed in Year 2.

These SL-CoVs, including four others isolated previously from this colony, Rs3367, RsSHC014, WIV1 and WIV16, are highly diversified in the S gene, but share similar sequence identity to SARS-CoV in ORF1ab (Fig 4). Genomic phylogenetic analysis showed that the SL-CoVs detected in this colony are more closely

related to SARS-CoVs from other geographic regions, especially three isolates, WIV16, Rs4874 and Rs4231 (Fig 5). Notably, among the 15 SL-CoVs, two isolates, Rs4084 from *Rhinolophus sinicus* and Rf4092 from *Rhinolophus ferrumequinum*, are highly similar to SARS-CoV in the ORF8 region (Fig 5). Rf4092 possessed a single ORF8 of the same length (369bp) as that in civet SARS-CoV SZ3, and the sequence showed only 10 nucleotide substitution (Fig 6). The ORF8 sequence of Rs4084 is highly similar to that of Rf4092, however in the region corresponding to the 29-bp deletion acquired in human SARS CoVs (e.g Tor2), a shorter deletion of only 5-bp is present, resulting in two overlapping ORF8s, ORF8a and ORF8b. The position of start codon and stop codon of the two ORFs were consistent with those in human strains (Fig 6).

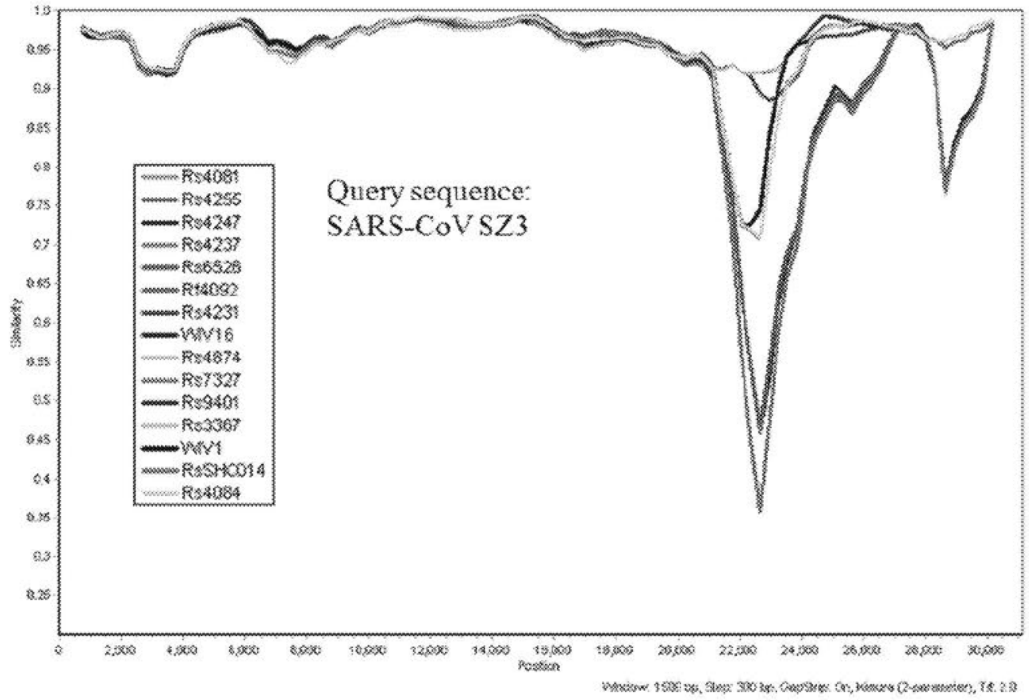


Fig 4. Simplot analysis of the 15 SL-CoVs identified from a single bat colony in Yunnan. SARS-CoV SZ3 is used as query sequence.

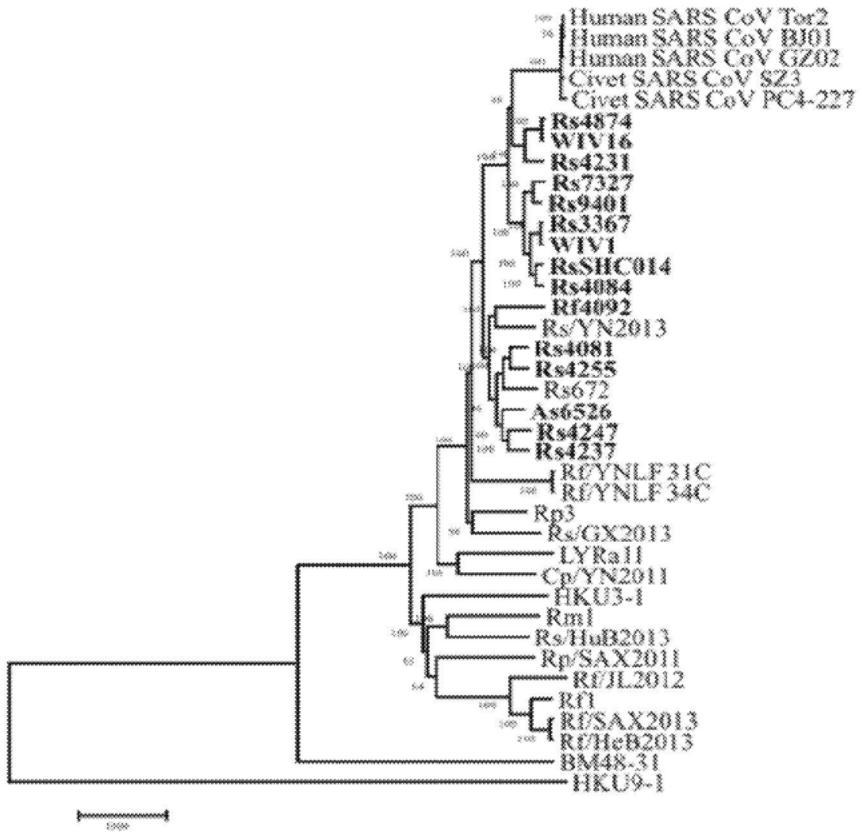


Fig 5. Phylogenetic analysis of full-length genome sequences of SL-CoVs and SARS-CoVs. Isolates identified in the single investigated bat colony in Yunnan in in bold.

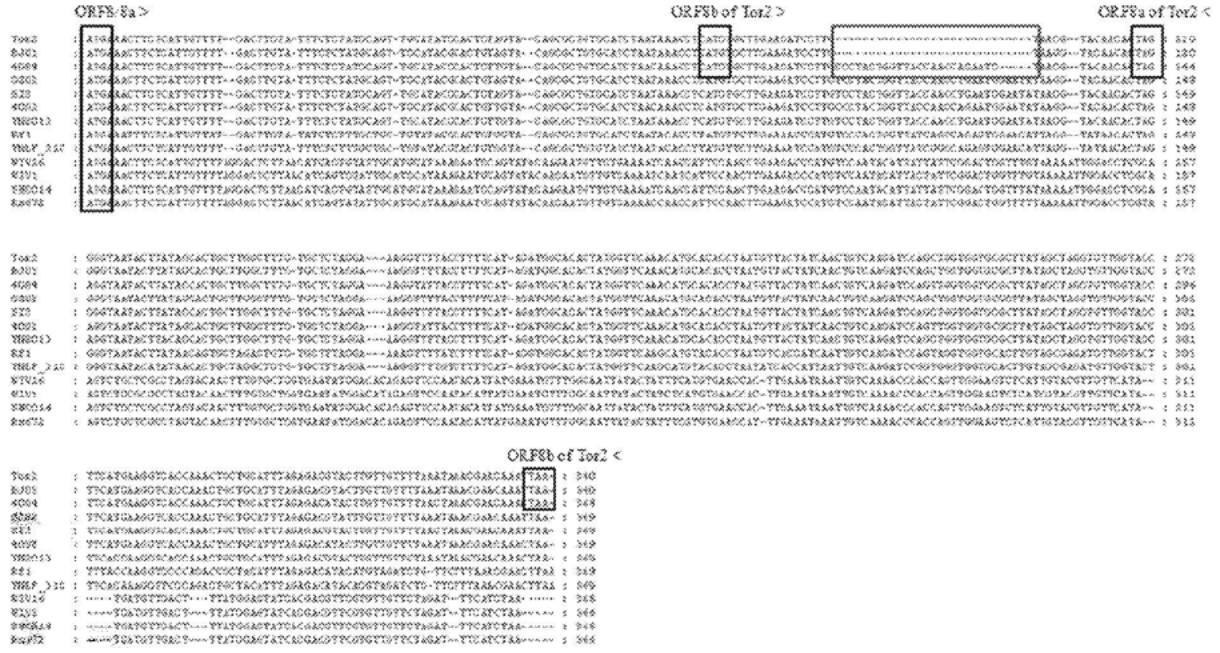
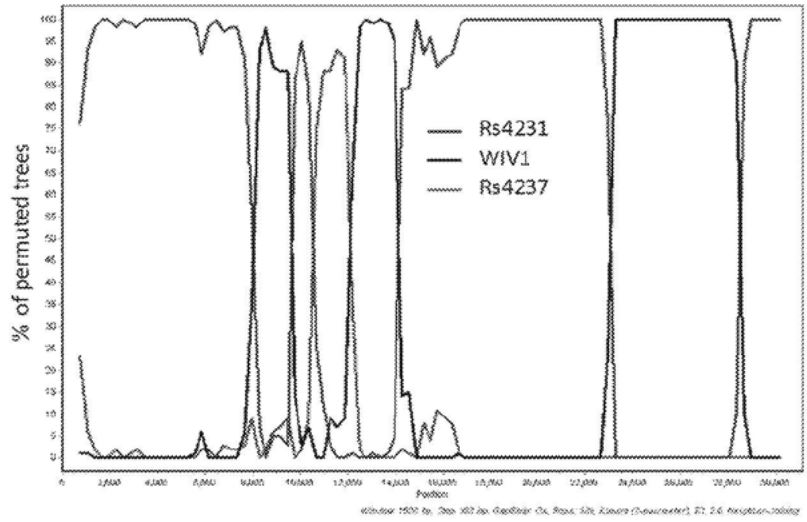


Fig 6. Alignment of ORF8 nucleotide sequences of SARS-CoV and bat SL-CoVs. The red box indicates the 29-nt deletion present in SARS-CoV of middle and late phase.

Recombination analysis of the full-length genome sequences reveals frequent recombination events among different SL-CoV strains circulating in this bat population. For example, WIV16 appears to be a recombination product of WIV1 and Rs4231. An important breakpoint is identified between the N-terminal domain (NTD) and RBD region in the S gene (Fig 7A). Consequently, WIV16 is identical to Rs4231 and WIV1 in NTD and RBD of the spike protein, respectively, and is highly homologous to SARS-CoV in both NTD and RBD. This makes it the SL-CoV most closely related to the direct progenitor of SARS-CoV discovered to date. Moreover, evidence is found to support the hypothesis that the direct progenitor of SARS-CoV was generated from recombination of WIV16 with Rf4092 at the site near ORF8. This work, which identifies diverse SL-CoVs highly homologous to SARS-CoV in different regions of the genome, suggests that rhinolophid bats are an evolutionary epicenter of SL-CoV and offers more insights into the evolutionary origin of SARS-CoV.

A.



B.

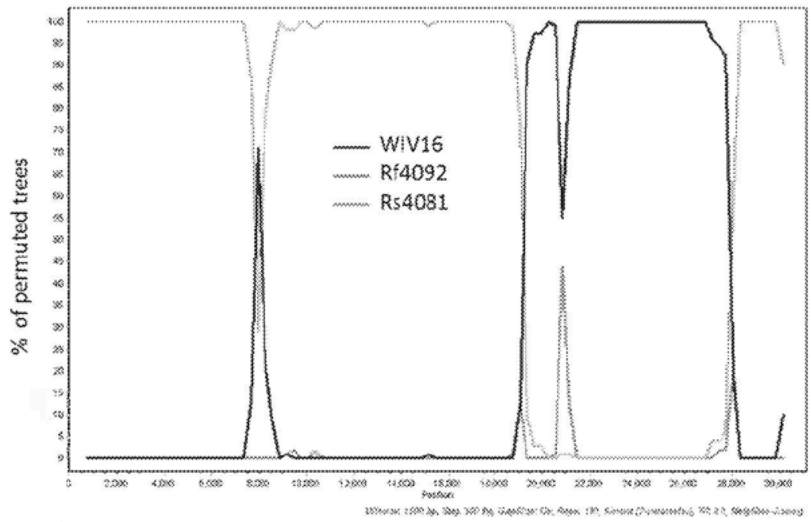


Fig 7 Bootscan analysis of full-length genome sequences of SL-CoVs. (A) WIV16 is used as query sequence. (B) SARS-CoV SZ3 is used as the query sequence. (Kimura model, window size, 1500bp, step size, 300bp)

Additional Year 2 items for Specific Aim 3:

- The infectious clone of WIV1 was successfully constructed using reverse genetic methods;
- Two chimeric bat SARS-like coronavirus strains were constructed by replacing the S gene in the backbone of WIV1;
- Permission to import mice with human ACE2 to China was obtained, so as to conduct the experimental infections proposed in our R01 specific aims.

Specific Goals Not Met.

- Comparative cophylogenetic analyses of bat host and CoV RdRp and Spike gene phylogenies, to assess patterns of evolutionary congruence and frequency of cross-species transmission (This will be conducted in year 3);
- Animal infection experiments of SARS-like coronaviruses were not done, because of the unavailability of mice with human ACE2 in Year 2. We now have secured these mice and will begin this work in year 3.
- Sampling of bat and other mammalian species in markets to screen for CoVs. We will begin this work in year 3.

Section C: Accomplishments: Publications

PUBLISHED

Xing-Yi Ge, Ning Wang, Wei Zhang, Ben Hu, Bei Li, Yun-Zhi Zhang, Ji-Hua Zhou, Chu-Ming Luo, Xing-Lou Yang, Li-Jun Wu, Bo Wang, Yun Zhang, Zong-Xiao Li, and Zheng-Li Shi. Coexistence of multiple coronaviruses in several bat colonies in an abandoned mineshaft. *Virologica Sinica* 31, 31–40 (2016).

Mei-Niang Wang, Wei Zhang, Yu-Tao Gao, Ben Hu, Xing-Yi Ge, Xing-Lou Yang, Yun-Zhi Zhang, Zheng-Li Shi. Longitudinal surveillance of SARS-like coronaviruses in bats by quantitative real-time PCR, *Virologica Sinica* 31(1): 78-80 (2016).

Cristin C. W. Young and Kevin J. Olival. Optimizing Viral Discovery in Bats. *PLoS ONE* 11(2) (2016).

Kevin J. Olival. To Cull, or Not To Cull, Bat is the Question. *Ecohealth* 13, 6–8 (2015).

Xing-Lou Yang, Ben Hu, Bo Wang, Mei-Niang Wang, Qian Zhang, Wei Zhang, Li-Jun Wu, Xing-Yi Ge, Yun-Zhi Zhang, Peter Daszak, Lin-Fa Wang, Zheng-Li Shi. Isolation and characterization of a novel bat coronavirus closely related to the direct progenitor of Severe Acute Respiratory Syndrome Coronavirus, *Journal of Virology* 90(6): 3253-6 (2015).

Ben Hu, Xingyi Ge, Lin-Fa Wang, Zhengli Shi. Bat origin of human coronaviruses. *Virology Journal* 12 (1): 221 (2015)

ACCEPTED, IN PRESS

Lei-Ping Zeng, Yu-Tao Gao, Xying-Yi Ge, Qian Zhang, Cheng Peng, Xinglou Yang, Bin Tan, Jing Chen, Aleksei Chmura, Peter Daszak, and Zheng-Li Shi. Bat SARS-like coronavirus WIV1 encodes an extra accessory protein ORFX involving in modulation of host immune response. *Journal of Virology* (in press, 2016)

B.4 What opportunities for training and professional development has the project provided?

We presented our project to graduate students, laboratory personnel, directors, and doctors from three Hospitals in Yunnan Province: Yunnan Provincial Institute of Endemic Diseases Control & Prevention (YNCDC); Dali Provincial Hospital; and The Third People's Hospital of Kunming. Select doctors at YNCDC (1) and Dali Provincial Hospital (3) were trained in the passive Hospital surveillance project protocols.

We trained graduate students from Dali School of Public Health (1) and the Wuhan University School of Public Health (3) in qualitative behavioral risk data collection methodologies and data collection technologies, survey data collection and analysis. These were also enrolled in and passed the Human Subjects Research Course provided by the Collaborative Institutional Training Initiative (CITI Program) at the University of Miami (http://citiprogram.org). The CITI Program is a leading provider of research education content with web based training materials serving millions of learners at academic institutions, government agencies, and commercial organizations in the U.S. and around the world.

C. PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

Yes

Publications Reported for this Reporting Period

Public Access Compliance	Citation
Complete	Yang XL, Hu B, Wang B, Wang MN, Zhang Q, Zhang W, Wu LJ, Ge XY, Zhang YZ, Daszak P, Wang LF, Shi ZL. Isolation and Characterization of a Novel Bat Coronavirus Closely Related to the Direct Progenitor of Severe Acute Respiratory Syndrome Coronavirus. J Virol. 2015 Dec 30;90(6):3253-6. PubMed PMID: 26719272; PubMed Central PMCID: PMC4810638.
Complete	Olival KJ. To Cull, or Not To Cull, Bat is the Question. Ecohealth. 2016 Mar;13(1):6-8. PubMed PMID: 26631385; PubMed Central PMCID: PMC4833651.

Non-compliant Publications Previously Reported for this Project

Public Access Compliance	Citation
Non-Compliant	(b) (4)

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

NOTHING TO REPORT

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period?

No

C.5 OTHER PRODUCTS AND RESOURCE SHARING

C.5.a Other products

NOTHING TO REPORT

C.5.b Resource sharing

NOTHING TO REPORT

D. PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	SSN	DOB	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
(b) (6)	Y	DASZAK, PETER	(b) (6)	(b) (6)	BS,PHD	PD/PI	(b) (4), (b) (6)					NA
	N	HOSSEINI, PARVIEZ RANA	(b) (6)	(b) (6)	BS,PHD	Co-Investigator						NA
(b) (6)	Y	Ross, Noam Martin		(b) (6)	PhD	Co-Investigator						NA
	N	OLIVAL, KEVIN J	(b) (6)	(b) (6)	PHD	Co-Investigator						NA
	N	KE, CHANGWEN			PHD	Co-Investigator				Center for Disease Control and Prevention of Guangdong Province	CHINA	NA
	N	ZHANG, SHUYI		(b) (6)	PHD	Co-Investigator				East China Normal University	CHINA	NA
	N	ZHANG, YUNZHI		(b) (6)	PHD	Co-Investigator				Yunnan Provincial Institute of Endemic Diseases Control & Prevention	CHINA	NA
	N	ZHU, GUANGJIAN		(b) (6)	PHD	Co-Investigator				East China Normal University	CHINA	NA
	N	GE, XINGYI			PHD	Co-Investigator				Wuhan Institute of Virology	CHINA	NA
	N	EPSTEIN, JONATHAN H	(b) (6)	(b) (6)	MPH,DVM,BA,PHD	Co-Investigator						NA
	N	CHMURA, ALEKSEI A	(b) (6)	(b) (6)	BS	Non-Student Research Assistant						NA
	N	SHI,		(b) (6)	PhD	Co-				Wuhan	CHINA	NA

		ZHENGLI				Investigator				Institute of Virology		

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award?

No

D.2.b New Senior/Key Personnel

Are there, or will there be, new senior/key personnel?

Yes

File uploaded: Noam Ross CV 2016.pdf

D.2.c Changes in Other Support

Has there been a change in the active other support of senior/key personnel since the last reporting period?

No

D.2.d New Other Significant Contributors

Are there, or will there be, new other significant contributors?

No

D.2.e Multi-PI (MPI) Leadership Plan

Will there be a change in the MPI Leadership Plan for the next budget period?

NA

Noam Ross

(b) (6)
http://www.noamross.net
@noamross

EDUCATION

University of California Davis, CA
Doctoral Candidate in Ecology Expected Completion Summer 2015

- Dissertation Committee: Alan Hastings (major professor, Ecology), David Rizzo (Plant Pathology), Jim Sanchirico (Natural Resource Economics)
- Dissertation Research: "Managing Emerging Forest Disease Under Uncertainty"

Brown University Providence, RI
Bachelor of Science in Environmental Science, Magna Cum Laude May 2006

- Honors Thesis: "Soil Organic Matter in Northern Mongolia: Permafrost and Land-Use interactions"
- Phi Beta Kappa, Sigma Xi, Environmental Science Honors, Rosenberger Prize for Outstanding Service

SCIENTIFIC PUBLICATIONS

- Carl Boettiger*, **Noam Ross***, Alan Hastings (2013) *Early Warning Signals: The Charted And Uncharted Territories*. Theoretical Ecology http://dx.doi.org/10.1007/s12080-013-0192-6
- Fuller, Kate, David Kling, Kaelin Kroetz, **Noam Ross**, and James N. Sanchirico (2013) *Economics and Ecology of Open-Access Fisheries*. In: Shogren, J.F., (ed.) Encyclopedia of Energy, Natural Resource, and Environmental Economics, Vol. 2 Encyclopedia of Energy, Natural Resource, and Environmental Economics p.39-49. Amsterdam: Elsevier. http://dx.doi.org/10.1016/B978-0-12-375067-9.00114-5

In preparation

- (b) (4)
-

**Co-equal authorship*

POSTERS

- **Ross, Noam**. "Optimal Control of Disease in Space: An Approach Using Individual-based Models," June 1-4, 2014. 12th Annual Conference of Ecology and Evolution of Infectious Disease, Fort Collins, Colorado.
- **Ross, Noam**. "Designing Protective Treatments for Forest Disease Using a Spatial Point Process Model," November 20-21, 2014. California Forest Pest Council Annual Meeting, McClellan, CA.
- **Ross, Noam**. "Optimal Control of Forest Disease Under Changing Community and Spatial Structure," November 4-18, 2013. Sustainable Management of Natural Resources Workshop, Mathematical Biosciences Institute, Columbus, OH.

