



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: [REDACTED] (b) (6)

Period Of Performance:
Budget Period: 07/24/2019 – 06/30/2021
Project Period: 06/01/2014 – 06/30/2025

Dear Business Official:

The National Institutes of Health hereby revises this award to reflect an increase in the amount of \$369,819 (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,

Emily Linde
Grants Management Officer
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Additional information follows

- 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) R01A1110964. 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 Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

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: Pursuant to the letter to EcoHealth Alliance, Inc. dated July 8, 2020, this award has been reinstated; however, all activities are suspended until such time as these concerns in the letter have been addressed to NIH's satisfaction.

Supersedes previous Notice of Award dated 04/27/2020. All other terms and conditions still apply to this award.

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/bmb15/bmb15toc.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.

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: Shaun W Gratton
Email: (b) (6) **Phone:** (b) (6)

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	\$170,325	\$170,123	\$170,123	\$170,123	\$170,123
Fringe Benefits	\$53,654	\$53,590	\$53,590	\$53,590	\$53,590
Personnel Costs (Subtotal)	\$223,979	\$223,713	\$223,713	\$223,713	\$223,713
Consultant Services	\$49,809	\$49,750	\$49,750	\$49,750	\$49,750
Materials & Supplies	\$20,170	\$14,850	\$14,850	\$14,850	\$14,850
Travel	\$15,045	\$15,027	\$15,027	\$15,027	\$15,027
Subawards/Consortium/Contractual Costs	\$229,923	\$229,651	\$229,651	\$229,651	\$229,651
Publication Costs		\$6,000	\$6,000	\$6,000	\$6,000
TOTAL FEDERAL DC	\$538,926	\$538,991	\$538,991	\$538,991	\$538,991
TOTAL FEDERAL F&A	\$123,054	\$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	\$384,547	\$309,340	\$309,340	\$309,340	\$309,340
F&A Costs 1	\$123,054	\$98,989	\$98,989	\$98,989	\$98,989

PI: DASZAK, PETER	Title: Understanding the Risk of Bat Coronavirus Emergence	
Received: 11/05/2018	FOA: PA18-484 Clinical Trial: Not Allowed	Council: 05/2019
Competition ID: FORMS-E	FOA Title: NIH Research Project Grant (Parent R01 Clinical Trial Not Allowed)	
2 R01 AI110964-06	Dual:	Accession Number: 4237214
IPF: 4415701	Organization: ECOHEALTH ALLIANCE, INC.	
Former Number:	Department:	
IRG/SRG: CRFS	AIDS: N	Expedited: N
<u>Subtotal Direct Costs</u> (excludes consortium F&A) Year 6: 515,358 Year 7: 515,358 Year 8: 515,358 Year 9: 515,358 Year 10: 515,358	Animals: Y Humans: Y Clinical Trial: N Current HS Code: (b) (4) HESC: N	New Investigator: N Early Stage Investigator: N
<i>Senior/Key Personnel:</i>		
	<i>Organization:</i>	<i>Role Category:</i>
PETER DASZAK	ECOHEALTH ALLIANCE, INC.	PD/PI
Zheng Li Shi	Wuhan Institute of Virology	Co-Investigator
Kevin Olival	EcoHealth Alliance	Co-Investigator
Ralph Baric	University of North Carolina	Co-Investigator
Noam Ross	EcoHealth Alliance	Co-Investigator
Alice Latinne	EcoHealth Alliance	Other (Specify)-Research Scientist
HongYing Li	EcoHealth Alliance	Other (Specify)-Research Scientist
Leilani Francisco	EcoHealth Alliance	Co-Investigator
Amy Sims	University of North Carolina at Chapel Hill	Co-Investigator
Emily Hagan	EcoHealth Alliance	Other (Specify)-Research Scientist
Guangjian Zhu	East China Normal University	Co-Investigator
Linfa Wang	Duke-NUS Medical School	Co-Investigator
Lili Ren	Institute of Pathogen Biology	Co-Investigator
Li Guo	Institute of Pathogen Biology	Co-Investigator
Peng Zhou	Wuhan Institute of Virology	Co-Investigator
Ben Hu	Wuhan Institute of Virology	Co-Investigator
Aleksei Chmura	EcoHealth Alliance	Other (Specify)-Research Scientist

APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

		3. DATE RECEIVED BY STATE	State Application Identifier
1. TYPE OF SUBMISSION*		4.a. Federal Identifier AI110964	
<input type="radio"/> Pre-application <input checked="" type="radio"/> Application <input type="radio"/> Changed/Corrected Application		b. Agency Routing Number	
2. DATE SUBMITTED	Application Identifier	c. Previous Grants.gov Tracking Number	
5. APPLICANT INFORMATION		Organizational DUNS*: 0770900660000	
Legal Name*: ECOHEALTH ALLIANCE, INC. Department: Division: Street1*: ECOHEALTH ALLIANCE, INC. Street2: 460 W 34TH ST City*: NEW YORK County: State*: NY: New York Province: Country*: USA: UNITED STATES ZIP / Postal Code*: 100012320			
Person to be contacted on matters involving this application Prefix: Dr. First Name*: Peter Middle Name: Last Name*: Daszak Suffix: Position/Title: PD/PI Street1*: 460 West 34th Street Street2: Suite 1701 City*: New York County: State*: NY: New York Province: Country*: USA: UNITED STATES ZIP / Postal Code*: 100012320 Phone Number*: (b) (6) Fax Number: 2123804465 Email: (b) (6)			
6. EMPLOYER IDENTIFICATION NUMBER (EIN) or (TIN)*		311726494	
7. TYPE OF APPLICANT*		M: Nonprofit with 501C3 IRS Status (Other than Institution of Higher Education)	
Other (Specify): <input checked="" type="radio"/> Small Business Organization Type <input type="radio"/> Women Owned <input type="radio"/> Socially and Economically Disadvantaged			
8. TYPE OF APPLICATION*		If Revision, mark appropriate box(es).	
<input type="radio"/> New <input type="radio"/> Resubmission <input checked="" type="radio"/> Renewal <input type="radio"/> Continuation <input type="radio"/> Revision		<input type="radio"/> A. Increase Award <input type="radio"/> B. Decrease Award <input type="radio"/> C. Increase Duration <input type="radio"/> D. Decrease Duration <input type="radio"/> E. Other (specify) :	
Is this application being submitted to other agencies?* <input type="radio"/> Yes <input checked="" type="radio"/> 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		13. CONGRESSIONAL DISTRICTS OF APPLICANT	
Start Date* Ending Date* 06/01/2019 05/31/2024		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: Suite 1701

City*: New York

County:

State*: NY: New York

Province:

Country*: USA: UNITED STATES

ZIP / Postal Code*: 100012317

Phone Number*: (b) (6) Fax Number: +12123804465 Email*: (b) (6)

15. ESTIMATED PROJECT FUNDING

a. Total Federal Funds Requested* \$3,586,760.00

b. Total Non-Federal Funds* \$0.00

c. Total Federal & Non-Federal Funds* \$3,586,760.00

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 penalties. (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. SFLL or OTHER EXPLANATORY DOCUMENTATION

File Name:

19. AUTHORIZED REPRESENTATIVE

Prefix: Dr. First Name*: Aleksei Middle Name: Last Name*: Chmura Suffix:

Position/Title*: Authorized Organizational Representative

Organization Name*: EcoHealth Alliance, Inc.

Department:

Division:

Street1*: 460 West 34th Street

Street2: Suite 1701

City*: New York

County:

State*: NY: New York

Province:

Country*: USA: UNITED STATES

ZIP / Postal Code*: 100012320

Phone Number*: (b) (6) Fax Number: 2123804465 Email*: (b) (6)

Signature of Authorized Representative*

Aleksei Chmura

Date Signed*

11/05/2018

20. PRE-APPLICATION File Name:**21. COVER LETTER ATTACHMENT** File Name: NIAID_COV_2018_Cover_Letter_Final.pdf

**424 R&R and PHS-398 Specific
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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*: ECOHEALTH ALLIANCE, INC.
 Street2: 460 W 34TH ST
 City*: NEW YORK
 County:
 State*: NY: New York
 Province:
 Country*: USA: UNITED STATES
 Zip / Postal Code*: 100012320
 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: University of North Carolina at Chapel Hill
 DUNS Number: 6081952770000
 Street1*: McGavran-Greenberg Hall
 Street2: Campus Box 7435
 City*: Chapel Hill
 County:
 State*: NC: North Carolina
 Province:
 Country*: USA: UNITED STATES
 Zip / Postal Code*: 275997435
 Project/Performance Site Congressional District*: NC-004

Project/Performance Site Location 2

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:
Country*: CHN: CHINA
Zip / Postal Code*: 430071
Project/Performance Site Congressional District*: 00-000

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: Institute of Pathogen Biology
DUNS Number: 5281563570000
Street1*: Dong Dan San Tiao, No. 9
Street2: Dongcheng District
City*: Beijing
County:
State*:
Province:
Country*: CHN: CHINA
Zip / Postal Code*: 100730
Project/Performance Site Congressional District*: 00-000

Additional Location(s) File Name:

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
1.a. If YES to Human Subjects	
Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input checked="" type="radio"/> No	
If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6 _ 7 _ 8	
If NO, is the IRB review Pending? <input checked="" type="radio"/> Yes <input type="radio"/> No	
IRB Approval Date: 03-15-2019	
Human Subject Assurance Number None	
2. Are Vertebrate Animals Used?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
2.a. If YES to Vertebrate Animals	
Is the IACUC review Pending? <input checked="" type="radio"/> Yes <input type="radio"/> No	
IACUC Approval Date: 03-15-2019	
Animal Welfare Assurance Number None	
3. Is proprietary/privileged information included in the application?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> 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? <input type="radio"/> Yes <input type="radio"/> No	
4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
6.a. If yes, identify countries: China	
6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename NIAID_COV_2019_PROJECT_SUMMARY_final.pdf
8. Project Narrative*	NIAID_COV_2019_NARRATIVE_Final.pdf
9. Bibliography & References Cited	NIAID_COV_2019_REFERENCES.pdf
10. Facilities & Other Resources	NIAID_COV_2019_FACILITIES_v01_PD.pdf
11. Equipment	NIAID_COV_2019_EQUIPMENT_v01.pdf

Project Summary: 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.

Renewal: Understanding the Risk of Bat Coronavirus Emergence

Project Narrative

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.

Facilities, Equipment, and Other Resources

EcoHealth Alliance, New York, USA (Drs. Daszak, Olival, Francisco, Ross)

EcoHealth Alliance is a New York-based 501(c) 3 non-profit institution that conducts scientific research on emerging zoonoses and global health capacity building. EcoHealth Alliance New York headquarters has (b) (4) square feet of office space including a meeting room and basic laboratory – freezer storage and light microscopy. The scientific staff (34 core scientists, 100+ field staff) is supported by a core admin staff of 18 who are available for work on this project and funded through private donor and federal support. EcoHealth Alliance does not support diagnostic facilities at its core headquarters and works in partnership with a network of leading diagnostic labs both in the USA and around the world.

EcoHealth Alliance is equipped with fiber optic Internet access and video conferencing facilities to facilitate easy communication between collaborators. EcoHealth Alliance employees have around-the-clock access to servers, VPNs, encryption software, IT support, and all necessary software including Git and Github (Hosted software revision/audit service), Sublime and Vim text editors, Vagrant and Oracle Virtualbox virtual machines, Google Apps (Hosted email and collaboration web based software), Ansible (Server provisioning software framework), Python, NodeJS, and R programming languages, Meteor (Javascript framework), Bash shell scripts, Jenkins (Continuous Integration server), Microsoft Office and Adobe CS6 running on both Apple Mac OS X, Ubuntu linux, and Windows Operating Systems. EcoHealth Alliance has a dedicated quad-core Linux server and another dedicated dual quad-core Mac Pro Server - each with 4TB hard drives. Either server individually or in combination may be used for intensive computational modeling and/or database processing by all the grantees. Access to the cloud and supercomputing services (Amazon) is provided by core funding to EcoHealth Alliance.

EcoHealth Alliance is the headquarters of a global network of over 70 partners that provides exceptional leverage for the core scientists. This network includes staff from: academic institutions at leading national universities; intergovernmental agencies (WHO, OIE, FAO, DIVERSITAS, IUCN); infectious disease surveillance laboratories including BSL-3 and -4 laboratories; national government agency offices and labs; locally-based wildlife conservation organizations in Asia, Africa and Latin America. EcoHealth Alliance is the headquarters of: The Consortium for Conservation Medicine (CCM); the journal *EcoHealth*; an NSF Research Coordination Network (EcoHealthNET); the IUCN Wildlife Health Specialist Group; and the OIE Wildlife Health Network. EcoHealth Alliance is a voting member of the IUCN and a partner in Columbia University's Earth Institute Center for Environmental Sustainability (EICES) and all senior scientific staff members are Adjunct Faculty at Columbia University's Department of Ecology, Evolution, and Environmental Biology or at the Mailman School of Public Health.

Institute of Pathogen Biology, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China (Drs. Ren, Guo)

The Institute of Pathogen Biology (IPB) is a key (flagship) institute within the Chinese Academy of Medical Sciences & Peking Union Medical College. IPB's mission is to conduct high quality research in basic and applied biology of critically important human pathogens. The ultimate goal is to conduct research and develop technology for better diagnosis, treatment, and prevention of infectious diseases. IPB specializes in multi-disciplinary approaches to pathogen research and technological development focused on improving China's capability to diagnose, treat and prevent infectious diseases.