PRESENTATIONS

- **Ross, Noam**, "Fungal Disease Mortality: Modeling for Management of Sudden Oak Death." Dec 1, 2014 Invited talk at EcoHealth Alliance, New York, NY.
- **Ross, Noam**, "Modeling forest disease using a macroparasite framework ," Agust 13, 2014. 99th Annual Ecological Society of America Meeting, Sacramento, CA.
- Ashander, Jamie, Kelly Gravuer, Megan Kelso, Mary E. Mendoza and **Noam Ross** "Managing River-Floodplains Systems: A Historical and Ecological Perspective" September 14, 2002. Presentation at NSF REACH IGERT Floodplains Workshop

AWARDS + FELLOWSHIPS (*Total received $225,429*)

- Don Dahlsten Memorial Grant ($325) — California Forest Pest Council, 2012
  Designing Protective Treatments for Forest Disease Using Spatial Point Process Models
- NSF IGERT Bridge Fellowship ($57,500) — UC Davis, CA, 2012
  Managing Emerging Forest Disease Under Uncertainty
- NSF IGERT Traineeship in Rapid Environmental Change ($115,00) — UC Davis, CA, 2010
  Modifying River-Floodplain Systems: A Historical and Ecological Approach
- UC Davis Graduate Group in Ecology Fellowship ($40,604) — UC Davis, CA, 2010
- NSF Research Experience for Undergraduates Fellowship ($8,000) — Acad. of Natural Sciences, PA, 2005
- Undergraduate Research Fellowship ($4,000) — Brown University, RI, 2003

SERVICE + PROJECTS

- **Workshop Instructor,** Software Capentry and Data Carpentry Foundations — Jan 2015–Present
- **Student Rep,** UC Davis Graduate Group in Ecology Executive Committee — Sep 2013–Present
- **Reviewer:** *Theoretical Ecology* (4 reviews) — Feb 2013–Present
- **Web Developer and Technology Chair,** Ecology Graduate Student Association — June 2013–Present
  Creator + Maintainer of graduate student blog, resources, and news site (egsa.ucdavis.edu)
- **Founder + Organizer,** Davis R Users' Group — Sep 2012–Present
  Created users group that provides tutoring and seminars to graduate students in 10+ departments
- **Contributor,** R packages `knitr, knitcitations, rcrossref, rethinking` — 2012-Present
- **Organizer:** NSF REACH IGERT Workshop on Multiple Goals in Floodplain Restoration — Sep 2012
- **Organizer,** UC Davis Conference on Ecology and the Business Sector — Apr 2011
- **Organizer**, UC Davis Graduate Group in Ecology Symposium — May 2010-2011
- **External Reviewer**, World Resources Institute Corporate Ecosystem Services Review — Jan 2008
- **External Reviewer**, McKinsey-Clinton Global Initiative Forestry Project — Mar 2008
- **Business Stewardship Volunteer,** NY Coastal Marine Resources Center — Feb-Apr 2007

OTHER WORK EXPERIENCE

GreenOrder — New York, NY
Analyst, Senior Analyst: Corporate Environmental Strategy + Governance — Sep 2006–Oct 2009

- Conducted environmental performance analysis for products in energy, transportation, and water sectors
- Created green product metrics system R&D stage-gating system for construction products manufacturer
- Managed engagement with equipment rental company to identify growth opportunities in green building
- Performed market and competitive analyses for a wide array of clients in retail, real estate financial and cleantech sectors; prepared and delivered client presentations; managed projects
- Managed analysts performing environmental product certifications and market research
- Developed firm seminar series and analyst training materials; conducted trainings on topics including auditing, statistical analysis, and environmental performance benchmarking
- Audited certifications for environmental products and facility performance

Wal-Mart — Providence, RI
Contract Researcher/Consultant: Energy Efficient Products Initiative — May-Sep 2006

- Developed forecasting model for sales of energy-efficient lamps at Wal-Mart stores
- Created guidelines for design of lamp recycling program

Brown University Facilities Management Providence, RI
Administrative, Research, + Teaching Assistant: Energy and Design Jan 2003–May 2006

- Developed energy-use and financial projections for university energy usage scenarios
- Performed background research and feasibility analysis for university energy efficiency projects
- Provided tutoring, logistical support and web design for two courses in sustainable design
- Responsible for maintenance of energy efficient, low-impact building

Hovsgol Lake Global Environmental Facility and Brown University Mongolia + Providence, RI
National Science Foundation REU Fellow, Thesis Research June 2005-May 2006
Advisor: Clyde Goulden

- Independent research on climate-land use interactions on permafrost soil carbon storage
  Plant surveys, soil pit excavation, soil physical and chemical analysis, soil microbial process incubations

Marine Biological Laboratory Ecosystems Center Woods Hole, MA
Semester in Environmental Science Student Aug-Dec 2004
Advisor: Charles Hopkinson

- Examined effects of nitrogen pollution on structure of microplankton food webs
- Microcosm experiments, fluorescence microscopy, dissolved nutrient analysis, planktonic growth incubations

Brown Center for Environmental Studies Providence, RI
Undergraduate Research Fellow Jun-Aug 2003
Advisor: Steven Hamburg

- Conducted research in biogeochemistry at Hubbard Brook Experimental Forest and surrounding region; oversaw soil pit excavation by undergraduate and graduate field crew
- Plant surveys, forest floor measurements, litter collection, soil pit excavation, soil physical and chemical analysis, GIS analysis in ESRI ArcMap

PUBLICATIONS IN POPULAR PRESS

- "Extinction Debt,"(Initial author) Wikipedia. Wikimedia Foundation, Inc., February 23, 2011 http://en.wikipedia.org/wiki/Extinction_debt
- "If Everyone Moves to the City, What Gets Left Behind?" *Good.is,* January 17, 2011. http://www.good.is/post/if-everyone-moves-to-the-city-what-is-left-behind/
- "Why the Ethanol Debate Isn't Helping Anyone," *GreenBiz.com*, Jun 3, 2009. http://www.greenbiz.com/blog/2009/06/03/why-ethanol-debate-isnt-helping-anyone
- "Four Lean, Green Strategies for an Uncertain Economy," (with Andrew Shapiro) *Harvard Business Review's Leading Green*, Oct 29, 2008. http://blogs.hbr.org/2008/10/4-lean-green-strategies-for-an/
- "What a Silent Spring Means for Business Risk," *GreenBiz.com*, Mar 6, 2007. http://www.greenbiz.com/blog/2007/03/05/what-silent-spring-means-business-risk

E. IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Dollar Amount	Country
211699	CHINA

F. CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

Yes

Is the research exempt from Federal regulations?

No

Does this project involve a clinical trial?

No

G.4.b Inclusion Enrollment Data

Report Attached: Understanding the Risk of Bat Coronavirus Emergence-PROTOCOL-001

G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?

No

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

No

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

Yes

G.8 PROJECT/PERFORMANCE SITES

Organization Name:	DUNS	Congressional	Address

		District	
Primary: EcoHealth Alliance, Inc.	077090066	NY-010	460 West 34th Street 17th Floor New York NY 100012317
Wuhan Institute of Virology	529027474		Xiao Hong Shan, No. 44 Wuchang District Wuhan
East China Normal University	420945495		3663 Zhongshan Beilu Shanghai
ECOHEALTH ALLIANCE	077090066		ECOHEALTH ALLIANCE, INC. 460 W 34TH ST NEW YORK NY 100012320
EcoHealth Alliance, Inc.	077090066	NY-010	460 West 34th Street 17th Floor New York NY 100012317
Wuhan Institute of Virology	529027474		Xiao Hong Shan, No. 44 Wuchang District Wuhan
East China Normal University	420945495		3663 Zhongshan Beilu Shanghai

G.9 FOREIGN COMPONENT

Organization Name: Wuhan Institute of Virology
Country: CHINA
Description of Foreign Component:
Principal Laboratory for all Research in China as per section G8 (above) and detailed in our Specific Aims

Organization Name: East China Normal University
Country: CHINA
Description of Foreign Component:
Principal Coordinating Team for all project field work as per section G8 (above) and detailed in our Specific Aims

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

No

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period?

No

G.12 F&A COSTS

Is there a change in performance sites that will affect F&A costs?

No

Inclusion Enrollment Report

Inclusion Data Record (IDR) #: 166195

Using an Existing Dataset or Resource: No

Delayed Onset Study ?: No

Clinical Trial: No

Enrollment Location: Foreign

NIH Defined Phase III Clinical Trial: No

Study Title: Understanding the Risk of Bat Coronavirus Emergence-PROTOCOL-001

Planned Enrollment

Planned Enrollment Total: 2,460

NOTE: Planned enrollment data exists in the previous format; the PD/PI did not enter the planned enrollment information in the modified format and was not required to do so. Only the total can be provided.

Cumulative Enrollment

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/Alaska Native	0	0	0	0	0	0	0	0	0	**0**
Asian	157	108	0	0	0	0	0	0	0	**265**
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	**0**
Black or African American	0	0	0	0	0	0	0	0	0	**0**
White	0	0	0	0	0	0	0	0	0	**0**
More than One Race	0	0	0	0	0	0	0	0	0	**0**
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	**0**
Total	**157**	**108**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**265**

A. COVER PAGE

Project Title: Understanding the Risk of Bat Coronavirus Emergence	
Grant Number: 5R01AI110964-05	**Project/Grant Period:** 06/01/2014 - 05/31/2019
Reporting Period: 06/01/2017 - 05/31/2018	**Requested Budget Period:** 06/01/2018 - 05/31/2019
Report Term Frequency: Annual	**Date Submitted:** 09/16/2020
Program Director/Principal Investigator Information: PETER DASZAK , PHD BS **Phone number:** (b) (6) **Email:** (b) (6)	**Recipient Organization:** ECOHEALTH ALLIANCE, INC. ECOHEALTH ALLIANCE, INC. 460 W 34TH ST 17TH FLOOR NEW YORK, NY 100012320 **DUNS:** 077090066 **EIN:** 1311726494A1 **RECIPIENT ID:** NIAID Coronavirus
Change of Contact PD/PI: N/A	
Administrative Official: ALEKSEI CHMURA 460 W 34th St., 17th Floor New York, NY 10001 **Phone number:** (b) (6) **Email:** (b) (6)	**Signing Official:** ALEKSEI CHMURA 460 W 34th St., 17th Floor New York, NY 10001 **Phone number:** (b) (6) **Email:** (b) (6)
Human Subjects: Yes HS Exempt: No Exemption Number: Phase III Clinical Trial:	**Vertebrate Animals:** Yes
hESC: No	**Inventions/Patents:** No

B. ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

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.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: Year 4 NIAID CoV Report_Final for eRA Commons.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: Year 4 NIAID CoV Training and Prof Devlp.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

1.Conference and University Lectures: PI Daszak, and Co-investigators Shi, Epstein, Olival, and Zhang gave invited University and Conference lectures including Harvard Univ. Columbia Univ., Tufts Univ., Mt. Sinai, the 2nd International Symposium on Emerging Viral Disease in China, the 2nd International Symposium on the Infectious Diseases of Bats in Colorado, Cell Symposia: Emerging and Re-emerging Viruses 2017 in Virginia, The International Union of Microbiological Societies 2017 National Academy of Sciences in Singapore, 2018 Borneo Quality of Life Conference in Malaysia, 2017 Chemical and Biological Defense Science and Technology (CBD S&T) in California, Prince Mahidol Award Conference in Bangkok, Collaboration for Environmental Evidence Meeting in Paris, US-China NSF Ecology and Evolution of Infectious Disease (EEID) Meeting, and others that included specific discussion of the current project and results.

2.Agency and other briefings: PI Daszak and Co-investigator Shi introduced this project and discussed new opportunities about predicting and preventing zoonoses within National Institute of Allergy and Infectious Disease Office, Defense Advanced Research Projects Agency, National Natural Science Foundation of China, Chinese Center for Disease Control and Prevention, US NASEM Forum on Microbial Threats, Chinese Academy of Sciences, and the Health Working Group at the US Embassy in Beijing.

3.Public outreach: PI Daszak and Co-investigator Shi, Epstein, Olival, have presented this work to the general public in a series of meetings over Year 4 including at Cosmos Club briefings that EcoHealth Alliances hosts in Washington DC, over 10 meetings on the China National Virome Project and the Global Virome Project in China, Europe, Australia, Southeast Asia and Latin America. Co-investigator Olival presented this work at a public event on Disease Transmission and Technologies in New York, co-investigator Ross presented this work at EcoHealth Webinar on wildlife trade network research. Zhu broadly introduced this work to the conservation and ecological research community in China through field training workshops.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

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

•To commence an in-depth analysis of data collected from the integrated biological behavioral surveillance from Yunnan, Guangxi, and Guangdong provinces, incorporating questionnaires and serological testing results.
•To initiate lab analysis of human samples collected from the passive hospital surveillance from four hospitals in Yunnan province: 1) Dali College Affiliated Hospital; 2) Dali Prefecture Hospital; 3) Kunming No. 3 People's Hospital, and 4) Chuxiong Prefecture Hospital. The goal will be to identify examples of CoV spillover events in China that may lead to illness.

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

•To repeat and continue in vivo experiments of SARSr-CoVs with spike variants on hACE-expressing transgenic mice (survival rate, histopathological analysis, etc) to evaluate the risk of cross-species infection of different SARSr-CoVs to humans;
•Continue searching for the receptor of SARSr-CoVs with deletions in the homologous region of SARS-CoV RBD (i.e. Rp3, Rs672), and SARSr-CoVs that are unable to utilize bat ACE2 (e.g. Rs4231).
•Continue the phylogeographic study of bat-CoV with newly collected samples to better understand the geographic distribution and evolution of bat-CoV genetic diversity in south China and SE Asia.

Specific Aim 3: Testing predictions of CoV inter-species transmission.

•Using the full-length infectious cDNA clone of MERS-CoV, chimeric viruses with the spikes of newly identified MERSr-CoVs will be constructed. The pathogenesis of these MERSr-CoVs will be tested on the human DPP4-expressing mouse model that has already been developed and validated in Y4.
•To conduct a population genetics study of Rhinolophus sinicus ACE2s, including the amplification of ACE2 genes from R. sinicus samples of different origin, test of the usage efficiency of R. sinicus ACE2s of different origins by SL-CoVs and kinetics study on the binding of SL-CoV RBD to different R. sinicus ACE2s.
•In collaboration with South China Agrricultural University, gather data on the spatial structure and barn-level mortality records to parameterize our mathematical model of virus spread that incorporates a meta-population structure in individual and use this to fit the model on a training set of farms and validate it on a hold-out set.
•Using the intra-farm transmission model, we will (a) determine the characteristics of a farm that determine the likelihood and size of an outbreak given a spillover event, and (b) determine whether SADS and PEDV outbreaks on farms can be distinguished by differing dynamics, as measured by transmission parameters in our intra-farm transmission model.

Year 4 Report: Understanding the Risk of Bat Coronavirus Emergence

Award Number: R01AI110964-03

Reporting Period: 06/01/2017 – 05/31/2018

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B.2 What was accomplished under these goals?

Summary

The results of the 4th year of our R01 work are detailed below. They include:

- Completed behavioral risk survey questionnaires and biological sample data collection for 1,585 people in Yunnan, Guangxi, and Guangdong provinces.
- Preliminary analysis of behavioral survey responses exploring key risk factors relating to potential viral zoonotic disease spillover in China, indicating notable differences among the respondents in Guangdong, Guangxi, and Yunnan.
- Completed serologic testing of collected human samples for MERS-CoV, SARSr-CoV, HKU9 CoV and HKU10 CoV, showing the serologic evidence of spillover of bat SARS-related CoVs (7 people in Yunnan province) and HKU9 CoV (2 people in Guangxi province).
- Testing of samples from 671 individual bats to identify diverse alpha- and beta-coronaviruses.
- Genetic diversity and genomic characterization of beta-coronaviruses in fruit bats and characterization of the full-length genome sequence of a novel HKU9-related CoV.
- Analysis of host-virus phylogeography for all bat CoV RdRp sequences collected by our group in China from 2008-2015 (Alpha-CoVs: n = 491; Beta-CoVs: n = 326) to identify the geographic areas that are likely sources of origin/diversity for this important group of viruses.
- Identification of two novel MERS-related CoVs that use DPP4 receptor.
- *In vivo* infection of SARSr-CoVs with variants of S protein in human ACE2 (hACE2) expressing mice.
- Identification of a novel bat-origin CoV (swine acute diarrhea syndrome coronavirus, SADS-CoV) causing a multi-farm outbreak of fatal acute diarrhea in piglets in Guangdong (published in *Nature* in April 2018).
- Development of an intra-farm transmission model to understand SADS-CoV spread and help predict and prevent future outbreaks.

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

During Year 4 we completed behavioral risk surveys and biological sample collection from people at selected sites in three provinces in southern China (Guangdong, Guangxi, and Yunnan) and began analyzing the results.

Behavioral Survey

We administered 1,585 surveys in Guangdong, Guangxi, and Yunnan provinces. Questions explored respondent health-seeking behavior, experiences with unusual illnesses, contact with wildlife and livestock, and general background information. Blood samples were collected from respondents and tested for SAS-related CoVs (SARSr-CoVs) and HKU10-CoV using serological assays. Survey data was analyzed by province to examine patterns among respondent characteristics and behavioral risk factors across provinces.

Respondent General Background Information

Of the 1,585 respondents who completed the survey, 420 were from Guangdong, 412 were from Guangxi, and 753 were from Yunnan. More females than males completed the survey in all provinces. The mean age of the overall survey sample was 52 years **(Figs. 1, 2)**.

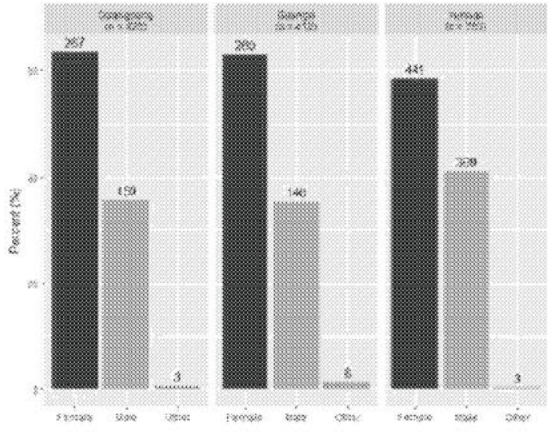


Figure 1: *Gender of respondents*

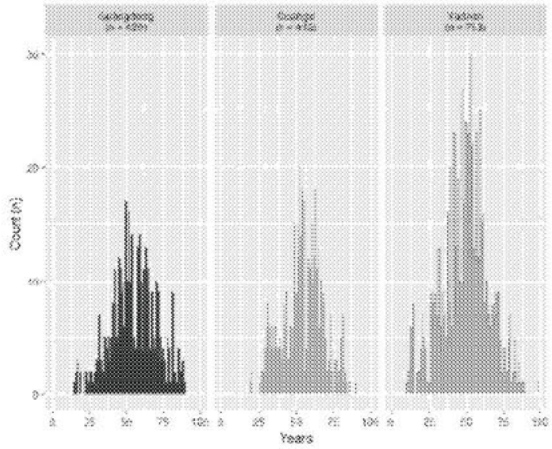


Figure 2: *Age distribution of respondents.*

Across all provinces, most respondents had lived in their respective locales for more than 5 years (96.3%) **(Fig. 3)** and earned less than 10,000 renminbi (RMB) annually (84.6%) **(Fig. 4)**. In 2016, the updated poverty standard in China was 3,000 RMB as defined by Poverty Alleviation Office of State Council. More families in Guangxi (61.8%) lived at or below the poverty level as compared to those in Guangdong (36.9%) and Yunnan (43.3%).