Human Resources. The department involved in this project consists of 30 staff members: 10 with a clinical medicine background, 12 biological research scientists, 3 bioinformaticists, 3 animal technicians, and 2 biochemists working on protein expression and purification.

Lab Facilities. The IPB includes the Ministry of Health Key Laboratory of Systems Biology of Pathogens, Christophe Merieux Laboratory, the AIDS Research Center, laboratories focused on Bacteriology, Virology, Mycology, Parasitology, and the Epidemiological Information Analysis Department. The institute has established platforms in metagenomics, transcriptome, morphology, molecular biology, and immunology. All of these are funded centrally and available to conduct the research proposed in the current R01.

BSL2 Facility. The institute has three laboratories of (b) (4) equipped as BSL2 space for virology, immunology and clinical sample preparation. Equipment includes an Illumina Hiseq 2500, Miseq and BGI 500, gel electrophoresis, power supplies, thermal cyclers, a programmable heat block, heat blocks, water baths, CO₂ incubators (2), several -70°C freezers, one -140°C freezer, refrigerators, DNA documentation system, DNA sequencing and computer assisted sequence analysis programs, several microfuges, Nikon and Zeiss microscopes with photographic and fluorescent capabilities, several class 2 environmental hoods, refrigerated water baths, real time thermocyclers, and spectrophotometers. The laboratory has an ELISA plate reader, an illuminometer, ELISA plate washer, spectrophotometers, and other equipment that is routinely used in characterizing antibody-protein interactions.

BSL 3 Facility. The institute shares an additional (b) (4) of BSL3 facilities equipped with sterile hoods (BSCIIA), CO₂ incubators, -70C freezer, an inverted Nikon fluorescent microscope, and equipment for virus isolation and culture, and molecular genetics research.

University of North Carolina at Chapel Hill, USA (Baric and Sims)

The Department of Epidemiology is an internationally recognized leader in epidemiologic research and training. The department offers research training in most specialized areas including cancer, cardiovascular diseases, environmental and occupational health, health services/clinical epidemiology, reproductive health and infectious diseases. The department's current faculty consists of 51 regular full-time faculty and 151 adjunct faculty members. The department has 218 graduate students enrolled, including 20 in the MPH program, 5 in the MSPH program, 20 in the MSCR program and 173 in the Ph.D. program. The Department of Epidemiology is headquartered in the four-story McGavran-Greenberg Building. The epidemiology administrative and office space occupies (b) (4) square feet and provides additional classroom space. Most of the department's research staff occupies a research annex consisting of approximately (b) (4) square feet of contiguous rental space in a commercial office building.

Dr. Baric has three laboratories of (b) (4) square feet each equipped as BL2 space for molecular biology, virology, immunology and recombinant DNA techniques, as laid out in the current R01 proposal. Equipment is available for gel electrophoresis, PCR, and BSL2 sample storage and handling facilities. It includes a DNA documentation system, DNA sequencing and computer assisted sequence analysis programs, several microfuges, a microscopy suite, 10+ IBM and Apple Pentium II/III computers with accompanying software, three thermocyclers, a fume hood, Nuclisens reader, hybridization oven, real time thermocyclers, three fluorescent inverted scopes with computer software (Olympus IX51), and a spectrophotometer. A Roche Light Cycler 480II is available for real time measurements. The laboratory has an ELISA plate reader, an illuminometer, 200 cages for animal maintenance and breeding in Seal-Safe housing, Bio Rad low pressure chromatography system, ELISA plate washer, spectrophotometers, and other equipment that is routinely used in characterizing antibody-protein interactions.

The Baric laboratory contains an additional (b) (4) square feet of newly renovated BSL3 facilities with enhanced features including shower in/shower out facility; dual anteroom access; Hepa filtered exhaust; redundant exhaust fans; card key access; an alarm system to Public Health/Campus Police; laboratory controlled combination lock; and Techniplast Sealsafe™ Hepa filtered animal housing for 300+ rodents. PAPR and tyvek suits are worn at all times in the BSL3 facility. The BL3 facilities are in an adjacent and attached building (b) (4) or in (b) (4), the latter space is directly adjacent to Dr. Baric's BSL2 laboratory resources. Each facility is equipped with sterile hoods (BSCIIA), four CO₂ incubators, gel electrophoresis equipment, thermal cyclers and power supplies, and related equipment necessary for virus cultivation and molecular genetic research. The facilities each house a -70°C freezer, an inverted Nikon fluorescent microscope with a digital camera, an ELISA plate reader and illuminometer. Both facilities contain rodent-sized Seal-Safe systems (~192 cages) for maintaining animals in a Hepa-filtered Air in/out environment, exhausted into the BSL3 Hepa-filtered exhaust system. An 8 chamber Buxco plethysmography system that allows for repetitive, noninvasive measures of the number of breaths, tidal volume, airway responsiveness, enhanced pause, and respiratory gases from live control and infected mice in a contained system is housed in the main BSL3 laboratory in (b) (4).

The Department of Epidemiology provides cold-room, autoclave, centralized dishwashing and a darkroom with an automated developer. The campus has central facilities for DNA oligonucleotide synthesis, histopathology, DNA sequencing, EM, light and confocal microscopy, automated PCR genotyping and Taqman facilities, and Fluorescent activated cell sorter facilities (FAC). As a member of the Department of Microbiology and Immunology and UNC Cancer center, Dr. Baric and his team have access to these facilities at a discounted cost. The University provides a variety of core services including: sequencing and deep sequencing cores, genomics cores, oligonucleotide synthesis cores, hybridoma cores, transgenic cores, structural biology cores, etc. typical of any world class research institution. Campus wide core facilities are available for oligonucleotide synthesis, Sanger and 454 sequencing, RNAseq, pathology and histology services, and Flow Cytometry. Approximately, 40,000 cages are available for CC RIX production in the (b) (4) on UNC Campus.

Wuhan Institute of Virology, Chinese Academy of Sciences, Hubei, China (Shi, Zhou, and Hu)

The Wuhan Institute of Virology (WIV), Chinese Academy of Sciences (CAS) is the only institute specializing in virology, viral pathology and virus technology among 19 other biological and biomedical research institutes in CAS. WIV is China's premier institute for virologic research. It consists of three research departments and one center: the Departments of Molecular Virology, of Bio-control, of Analytical Biochemistry and Biotechnology, and the Virus Resource and Bioinformation Center. It contains the Key Laboratory of Molecular Virology of CAS, the Joint-laboratory of Invertebrate Virology, an HIV Pre-screening Lab and the Hubei Engineering and Technology Research Center for Viral Diseases. The institute is further divided into 14 research groups, one of which (the Emerging Virus Laboratory) is headed by Dr. Zhengli Shi. The supporting system of the institute consists of an analytical equipment center, an experimental animal center, the editorial office of *Virologica Sinica* and a 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 Wuhan Institute of Virology is a World Health Organization collaborating center. It also has partnerships, research collaborations and contracts with universities and research institutes in more than 30 counties and regions including a long-time (>15 years) partnership with EcoHealth Alliance. There are 14 professors, 36 associated professors, and 47 assistant professors conducting research on virology and five of these have been awarded honors in the "Hundred Talents Project". In 2013, the first BSL-4 lab in China was opened at this Institute in a bespoke facility which was designed with the assistance of the US CDC and L'Institut Pasteur of France.

The WIV Emerging Virus Laboratory, headed by Dr. Shi, was set up to carry out exactly the sort of experimental activities on emerging viruses listed in the current R01 proposal. This lab possesses all necessary facilities for molecular biology and virology including a bank of -80°C freezers, PCR machines, gel electrophoresis and imaging systems, biosafety cabinets, super-clean benches, and cell culture rooms. A Core Facility Center was established at WIV to provide technological services to faculty, students, and visiting researchers. Core Facility Center equipment includes: a transmission electron microscope, ultracentrifugation machines, small animal *in vivo* imaging systems, confocal laser scanning microscopes, flow cytometry, a real-time qPCR system, and a high-throughput sequencing and analyzing system. In addition, WIV owns a complete biosafety research platform, which consists of the first national BSL-4 laboratory in China, and a cluster of BSL-3 and BSL-2 labs.

Equipment

EcoHealth Alliance (Daszak, Francisco, Olival, Ross)

EcoHealth Alliance is equipped with fiber optic Internet access and video conferencing facilities to facilitate easy communication between collaborators. EcoHealth Alliance employees have around the clock access to servers, VPNs, encryption software, IT support, and all necessary software including Git and Github (Hosted software revision/audit service), Sublime and Vim text editors, Vagrant and Oracle Virtualbox virtual machines, Google Apps (Hosted email and collaboration web based software), Ansible (Server provisioning software framework), Python, NodeJS, and R programming languages, Meteor (Javascript framework), Bash shell scripts, Jenkins (Continuous Integration server), Microsoft Office and Adobe CS6 running on both Apple Mac OS X, Ubuntu linux, and Windows Operating Systems. Additionally, EcoHealth Alliance has a dedicated quad-core Linux server and another dedicated dual quad-core Mac Pro Server - each with 4TB hard drives. Either server individually or in combination may be used for intensive computational modeling and/or database processing by all the grantees. Access to the cloud and supercomputing services (Amazon) is provided by core funding to EcoHealth Alliance.