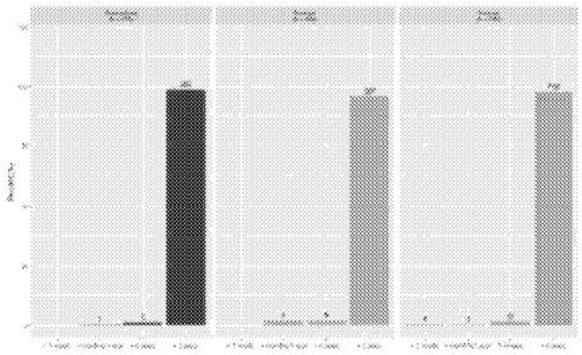


Figure 3: *Duration of residency.*

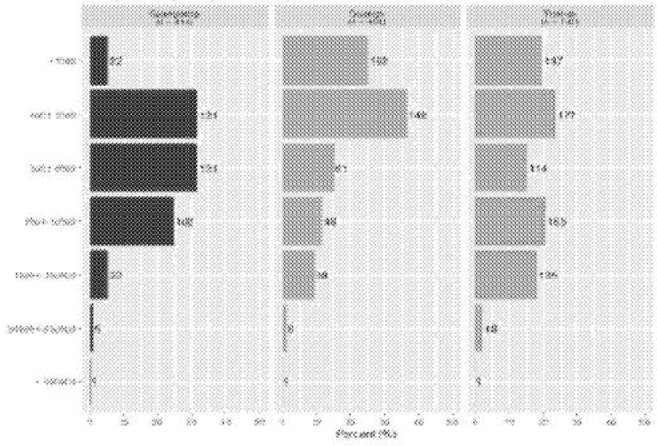


Figure 4: *Family annual per capita income (RMB).*

In Guangdong, Guangxi, and Yunnan, 73.9%, 57.0% and 69.6% of respondents, respectively, had a primary school-level education or less **(Fig. 5)**. Across all provinces the most common livelihood was crop production. In Yunnan, 699 out of 753 (92.8%) individuals from the province identified crop production as a livelihood activity. In comparison, 237 out of 420 (56.4%) individuals from Guangdong, and 260 out of 412 (63.1%) individuals from Guangxi **(Fig. 6)** named crop production as a livelihood in the last year. Respondents, however, where not restricted to defining a single livelihood, many indicated engaging in multiple types of livelihoods.

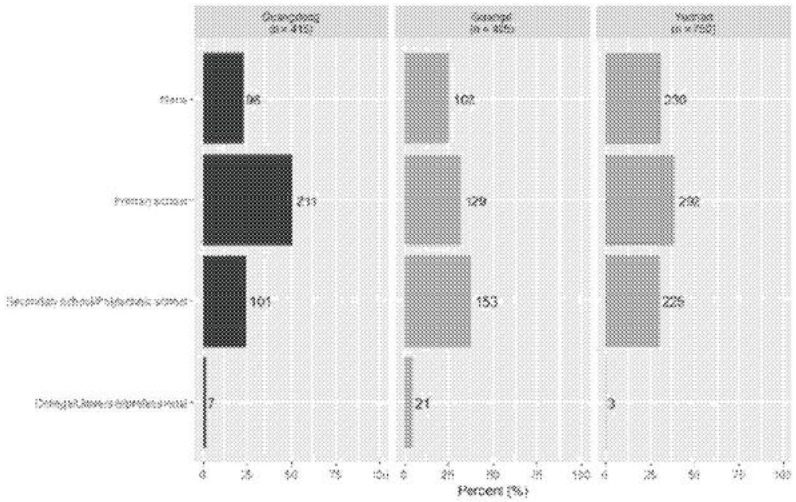


Figure 5: *Highest level of education completed*

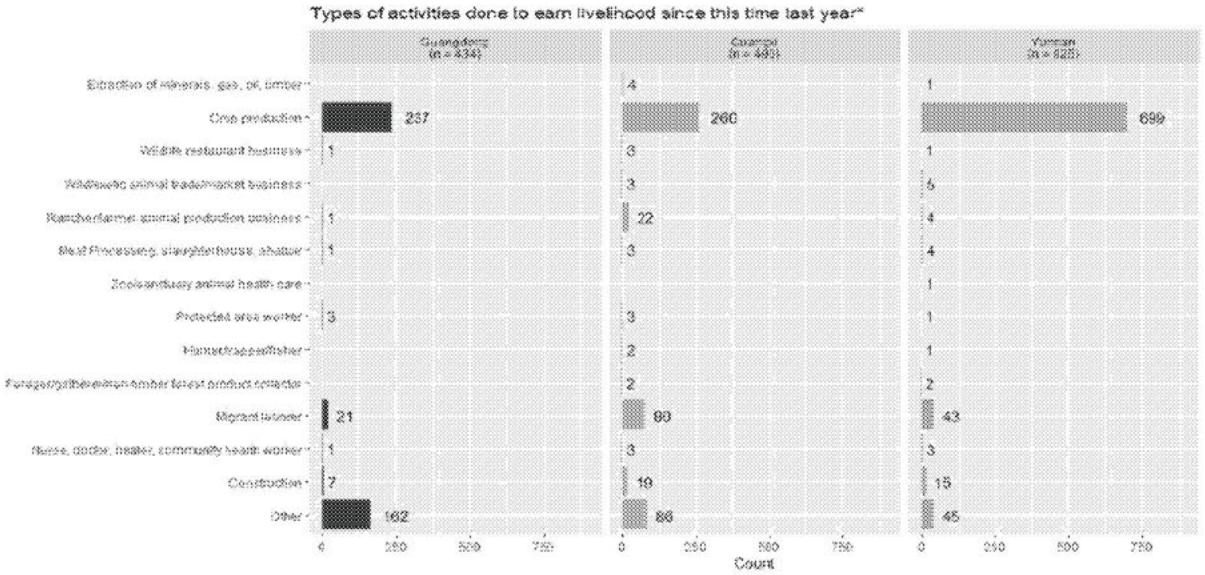


Figure 6: *Types of activities conducted to earn a livelihood since this time last year (above)*

In Guangdong, Guangxi, and Yunnan, 41.7%, 50.7% and 59.6% of respondents, respectively, indicated that they traveled outside of their village town or city in the past year. Among those who traveled, the average number of trips was 5 in Guangdong and Guangxi, and 6 in Yunnan. The average distance traveled by respondents in Guangdong and Yunnan were 113 Km and 118 Km, respectively, compared to 66 Km by respondents in Guangxi.

Health-Seeking Behavior and Experiences with Unusual Illnesses

When asked where they usually get treatment for illness or infection, the top 3 responses across all provinces in aggregate were hospitals, clinics, and pharmacies/dispensaries in descending order **(Fig. 7)**. However, within Yunnan, most respondents went to hospitals, followed by pharmacies, then clinics.

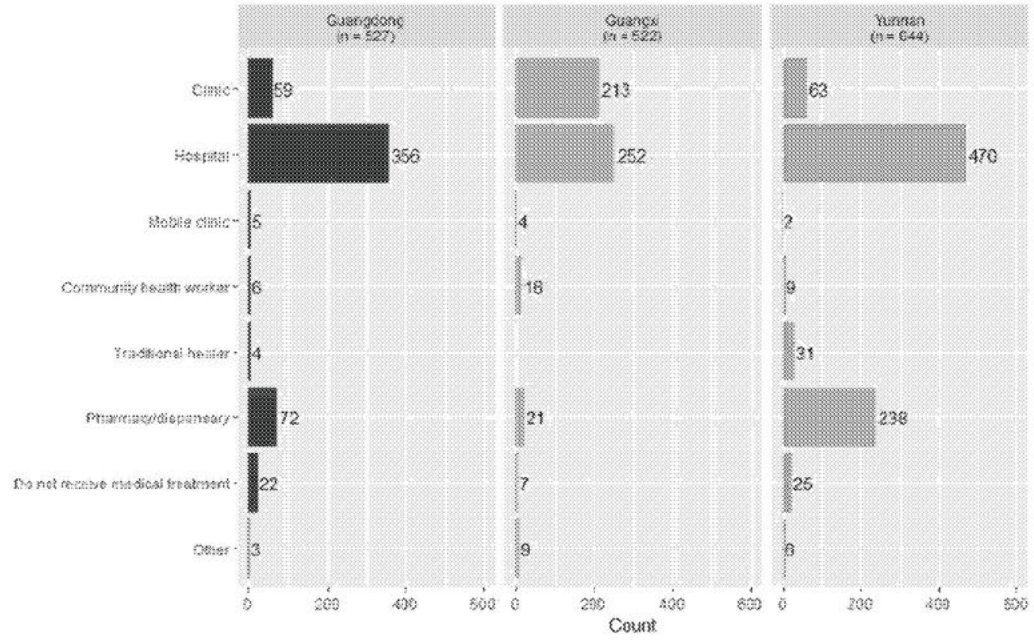
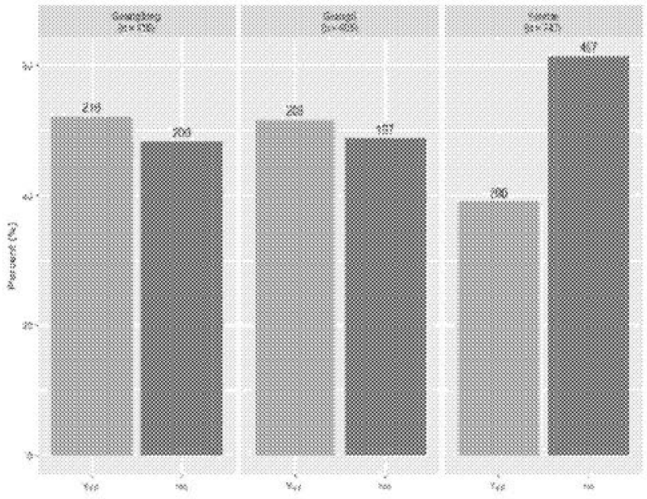


Figure 7: *Location where care was usually received for illness or infection.*

All survey respondents were asked whether they had experienced an unusual illness in their lifetime and in the past year, defined by a series of the most common symptoms associated with encephalitis, hemorrhagic fever (HF), severe acute respiratory infection (SARI), and influenza-like illness (ILI). Additional symptoms that were asked about included: fever with diarrhea or vomiting; fever with rash; and, persistent rash or sores on skin. Respondents were not restricted to selecting one illness and could provide multiple responses.

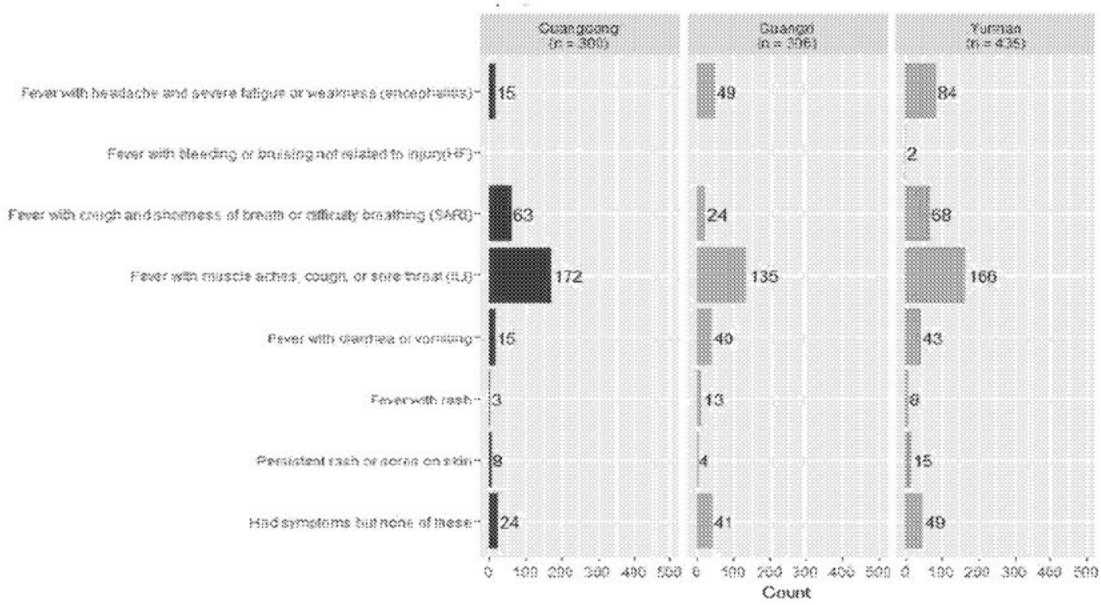
The proportion of respondents who had an unusual illness with any of the above-mentioned symptoms in their lifetime varied slightly by province. Between the three provinces, Yunnan had the fewest number of respondents who reported experiencing the symptoms provided (38.8%), compared to Guangdong and Guangxi (51.9% and 51.3%, respectively). Yunnan was also the only province where less than half of the respondents reported experiencing the symptoms provided **(Fig. 8)**.

Figure 8: *Respondent's experience of unusual illnesses.*



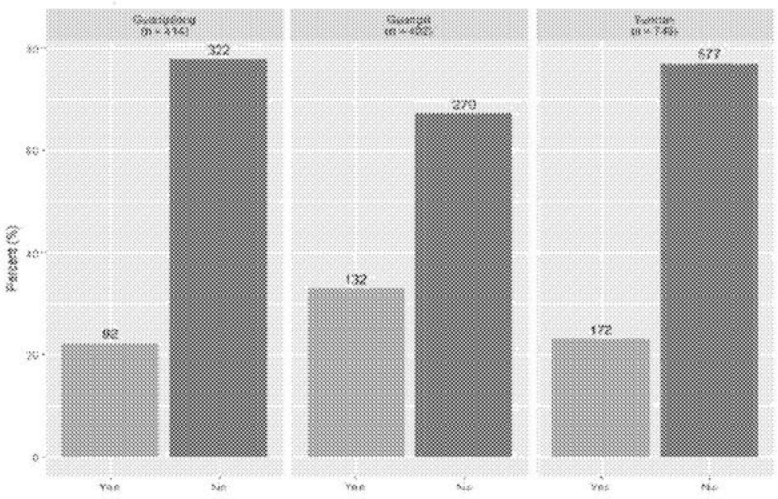
Across all three provinces, among those who had experienced any symptoms of unusual illness in their lifetimes, those associated with ILI were the most commonly reported. In Guangdong province, this was followed by symptoms associated with SARI, then by other symptoms not mentioned in the survey. In Guangxi province, the second most reported symptoms were ones associated with encephalitis, followed by other symptoms not mentioned in the survey. Similarly, in Yunnan, symptoms associated with encephalitis were the second most commonly reported, but this was followed by symptoms associated with SARI **(Fig. 9)**.

Figure 9: *Symptoms reported by people who had experienced unusual illness in their lifetime.*



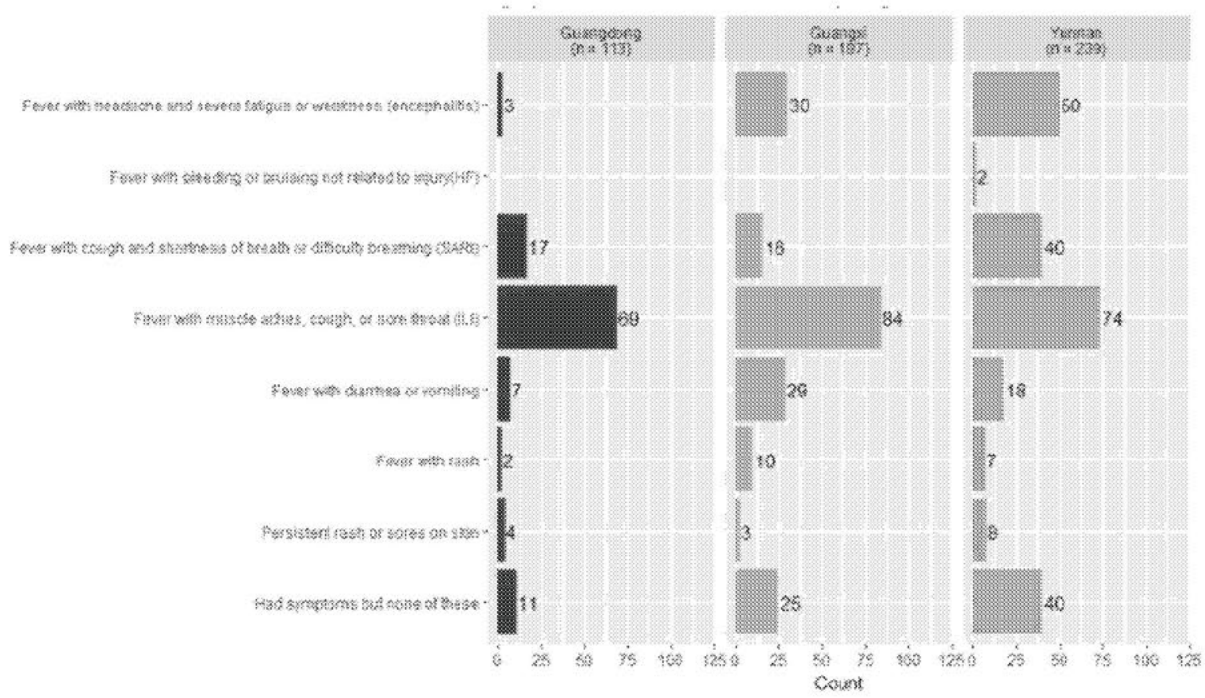
In each province, just under one-third of respondents who experienced the symptoms associated with an unusual illness in their lifetime indicated experiencing any of the symptoms in the past year – 22.2% in Guangdong, 32.8% in Guangxi and 23.0% in Yunnan **(Fig. 10)**.

Figure 10: *Whether respondents had experienced symptoms associated with an unusual illness, in the past year.*



Of the respondents who reported having symptoms of unusual illness in the past year, across all three provinces, symptoms associated ILI were the most commonly reported. In Guangdong province, this was followed by symptoms associated with SARI then by other symptoms not provided in the survey. In Guangxi, symptoms associated with ILI were followed by symptoms associated with encephalitis, then by fever with diarrhea or vomiting. In Yunnan, symptoms associated with ILI were followed by symptoms associated with encephalitis, then by both SARI and other symptoms not provided in survey **(Fig. 11)**.

Figure 11: *Symptoms experienced by those reporting unusual illness in the past year.*



When respondents were asked what caused the symptoms associated with unusual illness experienced in the past year, 64.4% in Guangxi (85 of 132 respondents), and 50.0% in both Guangdong and Yunnan (46 of 92 respondents and 86 of 172, respectively), said they did not know the cause **(Fig. 12)**. Only one respondent in Guangxi said their symptoms were due to

contact with animals (wild animals, specifically). Two respondents in Guangdong and one respondent in Guangxi said their symptoms were due to contact with animals (non-wild animals, specifically), whereas none of the respondents in Yunnan attributed their cause to contact with animals.

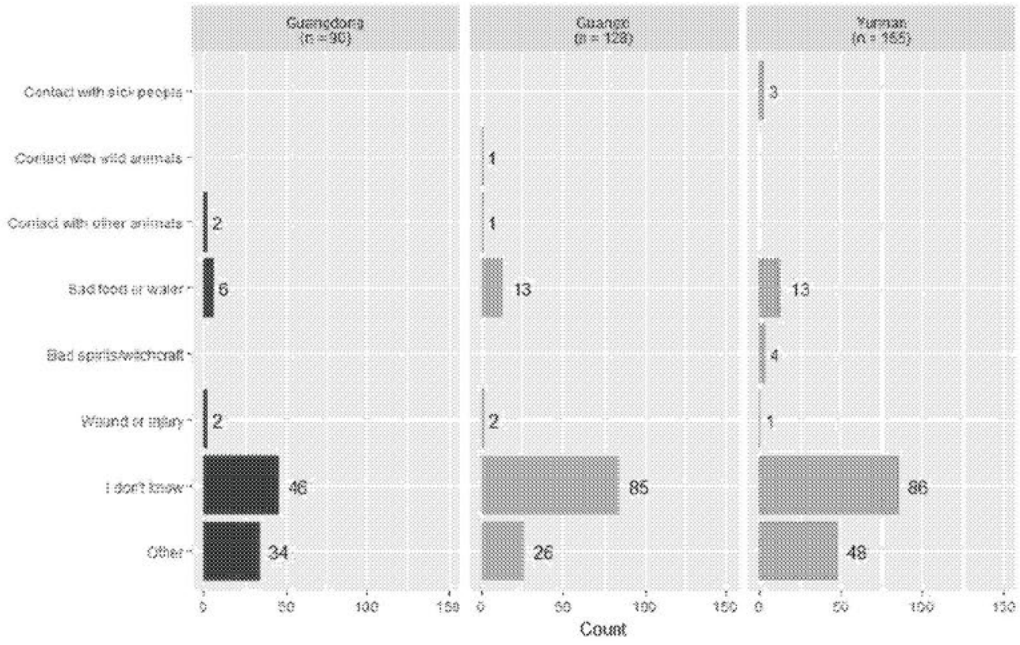
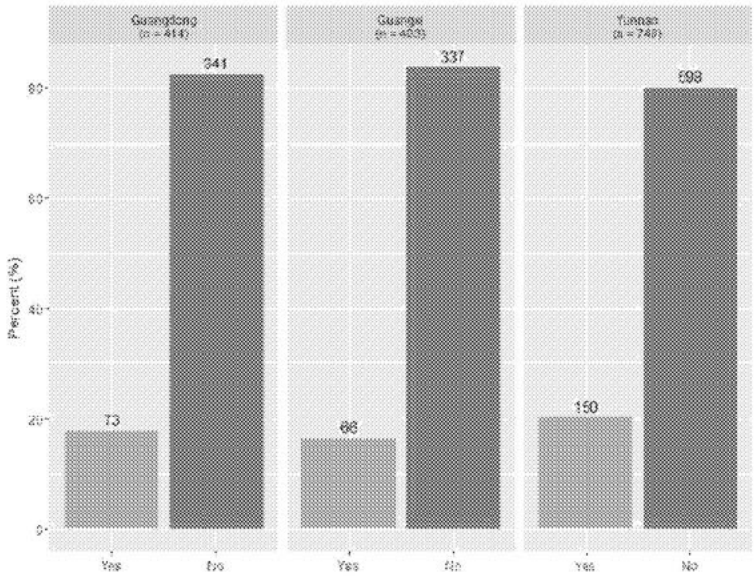


Figure 12: *Reported cause of sickness in the past year.*

Respondents reporting an unusual illness in the past year were asked if any of the people they lived with in the past year had symptoms similar to theirs, to assess possibilities of transmission among household members. Most respondents did not, across all three provinces: 82.4% in Guangdong, 83.6% in Guangxi and 79.9% in Yunnan **(Fig. 13)**.