Institute of Pathogen Biology (Ren, Guo)

The Institute of Pathogen Biology laboratories have equipment required for general microbiological, molecular, and biochemical work including microcentrifuges, agarose and polyacrylamide electrophoresis equipment, spectrophotometer, rocking and shaking platforms, bead-beater cell disruptor, and incubators (shaking and static). Major equipment relevant to this proposal which are available include:

BSL2 Facility. The institute has three laboratories of (b) (4) equipped as BSL2 space for the virology, immunology and clinical samples pretreatment. Equipment includes Illumina Hiseq 2500, Miseq and BGI 500, gel electrophoresis equipment, power supplies, thermal cyclers, a programmable heat block, heat blocks, water baths, CO₂ incubators (2), several -70°C freezers, one -140°C freezer, refrigerators, DNA documentation system, DNA sequencing and computer assisted sequence analysis programs, several microfuges, Nikon and Zeiss microscopes with photographic and fluorescent capabilities, several class 2 environmental hoods, refrigerated water baths, real time thermocyclers, and spectrophotometer. The laboratory has an ELISA plate reader, an illuminometer, ELISA plate washer, spectrophotometers, and other equipment that is routinely used in characterizing antibody-protein interactions.

BSL 3 Facility. The institute shares an additional (b) (4) of BSL3 facilities equipped with sterile hoods (BSCIIA), CO₂ incubators, -70°C freezer, an inverted Nikon fluorescent microscope with an assortment of filters, magnifications and digital camera, and related equipment necessary for virus cultivation and molecular genetic research.

Wuhan Institute of Virology (Shi, Zhou, Hu)

Institute of Virology's Emerging Virus Laboratory has equipment required for general microbiological, molecular, and biochemical work including microcentrifuges, agarose and polyacrylamide electrophoresis equipment, spectrophotometer, rocking and shaking platforms, bead-beater cell disruptor, and incubators (shaking and static). Major equipment relevant to this proposal which are available include: -80°C freezers, PCR machines, gel electrophoresis and imaging system, biosafety cabinets, super-clean benches, and cell culture rooms.

A Core Facility Center was established at Wuhan Institute of Virology to provide technological services to faculty, students, and visiting researchers. The equipment installed in the Core Facility Center include: transmission electron microscope, ultracentrifugation machines, small animal *in vivo* imaging systems, confocal laser scanning microscopes, flow cytometry, a real-time qPCR system, and a high-throughput sequencing and analyzing system.

In addition, the Wuhan Institute of Virology owns a complete biosafety research platform, which consists of the first national BSL-4 laboratory in China, and a cluster of BSL-3 and BSL-2 labs. These labs contain gel electrophoresis equipment, power supplies, thermal cyclers, programmable heat blocks, heat blocks, water

baths, CO₂ incubators, -70°C freezers, -140°C freezers, refrigerators, DNA documentation system, DNA sequencing and computer assisted sequence analysis programs, microfuges, Nikon and Zeiss microscopes with photographic and fluorescent capabilities, several class 2 environmental hoods, refrigerated water baths, real time thermocyclers, and spectrophotometers. The laboratory also has an ELISA plate reader, an illuminometer, ELISA plate washer, spectrophotometers, and other equipment that is routinely used in characterizing antibody-protein interactions.

University of North Carolina at Chapel Hill Baric Laboratory (Baric, Sims)

The three laboratories of the Baric Lab in the Department of Epidemiology have equipment required for general microbiological, molecular, and biochemical work including microcentrifuges, agarose and polyacrylamide electrophoresis equipment, spectrophotometer, rocking and shaking platforms, bead-beater cell disruptor, and incubators (shaking and static). Major equipment relevant to this proposal which are available include: gel electrophoresis equipment, power supplies, thermal cyclers, a programmable heat block, heat blocks, water baths, CO₂ incubators (2), several -70°C freezers, one -140°C freezer, refrigerators, DNA documentation system, DNA sequencing and computer assisted sequence analysis programs, several microfuges, two Nikon microscopes with photographic and fluorescent capabilities, several class 2 environmental hoods, refrigerated water baths, 10+ IBM and Apple Pentium II/III computers with accompanying software, three thermocyclers, a fume hood, Nuclisens reader, hybridization oven, real time thermocyclers, three fluorescent inverted scopes with computer software (Olympus IX51), and a spectrophotometer. A Roche Light Cycler 480II is available for real time measurements. The laboratory has an ELISA plate reader, an illuminometer, 200 cages for animal maintenance and breeding in Seal-Safe housing, Bio Rad low pressure chromatography system, ELISA plate washer, spectrophotometers, and other equipment that is routinely used in characterizing antibody-protein interactions.