Figure 13: *Whether household members had similar symptoms of unusual illness, in the past year*



Of the household members who experienced symptoms of unusual illness in the past year, the most commonly reported symptoms were those associated with ILI **(Fig. 14)**.

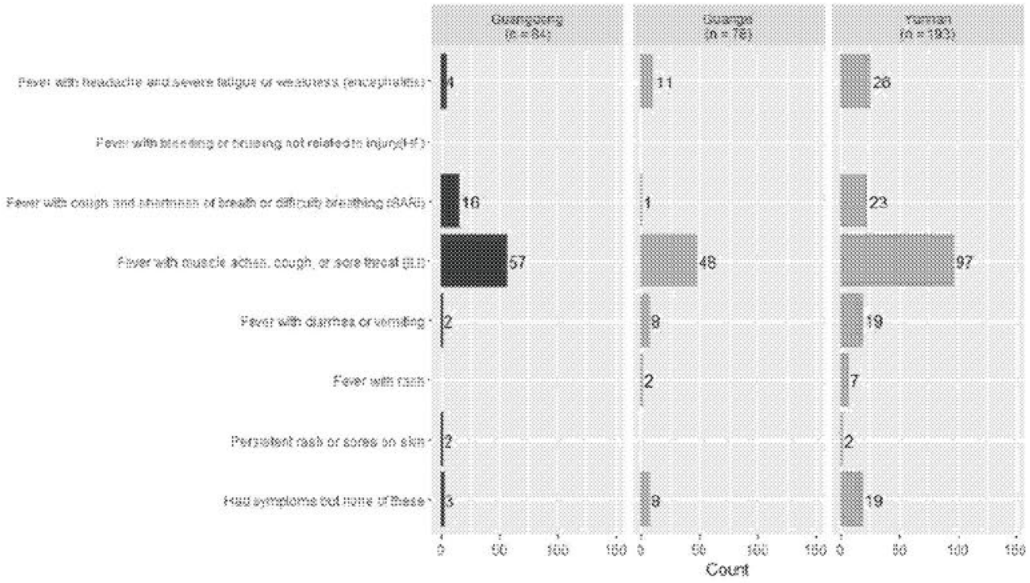


Figure 14: *Symptoms of household members who were ill, in past year.*

Respondents were also asked if any members of their household who experienced symptoms of unusual illness died as a result of their illness in the past year. Across all the three provinces, almost none had died from these illnesses **(Fig. 15)**.

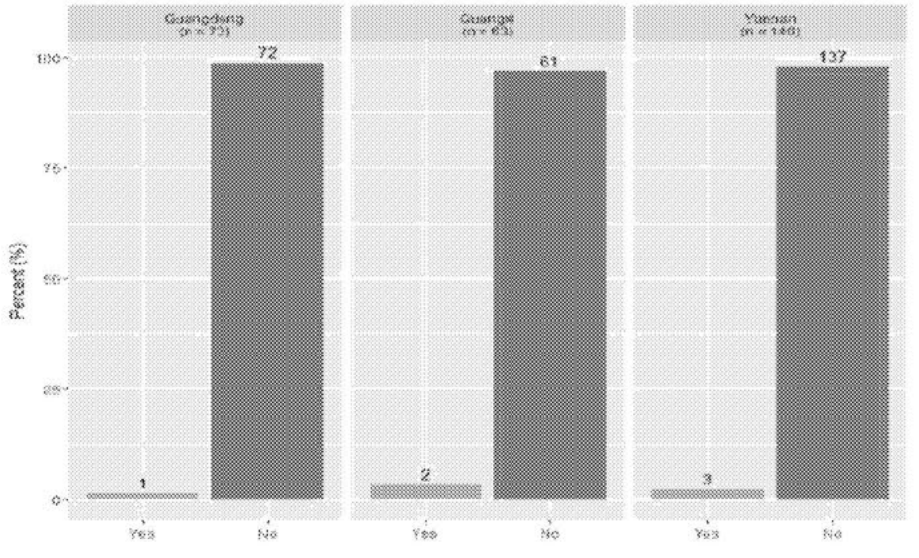


Figure 15: *Whether household members died from illness, in the past year.*

Contact with Animals

All respondents were asked about various types of animal contacts in their lifetime and in the past year. More than two-thirds of the respondents across all provinces, as well as in each of the provinces, reported raising an animal within their lifetime (71.2% in Guangdong, 77.7% in Guangxi, and 97.7% in Yunnan). More than half of the respondents in each province reported having animals come inside their dwellings (83.1 % in Guangdong, 60.2% in Guangxi, and 92.5% in Yunnan). More than half of respondents in each province reported handling live animals (51.5 % in Guangdong, 56.9% in Guangxi, and 62.9% in Yunnan) **(Table 1)**. Respondents from Yunnan had more types of contact with animals in their lifetime than those from Guangdong and Guangxi. With the exception of cooking or handling meat, organs, or blood from a recently killed animal and being scratched or bitten by an animal, the proportion of respondents from Yunnan who engaged in all types of animal activities was higher than the other provinces.

Type of animal contact (past year)	Guangdong		Guangxi		Yunnan	
	(n)	(%)	(n)	(%)	(n)	(%)
Lived with an animal as a pet	43	100 %	72	98.6 %	335	100 %
Handled live animals	212	100 %	226	98.3 %	332	99.7 %
Raised a live animal	296	100 %	312	99.4 %	518	99.8 %
Shared water source with animals for washing	47	100 %	19	95.0 %	97	100 %
Seen animal feces in or near food before you have eaten it	18	100 %	15	93.8 %	43	100 %
Eaten food after an animal has touched or damaged it	6	100 %	6	100 %	29	100 %
Animals come inside the dwelling where you live	345	100 %	239	98.0 %	493	100 %
Cooked or handled meat, organs, or blood from a recently killed animal	333	100 %	144	97.3 %	412	100 %
Eaten raw or undercooked meat or organs or blood	2	100 %	25	89.3 %	65	98.5 %
Eaten an animal that was not well/sick	--	--	1	100 %	6	100 %
Found a dead animal and collected it to eat, share, or sell	--	--	3	100 %	10	100 %
Been scratched or bitten by an animal	1	100 %	31	100 %	28	96.6 %
Slaughtered an animal	145	100 %	69	98.6 %	303	100 %
Hunted or trapped an animal	9	100 %	4	100 %	22	95.7%

Table 1: *Types of animal contact, within a respondent's lifetime.*

Respondents who reported having animal contact in their lifetime were also asked to indicate if they had the same type of animal contact in the past year **(Table 2)**. In the past year, across all three provinces and in each province, almost all respondents engaged in all contact types with the exception of eating an animal that was not well/sick, and finding a dead animal and collecting it to eat, share, or sell (0% for both in Guangdong).

Type of animal contact (lifetime)	Guangdong		Guangxi		Yunnan	
	(n)	(%)	(n)	(%)	(n)	(%)
Lived with an animal as a pet	43	10.4 %	73	18.1 %	335	62.9 %
Handled live animals	212	51.5 %	230	56.9 %	334	62.8 %
Raised a live animal	296	71.2 %	314	77.7 %	521	97.7 %
Shared water source with animals for washing	47	11.5 %	21	5.2 %	97	18.2 %
Seen animal feces in or near food before you have eaten it	18	4.4 %	16	3.9 %	43	8.1 %
Eaten food after an animal has touched or damaged it	6	1.5 %	6	1.5 %	29.0	5.4 %
Animals come inside the dwelling where you live	345	83.1 %	244	60.2 %	493	92.5 %
Cooked or handled meat, organs, or blood from a recently killed animal	333	80.4 %	148	36.7 %	413	77.5 %
Eaten raw or undercooked meat or organs or blood	2	0.5 %	28	6.9 %	68	12.8 %
Eaten an animal that was not well/sick	--	--	1	0.3 %	6	1.1 %
Found a dead animal and collected it to eat, share, or sell	--	--	3	0.7 %	10	1.9 %

Table 2: *Types of animal contact, in past year.*

Respondents who had animal contact in the past year were asked to identify the animals involved in the interaction. *(Figs. 16-26, below: the first two figures are enlarged to show row labels, which are identical for all)*. Cats and dogs were the most common pets reported across all provinces and in each province **(Fig. 16b)**.

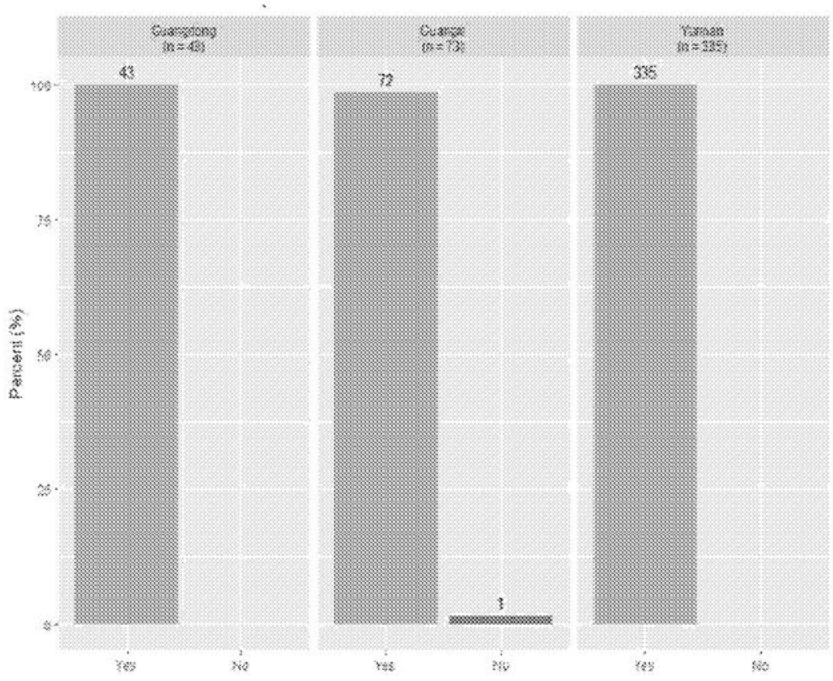
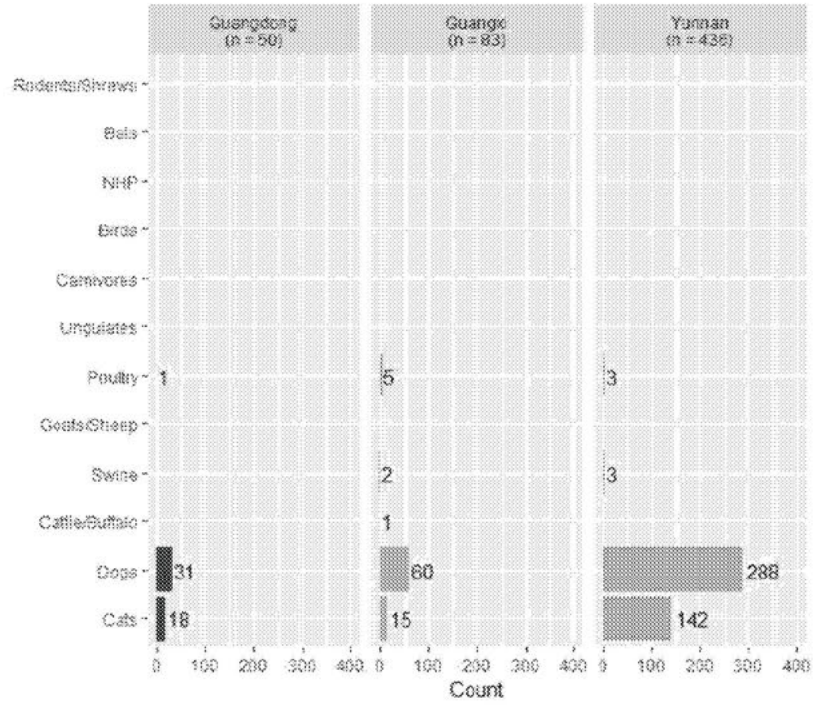


Figure 16a (top) & b (below): *(a) Whether respondents had lived with an animal as a pet, in the past year, and (b) among those who had, types of animal kept as pets.*



Poultry was the most common type of animal handled across all provinces as well as in each province, with 96.2%, 90.3%, and 92.8% of respondents handling animals in Guangdong, Guangxi and Yunnan, respectively **(Fig. 17b)**.

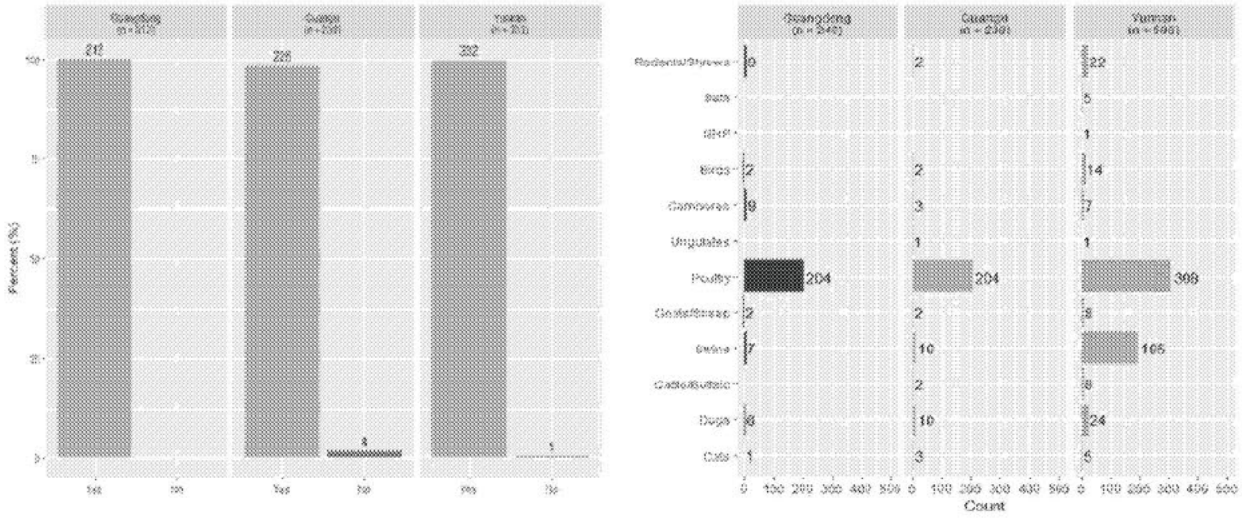
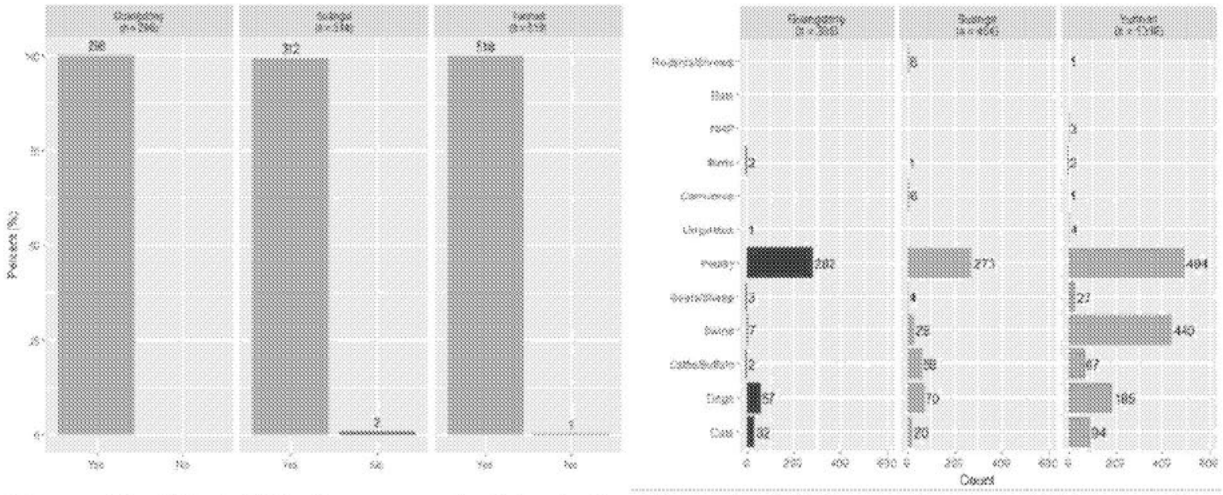


Figure 17a & b: *(a) Whether respondents had handled live animals, in the past year, and (b) among those who had, types of live animals handled.*

Poultry was also the most commonly raised animal in each of the three provinces; 95.3%, 87.5%, 95.4% in Guangdong, Guangxi, and Yunnan, respectively **(Fig. 18b)**.



Figures 18a & b: *(a) Whether respondents had raised live animals in the past year, and (b) among those who had, types of animals raised.*

In all three of the provinces, the most common type of animals found in respondent dwellings were rodents or shrews. In Guangdong and Yunnan, birds were the second most common animal type found in dwellings. In Guangxi province, birds along with poultry were the second most common animal type. Respondents in Guangdong and Yunnan reported that all 12 animal taxa had come inside their dwellings in the past year. Taxa seen in the dwellings of respondents from Guangdong and Yunnan and not Guangxi were non-human primates, ungulates, goats or sheep, swine, and cattle or buffalo **(Fig. 20b)**.

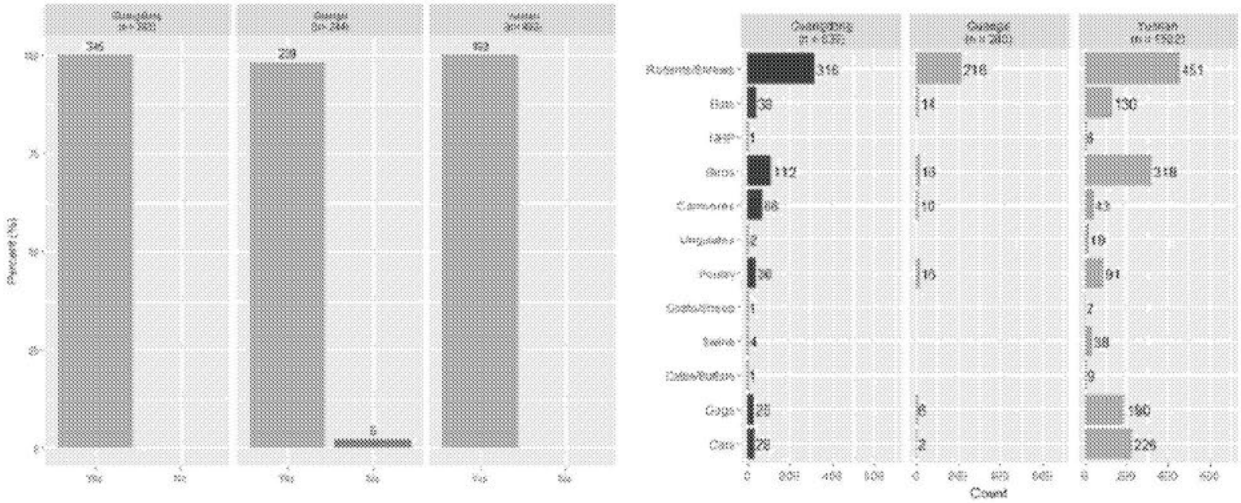


Figure 19a & b: *(a) Whether respondents had animals come inside dwelling, in the past year, and (b) among those who had, types of animals in dwelling.*

Almost all of the respondents who said they have cooked or handled meat, organs, or blood in their lifetime reported doing so in the past year. Common animal types that were cooked handled included poultry and swine in all three provinces **(Fig. 20)**.

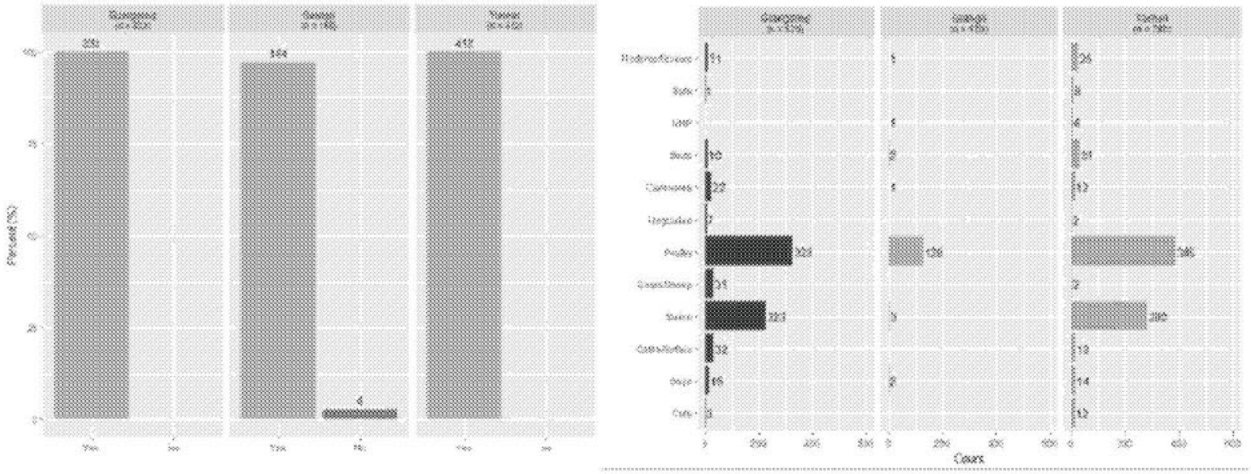


Figure 20a & b: *(a) Whether respondents had cooked or handled meat, organs or blood from a recently killed animal, in the past year, and (b) among those who had, types of animals whose meat, organs or blood was cooked or handled.*

More respondents in Yunnan reported eating raw or undercooked meat compared to respondents in Guangdong and Guangxi **(Fig. 21)**. In Yunnan, 96% of respondents who ate raw or undercooked meat in their lifetime did so in the past year. The types of animal products that were eaten raw or undercooked by respondents in Yunnan were mostly from swine. In Guangxi, the most commonly reported type of animal meat that had been eaten raw or undercooked was that of carnivores.

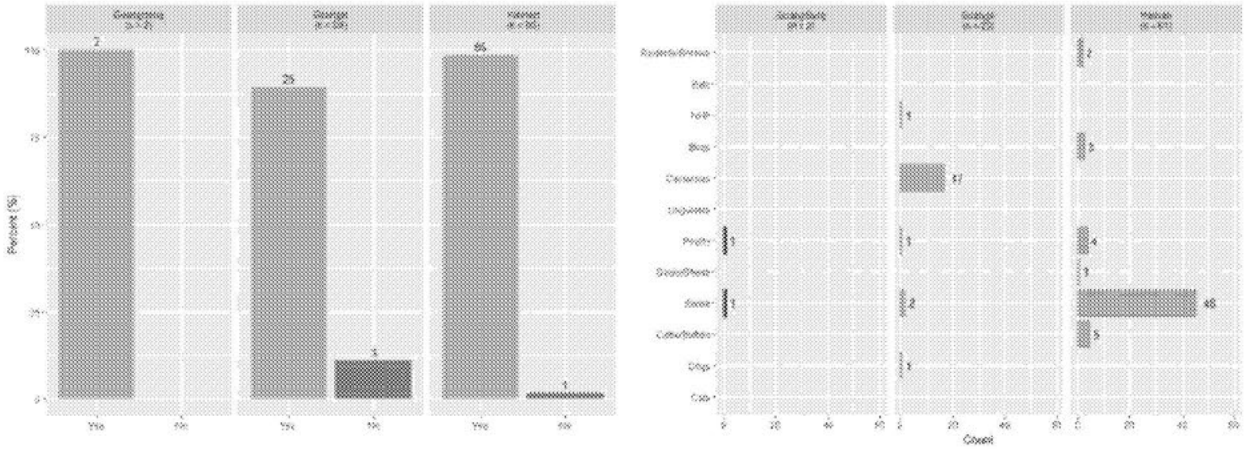


Figure 21 a & b: *(a) Whether respondents had eaten raw or undercooked meat or organs or blood, in the past year, and (b) among those who had, types of animals whose meat, organs or blood were eaten raw or undercooked.*

Across all provinces, a total of 13 respondents in Guangxi and Yunnan indicated that they collected an animal that was found dead to eat, share or sell. In Guandong, no respondents reported finding a dead animal and collecting it to eat, share, or sell. The most common type of animal collected across all provinces in aggregate was poultry. In Yunnan, poultry was the most common type of animal found dead and collected to eat, share or sell (80.0%), whereas dogs were the most common type in Guangxi (66.7%) **(Fig. 22)**.

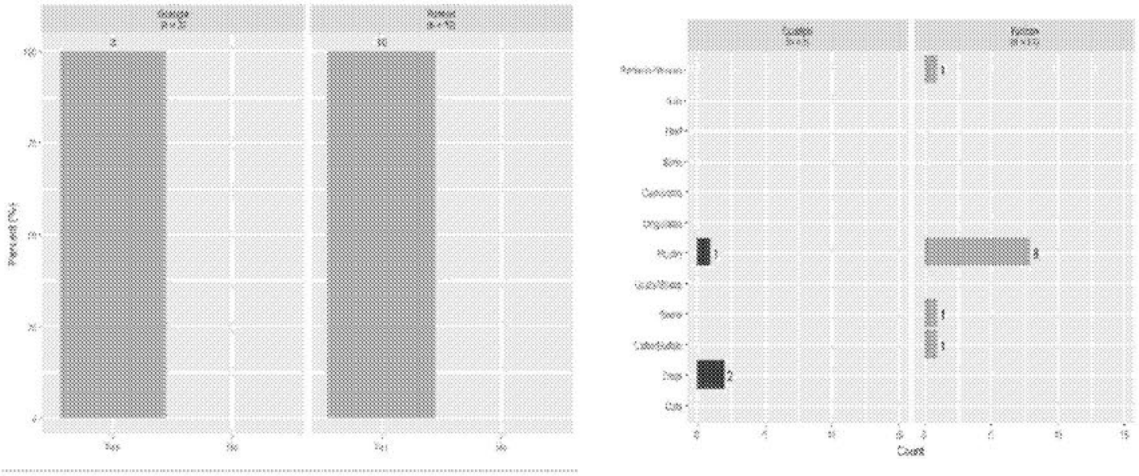


Figure 22 a & b: *(a) Whether respondents had found a dead animal and collected it to eat, share, or sell, in the past year, and (b) among those who had, types of animals that were found dead and collected to eat, share, or sell.*

In each province, almost all of the respondents who indicated being scratched or bitten by an animal in their lifetime said it occurred in the past year (100% in Guangdong, 98.6% in Guangxi, and 100% in Yunnan). In both Guangxi and Yunnan, dogs were the common type of animal that respondents said they were scratched or bitten by (64.5% in Guangxi and 50.0% in Yunnan). Cats were the second most common in Guangxi and Yunnan (9.6% in Guangxi, and 28.5% in Yunnan). Across all three provinces, only one respondent from Yunnan said that they were scratched or bitten by a bat **(Fig. 23)**.

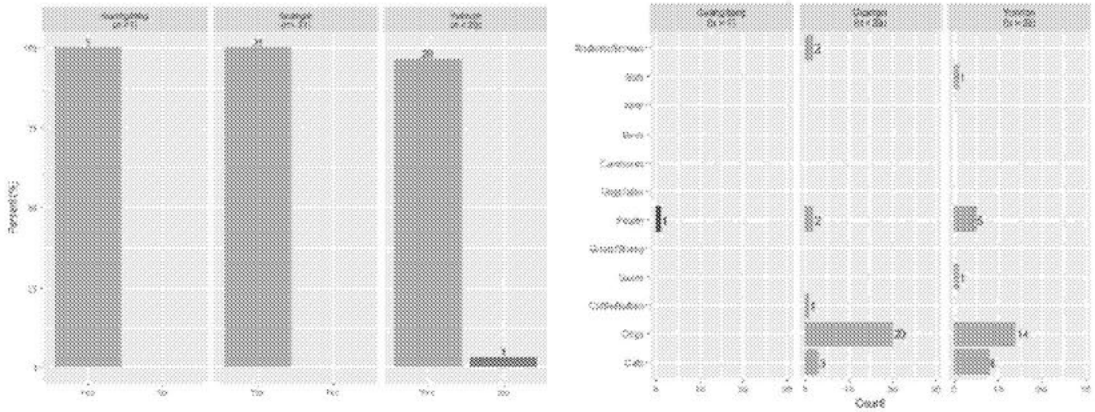


Figure 23 a & b: *(a) Whether respondents had been scratched or bitten by an animal, in the past year, and (b) among those who had, types of animals that scratched or bit respondents.*

Poultry was the most common type of animal slaughtered during the past year across all provinces as well as in each province (95.8% in Guangdong, 79.7% in Guangxi, and 94.1% in Yunnan). In addition to poultry, respondents in Yunnan also commonly only slaughtered swine (43.9%), compared to 1.4% in Guangdong and 7.3% in Guangxi **(Fig. 24)**.

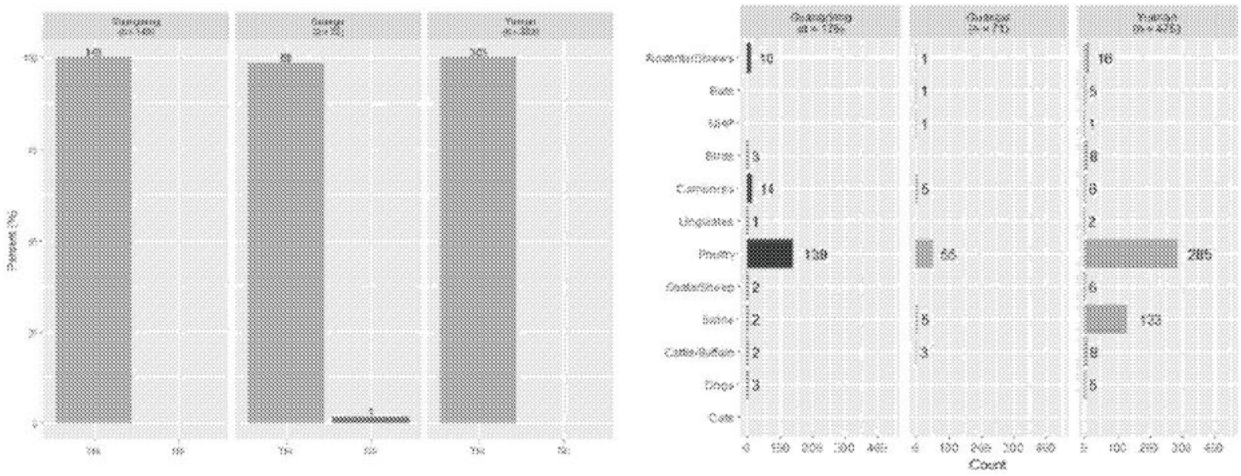


Figure 24 a & b: *(a) Whether respondents had slaughtered an animal, in the past year, and (b) among those who had, types of animals slaughtered.*

Carnivores were the most common taxa of animals hunted or trapped in the past year, in Guangdong and Guangxi. In Yunnan, rodents or shrews and birds were reported as the most common. Bats, non-human primates and dogs were animal types hunted by respondents in Yunnan but not by respondents in Guangdong and Guangxi **(Fig. 25)**.

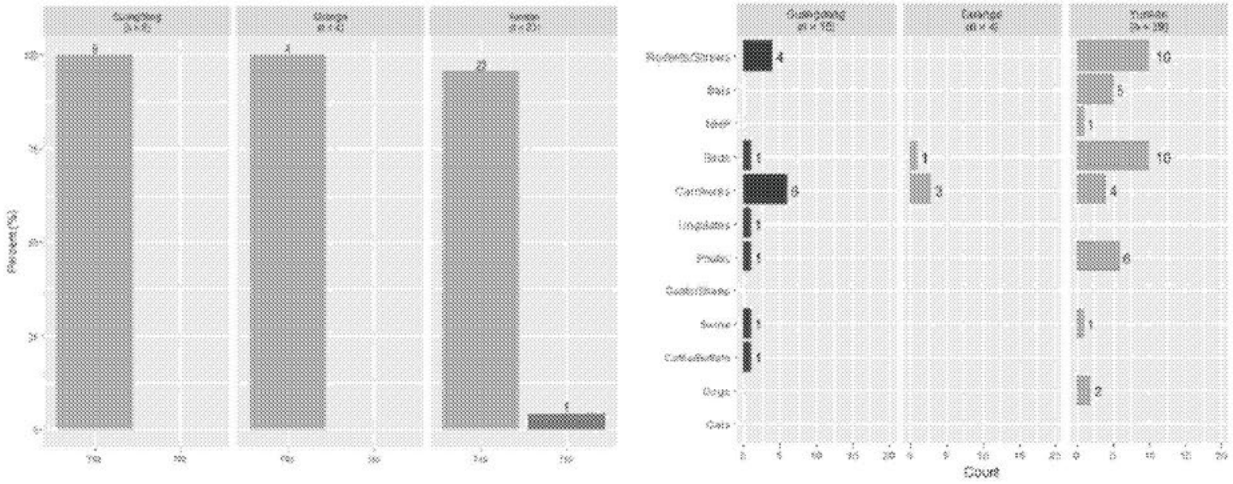


Figure 25 a & b: *(a) Whether respondents had hunted or trapped an animal, in the past year, and (b) among those who had, types of animals hunted or trapped.*

In examining bat-specific contact, across all provinces and within each province, the most common interaction with bats was finding them inside their houses. Respondents in Yunnan also hunted/trapped and handled bats, and were scratched/bitten by bats, whereas these did not occur in Guangdong or Guangxi **(Fig. 26)**.

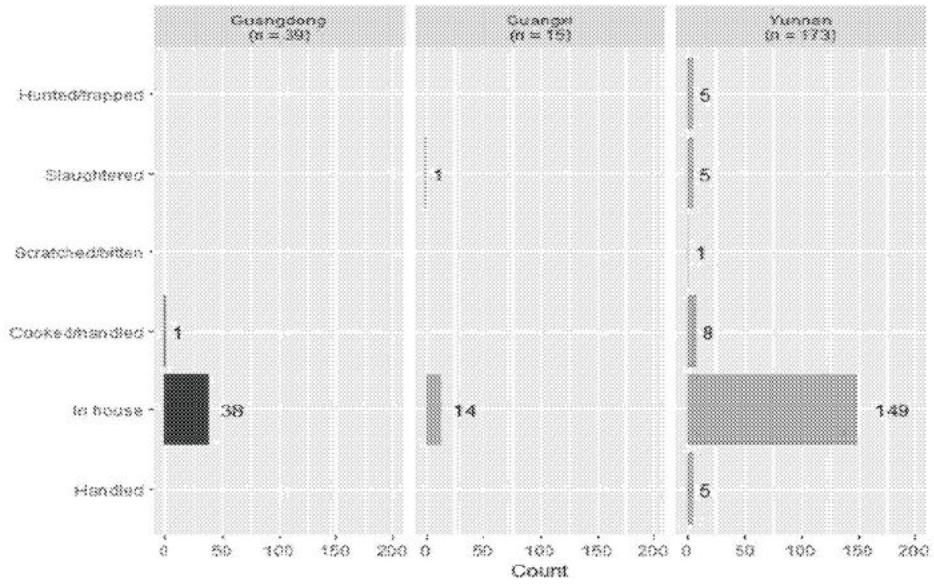


Figure 26: *Types of bat contact.*

After respondents were asked about their contact with wildlife and livestock, they were asked about their knowledge of whether animals can spread diseases and whether they were worried about diseases and disease outbreaks at wet markets. The proportion of respondents who thought that animals can spread disease was highest in Guangdong province (72.3%). In Guangxi and Yunnan, the proportion of those who thought animals could spread disease compared to those who thought that they did not were roughly equivalent – 47.5% versus 50.7% in Guangxi and 49.2% versus 49.3% in Yunnan **(Fig. 27)**.

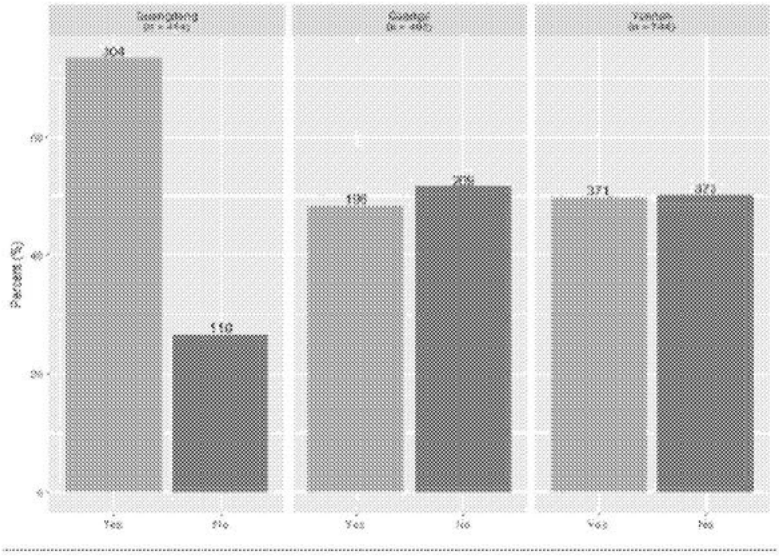


Figure 27: *Whether respondents thought that animals can spread disease.*

Similarly, when respondents were asked about whether they were worried about diseases or disease outbreaks in animals at wet markets, Guangdong had the highest proportion of respondents who said they were worried (67.3%). In both Guangxi and Yunnan, the proportion of respondents that was not worried (57.5% and 51.5%, respectively) was higher than the proportion that was worried **(Fig. 28)**

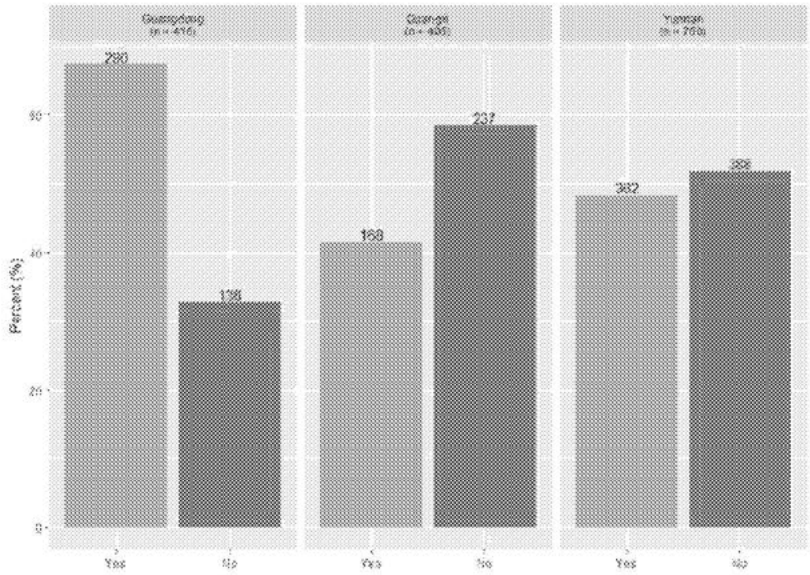


Figure 28: *Whether respondents were worried about diseases or disease outbreaks in animals at wet markets.*

Serological Evidence of Bat SARS-related CoV Infection in Humans

Respondents were asked to provide a biological sample to assess whether SARS-CoV spillover had occurred at the high-risk location where the survey has been implemented. A total of 1,530 serum samples were collected from 2016 to 2017 from individual residents in villages close to bat caves where coronaviruses were previously detected.

We developed an ELISA serology test using the purified NP protein of MERS-CoV, SARSr-CoV, HKU9 CoV and HKU10 CoV as coating antigen respectively and using Anti-Human IgG Monoclonal antibody as secondary antibody. All sera were screened for antibodies against these 4 bat-origin coronaviruses. Anti-SARSr-CoV NP IgG was detected in 10 samples, and 6 samples were positive for IgG against HKU10 NP. The 16 ELISA positive samples were further tested by confirmatory western blot, 7 samples from Yunnan province were confirmed positive for anti-SARSr-CoV, two samples (one from Guangdong province and one Guangxi province) were confirmed positive for anti-HKU10 **(Table 3)**.

Locations		Sample No.	NP Antibody Positive No.			
			HKU9 CoV	MERS CoV	SARSr-CoV	HKU10 CoV
Yunnan (2016)	Jinning	209			*6	
	Mengla	168			2 (*1)	
	Jinghong	212				2
	Lufeng	144				
Guangdong (2016)	Zengcheng	234			1	2
	Ruyuan	179				
Guangxi (2017)	Mashan	160			1	
	Guilin	224				*2
Total		1,530	0	0	*7	*2

Table 3 *Results of ELISA testing of human sera for antibodies to 4 different bat CoV species (*confirmed with western blot).*

Links Between ELISA Results and Behavior

Only one out of the seven SARS-related CoV seropositive respondents said that they had an unusual illness in their lifetime with reported symptoms similar to encephalitis or neural involvement. Two of the respondents said they had experienced symptoms in the past year with only one respondent specifying that they experienced epigastric pain and dizziness. The seven seropositive SARSr-CoV respondents reported various types of animal contacts in the past year. Three had lived with an animal as a pet, four handled a live animal, four raised a live animal, five saw animals inside their dwellings, five had cooked or handled meat, organs, or blood from a recently killed animals, one ate an animal that they knew was not well or sick, one was scratched or bitten by an animal, and four had slaughtered an animal. The only bat contact reported was by one respondent who saw a bat in their dwelling.

Both of the respondents who tested positive for HKU10-CoV antibodies said they had experienced an unusual illness in their lifetime, with symptoms associated with encephalitis and SARI. Neither respondent had experienced any symptoms of unusual illness in the past year. Both had reported handling and raising animals, with one indicating they saw animals come inside their dwelling, and one indicating cooking or handling meat, organs, or blood from a recently killed animal. No bat contact was reported by either of the respondents. Overall, five of the total nine SARS-related CoV and HKU10-CoV seropositive respondents reported being worried about disease or disease outbreaks at wet markets. Seven of the nine reported purchasing live animals from a wet market.