BSL3 Facility features include: shower in/shower out facility; dual anteroom access; Hepa filtered exhaust; redundant exhaust fans; card key access; an alarm system to Public Health/Campus Police; laboratory controlled combination lock; and Techniplast Sealsafe™ Hepa filtered animal housing for 300+ rodents. PAPR and tyvek suits are worn at all times in the BSL3 facility. The BL3 facilities are in an adjacent and attached building (b) (4) or in (b) (4); the latter space is directly adjacent to Dr. Baric's BSL2 laboratory resources. Each facility is equipped with sterile hoods (BSCIIA), four CO₂ incubators, gel electrophoresis equipment, thermal cyclers and power supplies, and related equipment necessary for virus cultivation and molecular genetic research. The facilities each house a -70°C freezer, an inverted Nikon fluorescent microscope with an assortment of filters, magnifications and digital camera, an ELISA plate reader and illuminometer. Both facilities contain rodent-sized Seal-Safe systems (~192 cages) for maintaining animals in a Hepa-filtered Air in/out environment, exhausted into the BSL3 Hepa-filtered exhaust system. An 8 chamber Buxco plethysmography system that allows for repetitive, noninvasive measures of the number of breaths, tidal volume, airway responsiveness, enhanced pause, and respiratory gases from live control and infected mice in a contained system is housed in the main BSL3 laboratory in

(b) (4)

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator				
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Degree Type:	PHD	Degree Year: 2000		
Attach Biographical Sketch*:	File Name:	SHI_Zhengli_Biosketch_Final.pdf		
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PROFILE - Senior/Key Person				
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Project Role*:	Co-Investigator	Other Project Role Category:		
Degree Type:	PHD	Degree Year: 2008		
Attach Biographical Sketch*:	File Name:	OLIVAL_Kevin_Biosketch_Final.pdf		
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PROFILE - Senior/Key Person				
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E-Mail*:	(b) (6)			
Credential, e.g., agency login:	(b) (6)			
Project Role*:	Other (Specify)	Other Project Role Category:	Research Scientist	
Degree Type:	MPH	Degree Year:	2013	
Attach Biographical Sketch*:	File Name:	HAGAN_Emily_Biosketch_Final.pdf		
Attach Current & Pending Support:	File Name:			

PROFILE - Senior/Key Person				
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E-Mail*:	(b) (6)			
Credential, e.g., agency login:	(b) (6)			
Project Role*:	Co-Investigator	Other Project Role Category:		
Degree Type:	PHD	Degree Year:	2012	
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Province:				
Country*:	SGP: SINGAPORE			
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E-Mail*:	(b) (6)			
Credential, e.g., agency login:	(b) (6)			
Project Role*:	Co-Investigator	Other Project Role Category:		
Degree Type:	PHD	Degree Year: 1986		
Attach Biographical Sketch*:	File Name:	WANG_Linfa_Final.pdf		
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PROFILE - Senior/Key Person				
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State*:				
Province:				
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Phone Number*:	(b) (6)	Fax Number:		
E-Mail*:	(b) (6)			
Credential, e.g., agency login:	(b) (6)			
Project Role*:	Co-Investigator	Other Project Role Category:		
Degree Type:	PHD	Degree Year: 2005		
Attach Biographical Sketch*:	File Name:	REN_Lili_Biosketch_Final.pdf		
Attach Current & Pending Support:	File Name:			

PROFILE - Senior/Key Person				
Prefix: Dr.	First Name*: Li	Middle Name	Last Name*: Guo	Suffix:
Position/Title*:	Professor			
Organization Name*:	Institute of Pathogen Biology			
Department:				
Division:				
Street1*:	No. 9 Dong Dan San Tiao			
Street2:	Dongcheng District			
City*:	Beijing			
County:				
State*:				
Province:				
Country*:	CHN: CHINA			
Zip / Postal Code*:	100730			
Phone Number*:	(b) (6)	Fax Number:		
E-Mail*:	(b) (6)			
Credential, e.g., agency login:	(b) (6)			
Project Role*:	Co-Investigator	Other Project Role Category:		
Degree Type:	MD	Degree Year: 2006		
Attach Biographical Sketch*:	File Name:	GUO_Li_Biosketch_Final.pdf		
Attach Current & Pending Support:	File Name:			