Specific Aim 1: Summary of Key Findings

Our analysis of the key risk factors relating to potential viral zoonotic disease spillover in China indicated some notable differences among the respondents in Guangdong, Guangxi, and Yunnan. With respect to demographic factors, Guangxi fared the lowest on key socio-economic

status indicators when compared to Guangdong and Yunnan provinces as reflected by the higher proportion of respondents in Guangxi living under the poverty level.

When assessing the type of animal contact and the associated animal taxa over the course of a respondent's lifetime, the results show that respondents in Yunnan engaged in greater contact with animals then those from Guangdong and Guangxi. For example, for 12 of the 14 animal contact types, a higher proportion of Yunnan respondents engaged in these respective activities than in Guangdong and Guangxi. Respondents in Yunnan also reported hunting bats, dogs, and non-human primates which were not reported to being hunted in Guangdong and Guangxi. Swine contact was higher in Yunnan for handling, raising, and slaughtering activities. When examining the various types of animal contact associated with bats only, our results also show that Yunnan respondents reported more varied types of contact with bats. Respondents in Yunnan indicated handling, being scratched by, slaughtering, and hunting bats, but these interactions did not occur in Guangdong or Guangxi. Additional analyses that examine predictors of animal contact in each province will be the focus of human behavioral analyses in Year 5 of the study.

Even though our sample population lives in areas that have dense and diverse bat populations, our results show an overall low proportion of respondents reporting hunting and trapping bats in all three provinces. The low proportion of hunting practice could be attributed to the success of conservation enforcement efforts undertaken by the government. These efforts may have effectively reduced the illegal practice of hunting wildlife or, as a consequence, moved the activity underground which made respondents less forthcoming about revealing their engagement in such practices. Further investigation into the potential causes is also warranted.

Our analyses also reveal differences in perceptions associated with zoonotic disease spillover between Guangdong, and Guangxi and Yunnan. For example, the proportion of respondents who thought that animals can spread disease was highest in Guangdong province at 72.3%, as compared to Guangxi (48.3%) and Yunnan (49.9%). Moreover, about two-thirds of respondents in Guangdong were worried about diseases and disease outbreaks in wet markets. These differences in perception observed in Guangdong compared to Guangxi and Yunnan could potentially be attributable to a heightened awareness of zoonotic disease emergence due to the 2001 SARS outbreak.

Finally, our serological testing results provide the first evidence ever of a bat SARSr-CoV spilling over into people in the wild. All of the SARSr-CoV positive individuals were from Yunnan province, which is the site of a cave in which we have identified a large diversity of SARSr-CoVs within the virome of which every genetic element of SARS-CoV can be identified. These findings warrant further investigations into the type of exposures that may have contributed to bat SARS-related CoVs to infect humans in this particular region. **They also highlight this region as a hotspot for SARSr-CoV future spillover risk.**

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

Bat CoV PCR Detection and Sequencing from Live-Sampled Bat Populations

We collected rectal swab and oral swab samples from 671 individual bats from 20 species in Guangdong and Guangxi provinces in southern China in Year 4 **(Table 4)**. 671 rectal swab samples were tested for CoV RNA and 154 (23.0%) were positive **(Table 5)**.

Date of Sampling	Sampling Locations	Rectal swabs	Oral swabs
May 10th 2017	Hezhou, Guangxi	6	6
May 11-12th 2017	Chongzuo, Guangxi	67	67
May 13th 2017	Nanning, Guangxi	66	66
May 17th, 2017	Beihai, Guangxi	23	23
May 19th 2017	Chongzuo, Guangxi	36	36
May 21st 2017	Yangshan, Qingyuan, Guangdong	46	46
May 22nd, June 7th 2017	Huidong, Huizhou, Guangdong	103	103
June 9th 2017	Nanning, Guangxi	71	71
June 9th 2017	Ningming, Chongzuo, Guangxi	63	63
September 10th 2017	Huidong, Huizhou, Guangdong	100	100
September 11th 2017	Yingde, Guangdong	90	90
Total		671	671

Table 4. *Bat samples collected for CoV surveillance in Year 4*

Species	Guangdong	Guangxi	Total
Rhinolophus sinicus	**9**/27	6	**9**/33
Rhinolphus rex		4	4
Rhinolophus pusilus	1	2	3
Rhinolophus pearsoni	5		5
Hipposideros armiger	24	8	32
Hipposideros larvatus	9	9	18
Hipposideros pomona		20	20
Hipposideros pratti	26		26
Aselliscus stoliczkanus		1	1
Miniopterus fuliginosus	1		1
Miniopterus pusillus	**29**/39		**29**/39
Myotis chinensis	**2**/27		**2**/27
Myotis daubentonii	2		2
Myotis ricketti	**86**/178		**86**/178
Pipistrellus abramus		2	2
Pipistrellus pipistrellus		2	2
Scotophilus kuhli		**24**/137	24/137
Tylonycteris pachypus		**4**/115	**4**/115
Tylonycteris robustula		3	3
Cynopterus sphinx		23	23
Total	126/339	28/332	154/671

Table 5*. Number of bat specimens tested and positive (bold) in Year 4*

A high prevalence of HKU6-related coronaviruses (48.3%), Scotophilus coronavirus 512 (17.5%), and coronavirus 1B (71.8%) was detected in *Myotis ricketii*, *Schotophilus khulii* and *Miniopterus pusillus*, respectively. SARS-related coronaviruses and HKU2-related coronaviruses were discovered in 4 and 5 *Rhinolophus sinicus* samples respectively from Guangdong. HKU4 coronaviruses were identified in 4 *Tylonycteris pachypus* from Guangxi **(Fig. 29)**.

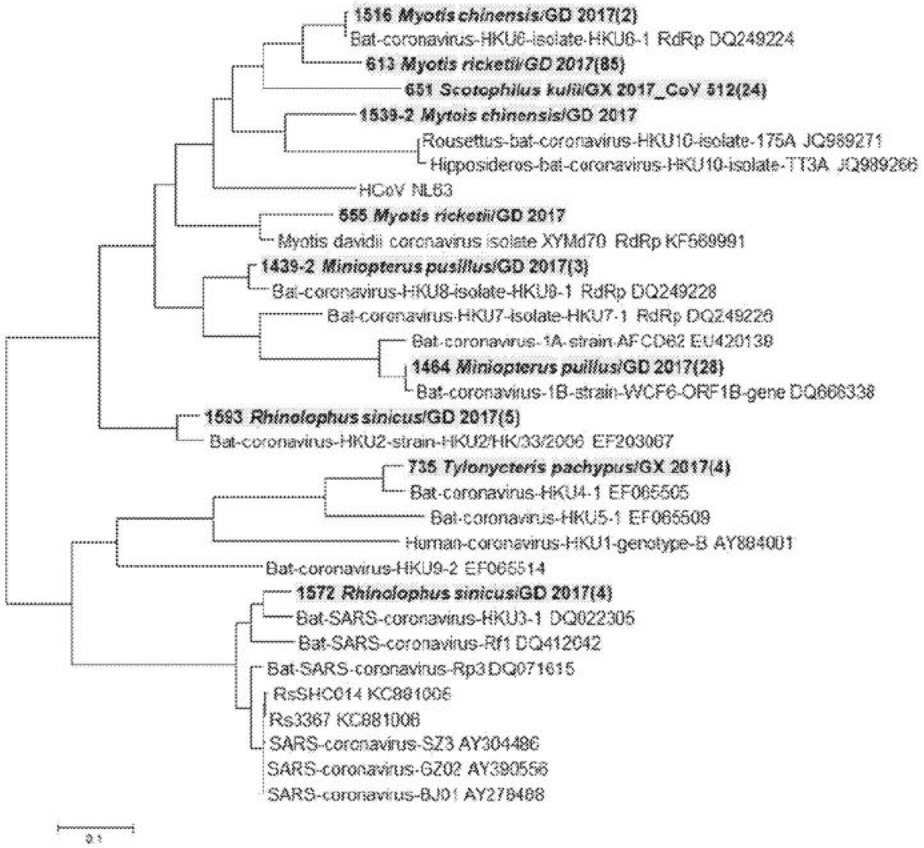


Figure 29: *Phylogenetic analysis of partial RdRp gene of CoV (440-nt partial sequence)*

Genetic Diversity and Genomic Characterization of Betacoronaviruses in Fruit Bats

In Year 4, we analyzed the genetic diversity of betacoronaviruses we have detected since 2009 in different species of fruit bats in Yunnan province, including *Eonycteris spelaea*, *Rousettus leschenaultia* and an unclassified *Rousettus* species. These viruses are classified into two betacoronavirus species, HKU9-CoV and GCCDC1-CoV. All HKU9-related viruses (n=46) were found in *Rousettus* spp. bats while GCCDC1-related viruses (n=13) from *E. spelaea*. Phylogenetic analysis of the full-length N gene suggests that HKU9-related CoVs are highly diverse and divided into 5 lineages with previously reported strains, and the GCCDC1-related CoVs were more similar between each other **(Fig. 30)**.

The full-length genome sequence of a novel HKU9-related CoV termed 2202 was determined. It shares 83% nt identity with other HKU9 strains, with the most divergent regions located in the S

protein, but shares only 68% aa identity with those of other HKU9 strains. Virus quantification revealed that intestine was the primary infected organ for HKU9-related CoVs while kidney and lungs could also be target tissues, suggesting potential for spillover through oral-fecal, respiratory, or uro-genitary routes.

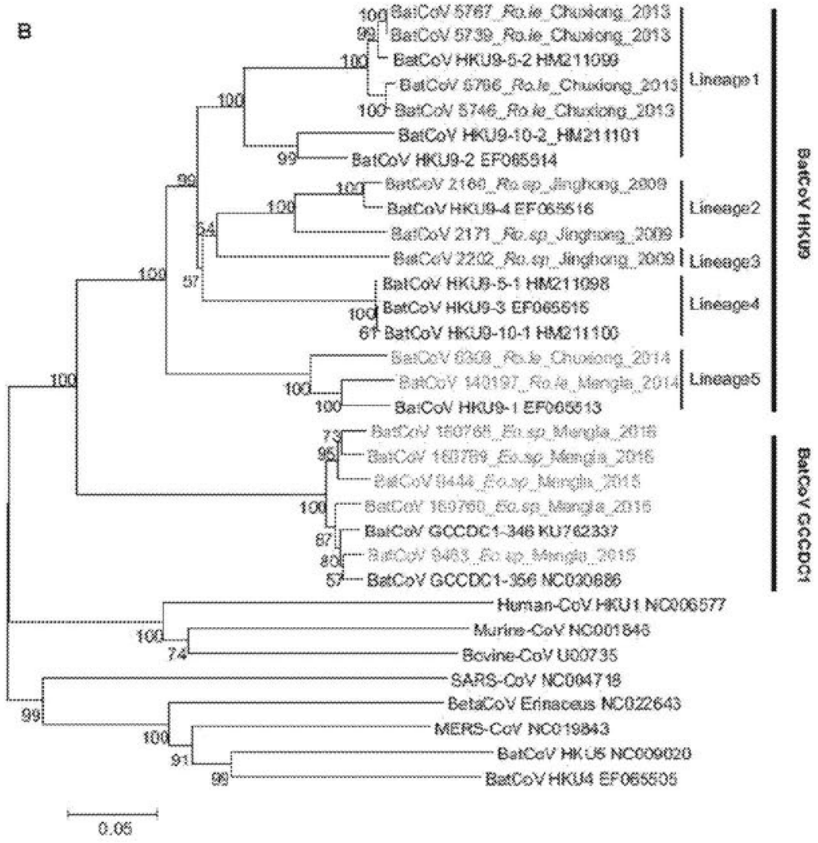


Figure 30. *Phylogenetic analysis of full-length N gene of HKU9 and GCCDC1 CoVs*

Bat Coronavirus Host-Virus Phylogeography in China

We used discrete ancestral character state reconstruction to estimate viral history and reconstructed the inferred bat host genus for each node within the phylogenetic tree **(Figs. 31, 32)**. The color of tree branches indicates the inferred ancestral host bat genus for the reconstructed phylogeny. *Rhinolophus* is the inferred ancestral host of lineages B and C (SARS-like CoVs and MERS-like CoVs, respectively). This genus played an important role in the diversification of Beta-CoVs. A larger host diversity is observed for Alpha-CoVs. Our dataset for this analysis includes all CoV RdRp sequences isolated from bat specimens collected by our team from 2008-2015 (Alpha-CoVs: n = 491 – Beta-CoVs: n = 326), including those collected under prior NIAID funding (1 R01 AI079231), funding from Chinese Federal Agencies, and a large majority from our current NIAID project. All Chinese bat CoV RdRp sequences available in GenBank were also added to our dataset (Alpha-CoVs: n = 226 – Beta-CoVs: n = 206).

Phylogenetic trees were reconstructed for Alpha- and Beta-CoVs separately using Bayesian inference (BEAST 1.8).

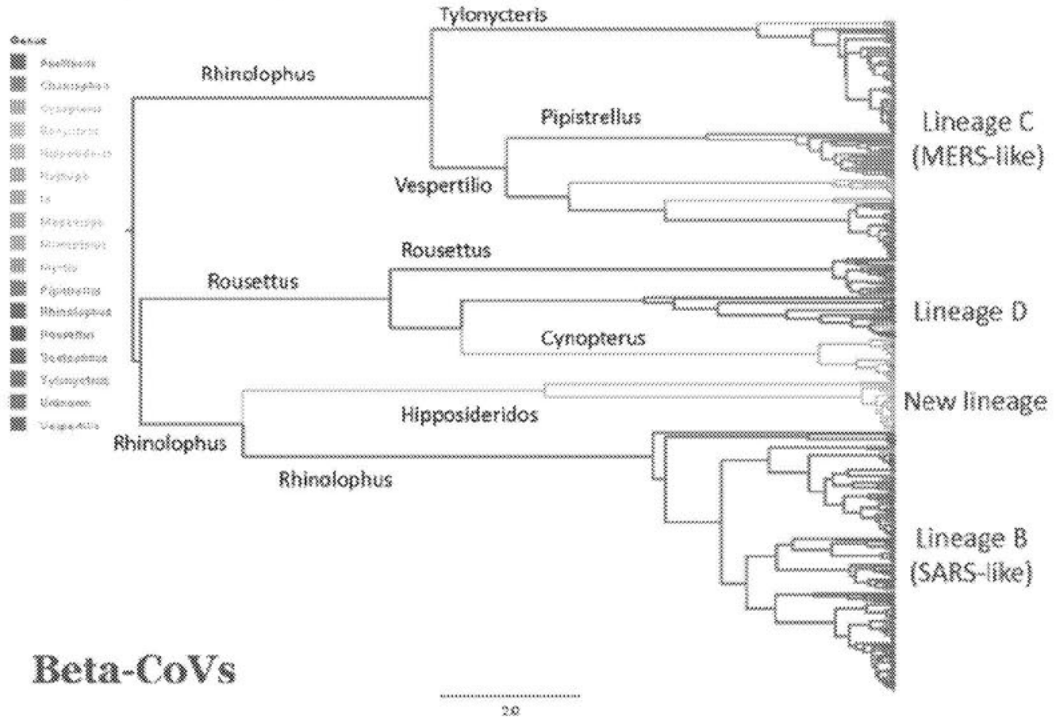


Figure 31. *Ancestral host reconstruction for Beta-CoVs, at a host genus level.*

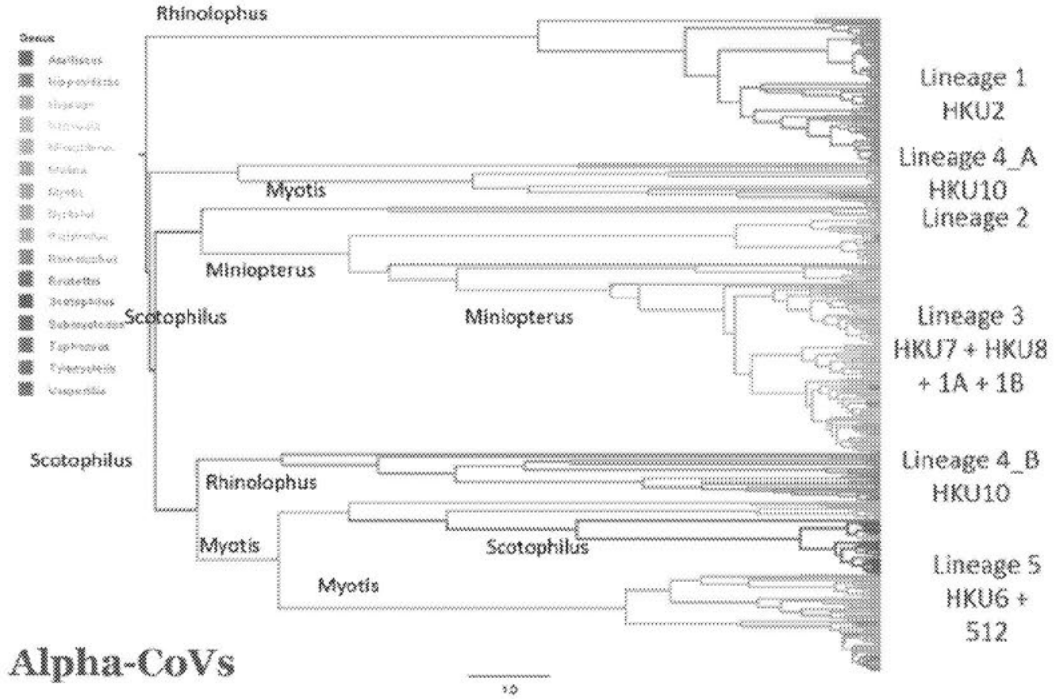


Figure 32. *Ancestral host reconstruction for Alpha-CoVs, at a host genus level.*

To better understand the geographic origins and extent of specific CoV clades, we also used discrete ancestral character state reconstruction in BEAST to reconstruct the ancestral location of each branch of the tree. We used SPREAD to visualize the tree in its geographic context and infer CoV spatial spread in China **(Fig. 33)**. These analyses allow us to identify the geographic areas that are likely sources of origin/diversity for this important group of viruses. The common ancestor of most Beta-CoVs lineages is located in Hong Kong and Guangdong. The common ancestor of most Alpha-CoV lineages was located in Yunnan province, and our results suggest they spread to other provinces from Yunnan.

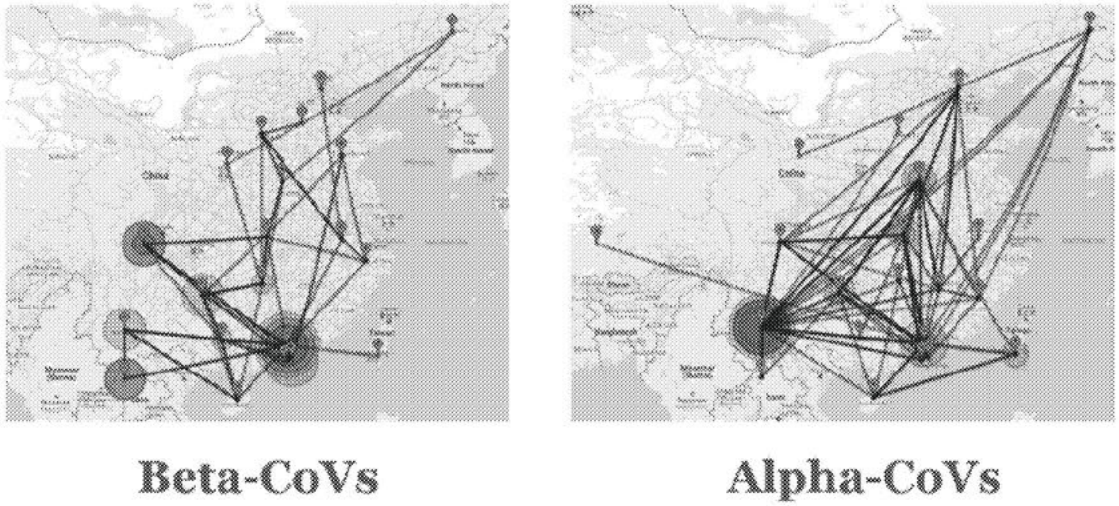


Figure 33. *Ancestral location reconstruction for Beta- and Alpha-CoVs. The bigger the circle is, the more ancestral the corresponding node is.*

Specific Aim 3: Testing Predictions of CoV Inter-Species Transmission

Identification of two novel MERS-related CoVs that use DPP4 receptor

Two novel MERSr-CoVs, BtCoV/li/GD/2013-845 and BtCoV/li/GD/2014-422, were identified from great evening bats (*Ia io*) in Guangdong province. Phylogenetic analysis of polyprotein 1 and the E, M, and N proteins suggests that the two novel strains are more closely related to MERS-CoV than to other lineage C Beta-CoVs. Their RdRp sequences are closely related to those of MERS-CoV and other MERSr-CoVs, with 94.4–97.0% aa identities. In contrast, they are divergent from MERS-CoV and other MERSr-CoVs in the spike protein, with only 58.9–64.7% aa identities. However, in the receptor-binding domain (RBD) of the spike protein, the two novel MERSr-CoVs are identical to MERS-CoV at six out of the 13 residues that directly interact with human DPP4 receptor, making them more similar to MERS-CoV than any other known lineage C BetaCoVs **(Fig. 34a)**. Protein–protein interaction assays demonstrated that the spike proteins of the novel MERSr-CoVs bind to both human and bat DPP4 **(Fig. 34b)**. Moreover, bat cells exogenously expressing human DPP4 support the entry of the retrovirus pseudotyped with BtCoV/li/GD/2014-422 spike, while the pseudovirus fails to enter cells that do not express DPP4. The results demonstrate that the spike protein of the newly identified MERSr-CoV recognizes the human DPP4 receptor.

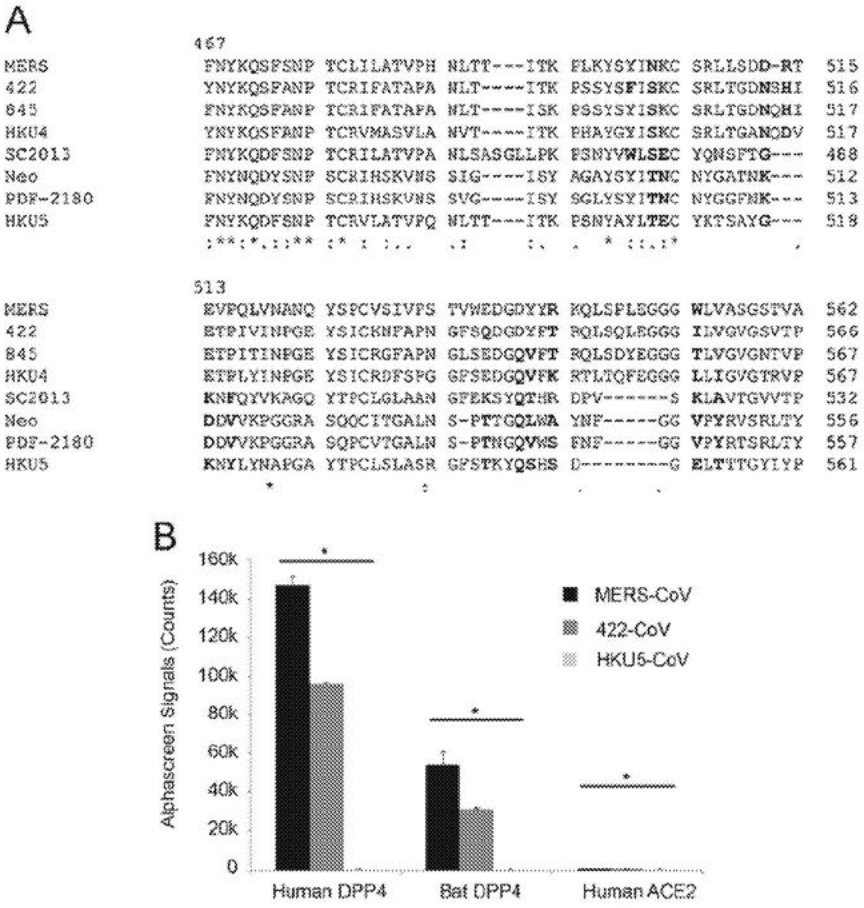


Figure 34. *BtCoV/li/GD/2014-422 RBD analysis (a) and DPP4-binding assay (b)*

In Vivo Infection of Human ACE2 (hACE2) Expressing Mice with SARSr-CoV S Protein variants

Using the reverse genetic methods we previously developed, infectious clones with the WIV1 backbone and the spike protein of SHC014, WIV16 and Rs4231, respectively, were constructed and recombinant viruses were successfully rescued. In Year 4, we performed preliminary *in vivo* infection of SARSr-CoVs on transgenic mice that express hACE2. Mice were infected with 10^5 pfu of full-length recombinant virus of WIV1 (rWIV1) and the three chimeric viruses with different spikes. Pathogenesis of the 4 SARSr-CoVs was then determined in a 2-week course. Mice challenged with rWIV1-SHC014S have experienced about 20% body weight loss by the 6th day post infection, while rWIV1 and rWIV-4231S produced less body weight loss. In the mice infected with rWIV1-WIV16S, no body weight loss was observed **(Fig. 35a)**. 2 and 4 days post infection, the viral load in lung tissues of mice challenged with rWIV1-SHC014S, rWIV1-WIV16S and rWIV1-Rs4231S reached more than 10^6 genome copies/g and were significantly higher than that in rWIV1-infected mice **(Fig. 35b)**. These results demonstrate varying pathogenicity of SARSr-CoVs with different spike proteins in humanized mice.

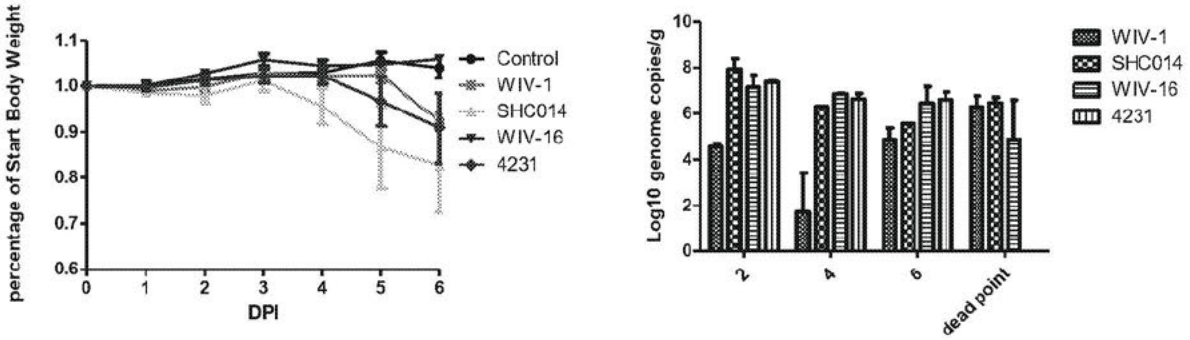


Figure 35. *In vivo infection of SARSr-CoVs in hACE2-expressing mice. (a, left) Body weight change after infection; (b, right) Viral load in lung tissues*

Additional Year 4 Results for Specific Aim 3:

Identification of a HKU2-related Coronavirus of Bat Origin that Caused Fatal Acute Diarrhea in Piglets

From October 2016, a series of fatal swine diarrhea disease outbreaks occurred in Guangdong province. By May 2017, it had resulted in death of 24,693 piglets across four farms. We identified a novel coronavirus as the etiological agent of the disease by metagenomic analysis, viral isolation and experimental infection, and named this "Swine Acute Diarrhea Syndrome coronavirus (SADS-CoV). During Year 4, we submitted and published a paper on this finding to *Nature* (Zhou *et al.*, 2018). The full-length genome of SADS-CoV shares 95% sequence identity to bat CoV HKU2. However, the S gene sequence identity is only 86%, suggesting that the previously reported HKU2-CoV is not the direct progenitor of SADS-CoV, but that they may have originated from a common ancestor.

Using a SADS-CoV specific qPCR assay based on its RdRp gene, SADS-related coronaviruses (SADSr-CoVs) were detected in rectal swabs of *Rhinolophus* bats collected from 2013 to 2016 in Guangdong. Full-length genome sequencing of 4 bat SADSr-CoVs revealed 96% to 98% overall genome sequence identity between SADSr-CoVs and SADS-CoV. Most importantly, the S protein of SADS-CoV shared more than 98% sequence identity with those of the two SADSr-CoVs (162149 and 141388), compared to 86% with HKU2-CoV (**Fig. *36a***). The phylogeny of S1 protein sequence showed strong co-evolutionary relationships with bat alphacoronavirus and their hosts, with swine SADS-CoV more closely related to SADSr-CoVs from *Rhinolophus affinis* than strains from *Rhinolophus sinicus* in which HKU2-CoV was found **(Fig. 36b)**. Analysis of the 33 SADS-CoV full genome sequences we were able to characterize from pigs suggests that viruses from the four farms may have been transmitted from their reservoir hosts independently. These findings highlight the importance of identifying coronavirus diversity and distribution in bats to mitigate future outbreaks that threaten livestock and public health.

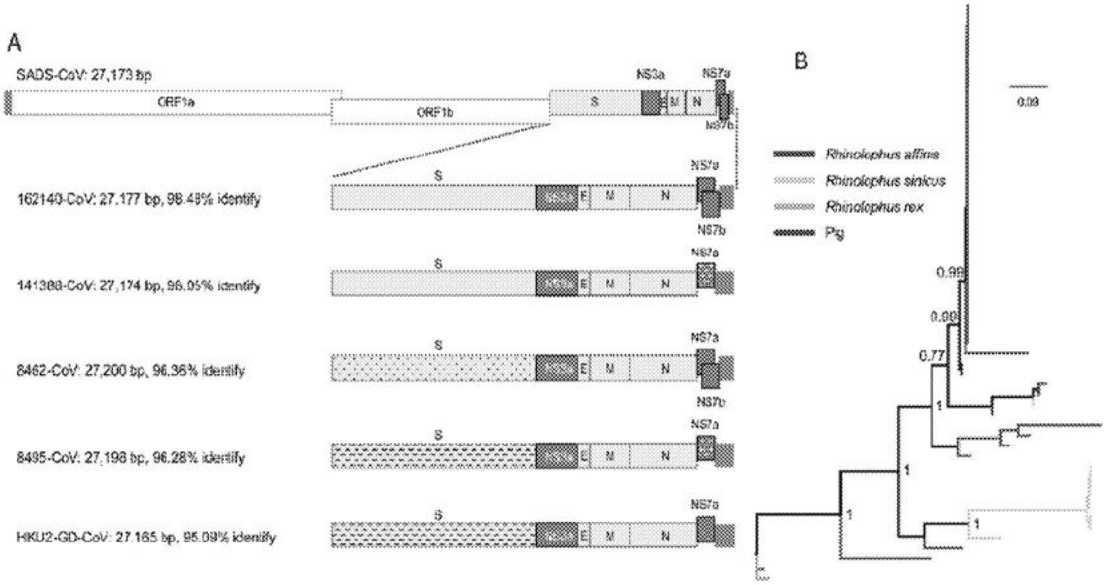
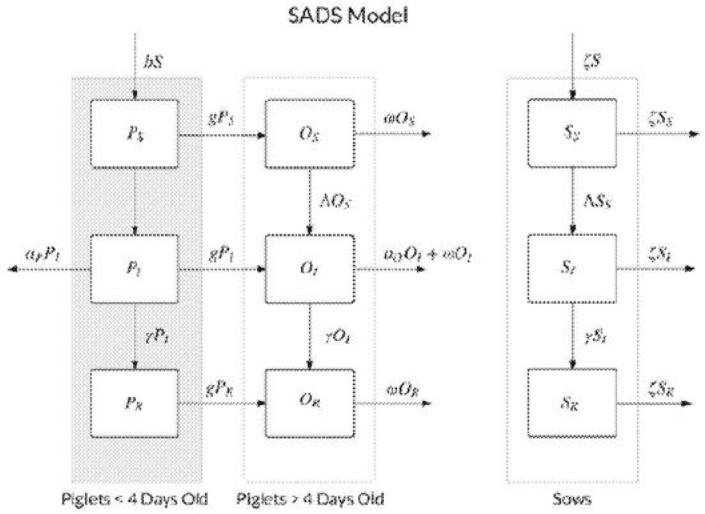


Figure 36. *Genome organization and comparison (a) and Phylogenetic analysis of S1 protein (b) of SADS-CoV and bat SADSr-CoVs*

Intra-Farm Transmission Model to Understand to Predict Future Transmission and Outbreak

To better understand amplification dynamics and assess the potential for future transmission resulting in large outbreaks, we developed an intra-farm, age-structured, stochastic transmission model for SADS-CoV **(Fig. 37)**. We developed multiple versions of this model to represent different hypotheses of disease transmission mechanisms and fit them to time-series data of reported deaths on multiple SADS-infected farms.



$$N = P_S + P_I + P_R + O_S + O_I + O_R + S_S + S_I + S_R$$

$$\Lambda = \beta \frac{(P_I + O_I + S_I)}{N}$$

Figure 37: *Schematic of intra-farm transmission mode.*

Our first model structure, which assumed equal mixing of animals across farms **(Fig. 38)** showed that age structure alone was insufficient to generate the temporal pattern of reported deaths on SADS-infected farms. Our second model structure **(Fig. 39)** represented individual barns on a farm as a series of pig-virus meta-populations. This structure was sufficient to re-create the dynamics of the series of rapid "mini-epidemics" that progressed in SADS-infected farms.

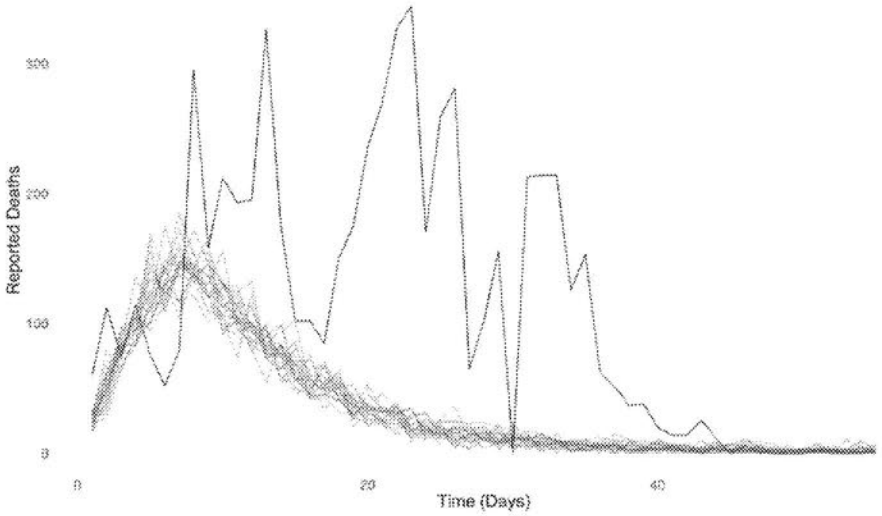


Figure 38: *Best-fit simulations (red) from an equal-mixing transmission model and actual reported death time series (black) on a SADS-infected farm.*

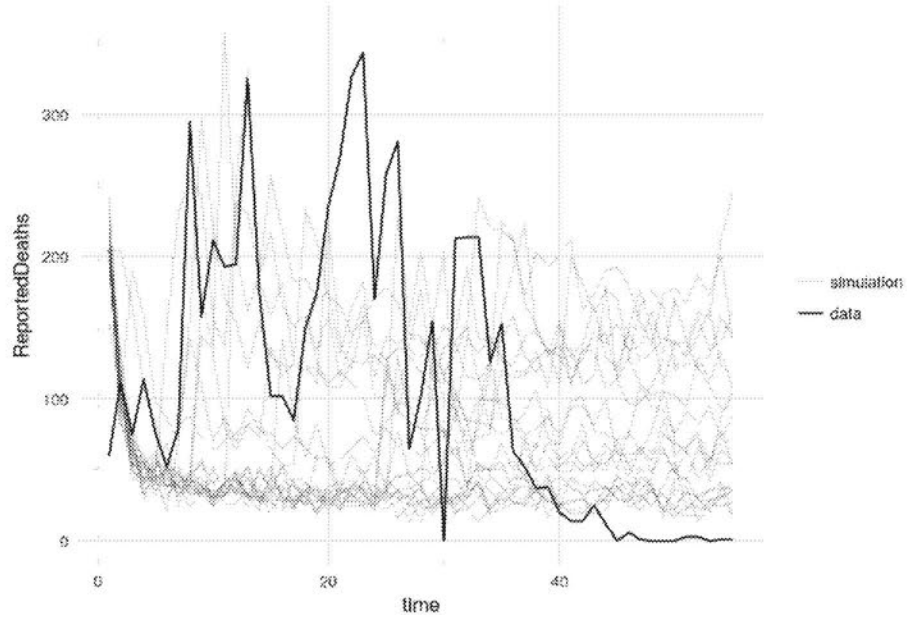


Figure 39: *Best-fit simulations (grey) from an metapopulation transmission model and actual reported death time series (black) on a SADS-infected farm.*

Specific Goals Not Meet

- The wild animal farm survey was piloted in early Y4, with data collected from seven wild animal farms, it was postponed due to the emergence of SADS-CoV where our group had focused on instead in Y4, but will be resumed in Y5 to continue collecting and analyzing data.
- The passive hospital surveillance has been piloted will continue in Year 4 to collect and test for CoVs.

B. 4 What opportunities for training and professional development has the project provided?

1. Conference and University lectures: We provided human subject research trainings to chief physicians and nurses at local clinics, staff from Yunnan Institute of Endemic Diseases Control and Prevention, students from Dali College and Wuhan University for both qualitative and quantitative research.

2. Agency and other briefing: Dr. Guangjian Zhu was invited by the Guangdong Institute of Applied Nature Resources, Guangdong Academy of Sciences to provide training to 8 field team members regarding biosafety and PPE use, bats and rodents sampling. Dr. Zhengli Shi participated in the US National Science Foundation-funded EcoHealthNet (grant to EcoHealth Alliance – Epstein PI) that provides research exchange opportunities to undergraduate and graduate-level students.

3. Public outreach: PI Daszak, and Co-investigators Shi, Epstein, and Olival presented the results of this project to the public via interviews with national central and local television, social media, newspaper and journals in China and the US.

C. PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

Yes

Publications Reported for this Reporting Period

Public Access Compliance	Citation
Complete	Luo CM, Wang N, Yang XL, Liu HZ, Zhang W, Li B, Hu B, Peng C, Geng QB, Zhu GJ, Li F, Shi ZL. Discovery of Novel Bat Coronaviruses in South China That Use the Same Receptor as Middle East Respiratory Syndrome Coronavirus. Journal of virology. 2018 July 1;92(13). PubMed PMID: 29669833; PubMed Central PMCID: PMC6002729; DOI: 10.1128/JVI.00116-18.
Complete	Field HE. Evidence of Australian bat lyssavirus infection in diverse Australian bat taxa. Zoonoses and public health. 2018 September;65(6):742-748. PubMed PMID: 29785730; PubMed Central PMCID: PMC6249124; DOI: 10.1111/zph.12480.
Complete	Eskew EA, Olival KJ. De-urbanization and Zoonotic Disease Risk. EcoHealth. 2018 December;15(4):707-712. PubMed PMID: 30120670; PubMed Central PMCID: PMC6265062; DOI: 10.1007/s10393-018-1359-9.
Complete	Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. Nature reviews. Microbiology. 2019 March;17(3):181-192. PubMed PMID: 30531947; PubMed Central PMCID: PMC7097006; DOI: 10.1038/s41579-018-0118-9.
Complete	Li HY, Zhu GJ, Zhang YZ, Zhang LB, Hagan EA, Martinez S, Chmura AA, Francisco L, Tai H, Miller M, Daszak P. A qualitative study of zoonotic risk factors among rural communities in southern China. International health. 2020 February 12;12(2):77-85. PubMed PMID: 32040190; PubMed Central PMCID: PMC7017878; DOI: 10.1093/inthealth/ihaa001.

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Nothing to report

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization? No

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
(b) (6)	Y	DASZAK, PETER	BS,PHD	PD/PI	(b) (4), (b) (6)					NA
(b) (6)	N	Chmura, Aleksei	BS,PHD	Non-Student Research Assistant						NA
(b) (6)	N	Ross, Noam Martin	PhD	Co-Investigator						NA
(b) (6)	Y	Olival, Kevin J.	PHD	Co-Investigator						NA
(b) (6)	Y	Zhang, Shu-yi	PHD	Co-Investigator				East China Normal University	CHINA	NA
	N	ZHU, GUANGJIAN	PHD	Co-Investigator				East China Normal University	CHINA	NA
	N	GE, XINGYI	PHD	Co-Investigator				Wuhan Institute of Virology	CHINA	NA
	N	KE, CHANGWEN	PHD	Co-Investigator				Center for Disease Control and Prevention of Guangdong Province	CHINA	NA
	Y	ZHANG, YUNZHI	PHD	Co-Investigator				Yunnan Provincial Institute of Endemic Diseases Control & Prevention	CHINA	NA
(b) (6)	N	EPSTEIN, JONATHAN H	MPH,DVM,BA,PHD	Co-Investigator						NA
(b) (6)	N	SHI, ZHENGLI	PhD	Co-Investigator				Wuhan Institute of Virology	CHINA	NA

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award?

No

D.2.b New Senior/Key Personnel

Are there, or will there be, new senior/key personnel?

No

D.2.c Changes in Other Support

Has there been a change in the active other support of senior/key personnel since the last reporting period?

No

D.2.d New Other Significant Contributors

Are there, or will there be, new other significant contributors?

No

D.2.e Multi-PI (MPI) Leadership Plan

Will there be a change in the MPI Leadership Plan for the next budget period?

NA

E. IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Dollar Amount	Country
$201,422	CHINA

F. CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

Sub-Project ID:	Study ID	Study Title:	Delayed Onset	Clinical Trial	NCT	NIH-Defined Phase 3	ACT
	58010	Understanding the Risk of Bat Coronavirus Emergence-PROTOCOL-001	NO	NO		NO	

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

No

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

Yes

G.8 PROJECT/PERFORMANCE SITES

Organization Name:	DUNS	Congressional District	Address
Primary: EcoHealth Alliance, Inc.	077090066	NY-010	460 West 34th Street 17th Floor New York NY 100012317
Wuhan Institute of Virology	529027474		Xiao Hong Shan, No. 44 Wuchang District Wuhan NONE
East China Normal University	420945495		3663 Zhongshan Beilu Shanghai NONE
ECOHEALTH ALLIANCE	077090066		ECOHEALTH ALLIANCE, INC. 460 W 34TH ST

			NEW YORK NY 100012320

G.9 FOREIGN COMPONENT

Organization Name: Wuhan Institute of Virology
Country: CHINA
Description of Foreign Component:
Principal Laboratory for all Research in China as per section G8 (above) and detailed in our Specific Aims

Organization Name: Wuhan School of Public Health
Country: CHINA
Description of Foreign Component:
Principal Coordinating Team for all project field work as per section G8 (above) and detailed in our Specific Aims

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

No

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period?

No

G.12 F&A COSTS

Is there a change in performance sites that will affect F&A costs?

No

Section 1 - Basic Information (Study 58010)

OMB Number: 0925-0001 and 0925-0002

Expiration Date: 03/31/2020

1.1. Study Title *

Understanding the Risk of Bat Coronavirus Emergence-PROTOCOL-001

1.2. Is this study exempt from Federal Regulations * Yes • No

1.3. Exemption Number 1 2 3 4 5 6 7 8

1.4. Clinical Trial Questionnaire *

1.4.a. Does the study involve human participants?	• Yes	No
1.4.b. Are the participants prospectively assigned to an intervention?	Yes	• No
1.4.c. Is the study designed to evaluate the effect of the intervention on the participants?	Yes	• No
1.4.d. Is the effect that will be evaluated a health-related biomedical or behavioral outcome?	Yes	• No

1.5. Provide the ClinicalTrials.gov Identifier (e.g. NCT87654321) for this trial, if applicable

Section 2 - Study Population Characteristics (Study 58010)

2.1. Conditions or Focus of Study

2.2. Eligibility Criteria

2.3. Age Limits	Min Age:	Max Age:
2.4. Inclusion of Women, Minorities, and Children		
2.5. Recruitment and Retention Plan		
2.6. Recruitment Status	Not yet recruiting	
2.7. Study Timeline		

Inclusion Enrollment Reports

IER ID#	Enrollment Location Type	Enrollment Location
IER 58010	Foreign	

Inclusion Enrollment Report 58010

Using an Existing Dataset or Resource* : Yes • No

Enrollment Location Type* : Domestic • Foreign

Enrollment Country(ies): CHN: CHINA

Enrollment Location(s):

Comments:

Planned

Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/ Alaska Native	0	0	0	0	0
Asian	1230	1230	0	0	2460
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
Black or African American	0	0	0	0	0
White	0	0	0	0	0
More than One Race	0	0	0	0	0
Total	1230	1230	0	0	2460

Cumulative (Actual)

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/ Alaska Native	0	0	0	0	0	0	0	0	0	0
Asian	980	616	0	0	0	0	0	0	0	1596
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0
Black or African American	0	0	0	0	0	0	0	0	0	0
White	0	0	0	0	0	0	0	0	0	0
More than One Race	0	0	0	0	0	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	0
Total	980	616	0	0	0	0	0	0	0	1596

Section 3 - Protection and Monitoring Plans (Study 58010)

3.1. Protection of Human Subjects

3.2. Is this a multi-site study that will use the same protocol to conduct non-exempt human subjects research at more than one domestic site?	Yes	No	N/A

If yes, describe the single IRB plan

3.3. Data and Safety Monitoring Plan

3.4. Will a Data and Safety Monitoring Board be appointed for this study?	Yes	No

3.5. Overall structure of the study team

Section 4 - Protocol Synopsis (Study 58010)

4.1. Brief Summary

4.2. Study Design

4.2.a. Narrative Study Description

4.2.b. Primary Purpose

4.2.c. Interventions

Type	Name	Description

4.2.d. Study Phase

Is this an NIH-defined Phase III Clinical Trial? Yes • No

4.2.e. Intervention Model

4.2.f. Masking Yes No

Participant	Care Provider	Investigator	Outcomes Assessor

4.2.g. Allocation

4.3. Outcome Measures

Type	Name	Time Frame	Brief Description

4.4. Statistical Design and Power

4.5. Subject Participation Duration

4.6. Will the study use an FDA-regulated intervention? Yes No

4.6.a. If yes, describe the availability of Investigational Product (IP) and Investigational New Drug (IND)/ Investigational Device Exemption (IDE) status

4.7. Dissemination Plan

PI: **DASZAK, PETER**	Title: Understanding the Risk of Bat Coronavirus Emergence	
Received: 06/05/2013	FOA: PA11-260	Council: 01/2014
Competition ID: ADOBE-FORMS-B2	FOA Title: RESEARCH PROJECT GRANT (PARENT R01)	
1 R01 AI110964-01	Dual:	Accession Number: 3595101
IPF: 4415701	Organization: ECOHEALTH ALLIANCE, INC.	
Former Number:	Department:	
IRG/SRG: CRFS	AIDS: N	Expedited: N
Subtotal Direct Costs (excludes consortium F&A) Year 1: 499,993 Year 2: 499,469 Year 3: 499,978 Year 4: 499,953 Year 5: 499,974	Animals: Y Humans: Y Clinical Trial: N Current HS Code: (b) (4) HESC: N	New Investigator: N Early Stage Investigator: N

Senior/Key Personnel:	*Organization:*	*Role Category:*
Peter Daszak	EcoHealth Alliance, Inc.	PD/PI
ZhengLi Shi	Wuhan Institute of Virology	Co-Investigator
ShuYi Zhang	East China Normal University	Co-Investigator
Changwen Ke	CDC and Prevention of Guangdong Province	Co-Investigator
Jonathan Epstein	EcoHealth Alliance	Co-Investigator
Kevin Olival	EcoHealth Alliance	Co-Investigator
Parviez Hosseini	EcoHealth Alliance	Co-Investigator
XingYi Ge	Wuhan Institute of Virology	Co-Investigator
Guanjin Zhu	Guangdong Entomological Institute	Co-Investigator
Yun-Zhi Zhang	Yunnan Center for Disease Control	Co-Investigator

Additions for Review

Accepted Publication	News of manuscripts acceptance

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_KS [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) (4)

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	POSITION TITLE
Parviez R Hosseini	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 8/5/13 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: 077090060000

* 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: 077090660000

* 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: 077090060000

* 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: 077090060000

* 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: 077690060000

* 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: 077090660000

* 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: 077690060000

* 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: 077090660000

* 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: 077090060000

* 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: 077090060000

* 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:** r Project q 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) (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 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:** r Project q 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:** r Project q 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:** r Project q 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) (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 2

*** ORGANIZATIONAL DUNS:** 5290274740000

*** Budget Type:** r Project q 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:** r Project q 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:** r Project q 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) (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 3

*** ORGANIZATIONAL DUNS:** 5290274740000

*** Budget Type:** r Project q 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:** r Project q 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:** r Project q 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:** r Project q 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:** r Project q 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:** r Project q 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:** r Project q 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:** r Project q 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 12.0 months 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:** r Project q 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) (b) (4), (b) (6)

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

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

*** ORGANIZATIONAL DUNS:** 4209454950000

*** Budget Type:** r Project q 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:** r Project q 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:** r Project q 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:** r Project q 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:** r Project q 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:** r Project q 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:** r Project q 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:** r Project q 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:** r Project q 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:** r Project q 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:** r Project q 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:** r Project q 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:** r Project q 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:** r Project q 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) 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?**

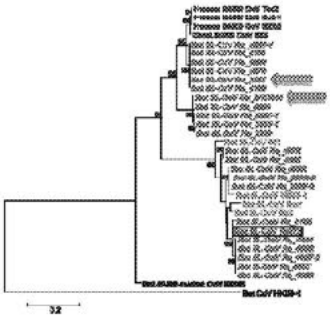


Figure 1. Phylogenetic tree of receptor binding domain sequences of SARS-CoVs (Red), bat SARS-like CoVs discovered by our group in the last 2 years (Blue), and bat SL-CoVs that we published previously in our paper proposing a bat-origin for SARS in 2005 (Green) (*3*). In 2012, we isolated two novel SL-CoVs (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*).

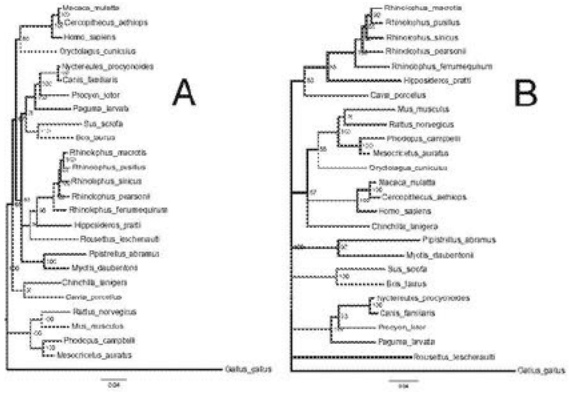


Figure 2. Mammal ACE2 phylogeny using: A) nucleotide data (~2400bp) of ACE2 gene; B) translated protein sequences of same ACE2 genes. All mammal species with available data, including primates (purple), lagomorphs (pink); carnivores (blue); ungulates (green), rodents (brown), and bats (red). Bats are 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.

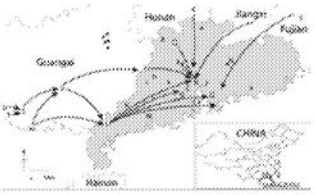


Figure 5: Proposed sampling sites in Southern China (Guangdong, Guangxi, and Fujian Provinces) for the current study. Arrows indicate wildlife trade routes. Letters indicate wild animal markets in Guangdong (A-R), Guangxi (S-W), Hunan (X) and Fujian (Y).

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**).

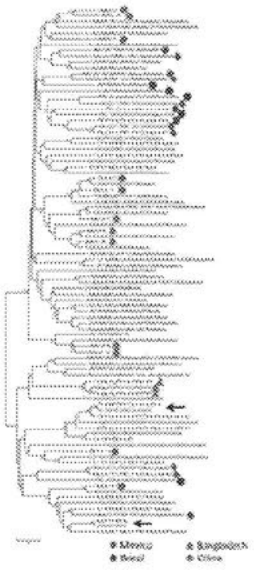
C1c) Data analysis: Human sera and stool samples will be tested at provincial CDC labs (see **letters of support**) and animal samples will be screened at the Wuhan Institute of Virology (Co-I, Shi). Serum or plasma samples will be tested for CoV antibodies using ELISAs specific for SARS-CoV and bat 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**).

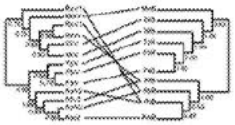


Figure 7 (left): Host-pathogen co-phylogeny of bat-CoVs from China (*43*). Bat genera: R, *Rhinolophus*; Mm *Miniopterus*; Mr, *Myotis*; P, *Pipistrellus*; V= viral sequence, B= bat sequence. This figure suggests rhinolophid CoVs may have a greater ability to jump hosts. Warrants further investigation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

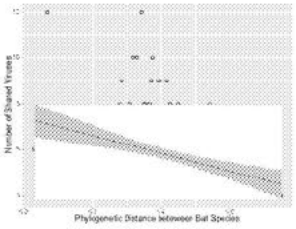


Fig 8. Scatterplot showing a decrease in the number of shared viruses with decreasing phylogenetic relatedness among bat species. Dataset includes all bat species pairs with >3 shared viruses for ~200 bat-virus associations form the literature (Olival, unpublished). Pairwise phylogenetic distance from 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) otherwise $$f_m(s_1, s_2, \ldots, s_m) = \exp\left(-R_0^{(m)}(1-s_m)\right)$$

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 $\mathbf{R}_0 = \boldsymbol{\chi\phi\tau}$, where $\boldsymbol{\tau}$ is the duration of infectiousness, and $\boldsymbol{\chi}$ is the rate of contact. Our receptor binding studies and predictive GLM models of host range will be used to inform $\boldsymbol{\phi}$, 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, $\mathbf{R}_0 = \boldsymbol{\chi\phi\tau}$, 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' $\boldsymbol{\Omega}_k$ 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 $\mathbf{R}_0 = \boldsymbol{\chi\phi\tau}$ 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.

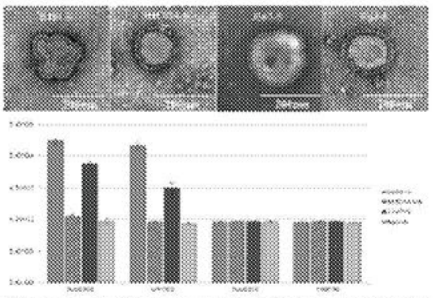


Figure 9: Top panel: HIV pseudovirus carrying spike proteins from human SARS-CoV (BJ01-S) and bat SARS-like CoV (SHC014-S, 3367-S and Rp-S). Bottom panel: Infectivity assay with the above pseudoviruses in HeLa cell lines expressing ACE2 from human, civet and bat.

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.

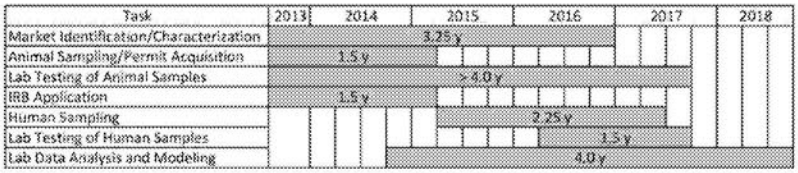
C3c) *In vitro* studies: We will isolate bat-CoVs using Vero E6 cell (susceptible SARS-CoV and MERS-CoV) and primary or transformed bat cell lines that we have developed from *Myotis davidii, Rhinolophus sinicus, Myotis chinensis, Rousettus leschenaultia* and other bats of China (*124, 125*). CoV PCR-positive 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, there 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.

上海市疾病预防控制中心
Shanghai Municipal Center for Disease Control and Prevention
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电话(Tel)：+86-21-62758710 传真(Fax)：+86-21-62756323 网址(Website)：http://www.scdc.sh.cn

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

Address: Xiaohongshan 44, Wuchang, Wuhan 430071, Hubei, P. R. China
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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. Jinren 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.

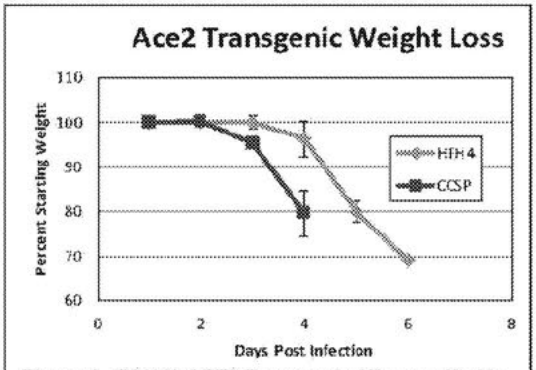

Figure 1. FOXJ1 ACE2 Transgenic Mice are Highly Susceptible to wildtype SARS-CoV Infection. Two different lines were infected with wildtype SARS-virus and clinical disease evaluated at different times postinfection.

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

地址：广州市番禺区大石街前锋路160号 邮编：511430
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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

A. COVER PAGE

Project Title: Understanding the Risk of Bat Coronavirus Emergence	
Grant Number: 5R01AI110964-04	**Project/Grant Period:** 06/01/2014 - 05/31/2019
Reporting Period: 06/01/2016 - 05/31/2017	**Requested Budget Period:** 06/01/2017 - 05/31/2018
Report Term Frequency: Annual	**Date Submitted:** 04/12/2017
Program Director/Principal Investigator Information: PETER DASZAK , BS PHD **Phone number:** (b) (6) **Email:** (b) (6)	**Recipient Organization:** ECOHEALTH ALLIANCE, INC. ECOHEALTH ALLIANCE, INC. 460 W 34TH ST 17TH FLOOR NEW YORK, NY 100012320 **DUNS:** 077090066 **EIN:** 1311726494A1 **RECIPIENT ID:**
Change of Contact PD/PI: N/A	
Administrative Official: ALEKSEI CHMURA 460 W 34th St., 17th Floor New York, NY 10001 **Phone number:** (b) (6) **Email:** (b) (6)	**Signing Official:** ALEKSEI CHMURA 460 W 34th St., 17th Floor New York, NY 10001 **Phone number:** (b) (6) **Email:** (b) (6)
Human Subjects: Yes HS Exempt: No Exemption Number: Phase III Clinical Trial:	**Vertebrate Animals:** Yes
hESC: No	**Inventions/Patents:** No

B. ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

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.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

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B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

1.Conference and University Lectures: PI Daszak, and Co-investigators Shi, Epstein, Olival, and Zhang gave invited University and Conference lectures including Avoiding Catastrophe Meeting at Concordia Univ., Harvard Univ. Columbia Univ., National Academy of Sciences, World Humanitarian Summit in Turkey, NEIDL Symposium in Boston, Global Pandemic Policy Summit at Texas A&M Univ., One Health EcoHealth Congress in Australia, WHO briefing, Rockefeller Planetary Health meeting, 17th International Bats Conference, China National Global Virome Project Initiative Meeting, and others that included specific discussion of the current project and results.

2.Agency and other briefings: PI Daszak and Co-investigator Shi introduced this project to potential collaborators within Rockefeller Foundation, WHO, FAO, International Collaboration Bureau of Chinese Academy of Sciences, Beijing Genomic Institute, National Natural Science Foundation of China, Institute of Pathogen Biology, Chinese Academy of Medical Science & Peking Union Medical College, and Chinese CDC.

3.Public outreach: PI Daszak and Co-investigator Shi presented this work to members of NSF, NIH, U.S. CDC, the State of Forestry Administration of China, and the general public at the China National Virome Project Initiative Meeting hosted by Chinese CDC and Chinese Academy of Sciences (2017); Co-investigator Olival presented this work at the NYC Medtech Forum to the public (2016); Research Technician Dr. Guangjian Zhu presented this work at the China Conservation Expo to the conservation groups in China (2016). Co-Investigator Y-Z Zhang presented this project to the provincial infectious disease hospital Kunming No.3 People's Hospital in Yunnan province (2016).

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

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

•To commence the analysis of data collected from the integrated biological behavioral surveillance questionnaires from Yunnan, Guangxi, and Guangdong provinces, linking to the viral and serological testing results of biological samples.

•Following the successful pilot of wildlife trade network research in Lipu, Guilin, Guangxi province in Year 3, we will continue the Wild Animal Farms Survey in Guangxi, and expand to Yunnan and Guangdong in Year 4, with Institutional Review Board approvals from both Yunnan Institute of Endemic Diseases Control and Prevention and Hummingbird #2016-55, to:

−Generate a network model of wildlife trade
−Model trade flows in the wildlife farmer networks to identify locations of high potential for viral recombination
−Update survey instrument for "second wave" network interviews

•We will continue the passive hospital surveillance with anonymized, surveillance data collection from acutely ill hospital in-patients who 1) satisfy syndromic eligibility criteria; 2) have complete medical records; 3) non-normative laboratory confirmed diagnostic results; and suspected acute viral infection.

Research has been successfully piloted in four hospitals in Yunnan province: 1) Dali College Affiliated Hospital; 2) Dali Prefecture Hospital; 3) Kunming No. 3 People's Hospital, and 4) Chuxiong Prefecture Hospital, 120 biological samples have been collected, with approval from the Institutional Review Boards of the School of Public Health of Wuhan University and Hummingbird IRB

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

•The genomic characterization of SL-CoVs in Year 3 was focused on Rhinolophus sinicus in Yunnan, our plan for Year 4 is to obtain complete S gene, RdRp gene or full-length genome sequences of more SL-CoVs from a broader range of bat species identified all over China and conduct a more comprehensive evolution study on SL-CoVs in bats.

•To search for the receptor of SL-CoV with deletions in the homologous region of SARS-CoV RBD (i.e. Rp3, Rs672), and SL-CoVs which has been demonstrated to be unable to utilize bat ACE2 (i.e. Rs4231) whose receptors may be some molecules other than ACE2.

•To conduct population genetics study of Rhinolophus sinicus ACE2s, which includes: the amplification of ACE2 genes from Rhinolophus sinicus samples of different origin, test of the usage efficiency of Rhinolophus sinicus ACE2s of different origins by SL-CoVs and kinetics study on the binding of SL-CoV RBD to different Rhinolophus sinicus ACE2s.

•Phylogeographic study of bat-CoV to better understand the geographic distribution and evolution of bat-CoV genetic diversity in south China.

•Phylogeographic study of bat host (Rhinolophus) species to assess the connectivity of bat populations and infer their historical movements and demographic history to improve our understanding of CoV transmission among bat populations in southern China.

•Cophylogenetic analyses of bat host and CoV phylogenies to assess frequency of cross-species transmission. Comparison of Alpha- and Beta-CoV cophylogenetic patterns building on Year 3 analyses using published sequences.

Specific Aim 3: Testing predictions of CoV inter-species transmission.

•Using the reverse genetic method, we will construct chimeric viruses with the backbone of MERS-CoV and the S genes from diverse newly identified bat MERS-related coronaviruses, and examine the pathogenicity of bat MERS-related coronaviruses on cell and animal levels.

•The animal infection experiments are planned to be conducted in following years to study the pathogenicity of diverse SL-CoVs and MERS-related CoV that we identified in Chinese bats.

•Surveillance of infection in human populations by bat-borne CoVs in Guangxi and Guangdong provinces in previously identified areas with human populations of high risk of exposure to bats. PCR and ELISA will be used, respectively, for detection of viral nucleic acids and antibodies against the viral nucleocapsid protein or spike protein.