PROFILE - Senior/Key Person				
Prefix: Dr.	First Name*: Peng	Middle Name	Last Name*: Zhou	Suffix:
Position/Title*:	Principal Investigator			
Organization Name*:	Wuhan Institute of Virology			
Department:				
Division:				
Street1*:	Xiao Hong Shan, No. 44			
Street2:				
City*:	Wuhan			
County:				
State*:				
Province:				
Country*:	CHN: CHINA			
Zip / Postal Code*:	430071			
Phone Number*:	(b) (6)	Fax Number:		
E-Mail*:	(b) (6)			
Credential, e.g., agency login:	(b) (6)			
Project Role*:	Co-Investigator	Other Project Role Category:		
Degree Type:	PHD	Degree Year: 2011		
Attach Biographical Sketch*:	File Name:	ZHOU_Peng_Biosketch_Final.pdf		
Attach Current & Pending Support:	File Name:			

PROFILE - Senior/Key Person				
Prefix: Dr.	First Name*: Ben	Middle Name	Last Name*: HU	Suffix:
Position/Title*:	Research Scientist			
Organization Name*:	Wuhan Institute of Virology			
Department:				
Division:				
Street1*:	Xiao Hong Shan, No. 44			
Street2:				
City*:	Wuhan			
County:				
State*:				
Province:				
Country*:	CHN: CHINA			
Zip / Postal Code*:	430071			
Phone Number*:	(b) (6)	Fax Number:		
E-Mail*:	(b) (6)			
Credential, e.g., agency login:	(b) (6)			
Project Role*:	Co-Investigator	Other Project Role Category:		
Degree Type:	PHD	Degree Year:	2015	
Attach Biographical Sketch*:	File Name:	HU_Ben_Biosketch_final.pdf		
Attach Current & Pending Support:	File Name:			

PROFILE - Senior/Key Person				
Prefix: Dr.	First Name*: Aleksei	Middle Name	Last Name*: Chmura	Suffix:
Position/Title*:	Research Scientist			
Organization Name*:	EcoHealth Alliance			
Department:				
Division:				
Street1*:	460 West 34th Street			
Street2:	Suite 1701			
City*:	New York			
County:				
State*:	NY: New York			
Province:				
Country*:	USA: UNITED STATES			
Zip / Postal Code*:	100012317			
Phone Number*:	(b) (6)	Fax Number:	+12123804465	
E-Mail*:	(b) (6)			
Credential, e.g., agency login:	(b) (6)			
Project Role*:	Other (Specify)	Other Project Role Category:	Research Scientist	
Degree Type:	PHD	Degree Year:	2018	
Attach Biographical Sketch*:	File Name:	CHMURA_Aleksei_Biosketch_Final.pdf		
Attach Current & Pending Support:	File Name:			

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

BIOGRAPHICAL SKETCH
DO NOT EXCEED FIVE PAGES.

NAME: Peter Daszak

eRA COMMONS USER NAME (credential, e.g., agency login): (b) (6)

POSITION TITLE: President & Chief Scientist

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Bangor University, UK	B.S (hons)	07/1986	Zoology
University of East London, UK	Ph.D.	03/1993	Infectious Diseases

A. Personal Statement

I have the broad expertise in emerging viral zoonoses, and scientific management experience to support this proposed work that involves an international interdisciplinary team working on field collection of wildlife and human samples, human behavioral risk surveys, modeling and analytics, and viral characterization *in vitro* and *in vivo*. I am President and Chief Scientist of EcoHealth Alliance, a US-based 501 (c) 3 institution that conducts research on emerging zoonoses and global health capacity building. My 20+ years of NIH-funded research focuses on understanding the links among disease emergence in wildlife, livestock and people, particularly viral zoonoses. This includes identifying the bat origin of SARS-CoV and SADS-CoV, analyzing the ecology of West Nile, Nipah and Hendra virus emergence, publishing the first unbiased analysis of global emerging disease hotspots, and developing the scientific rationale for the Global Virome Project (GVP). Over the past 18 years I have been the PI on 4 multidisciplinary R01s that use modeling, epidemiology, laboratory and field science to test hypotheses on the emergence of wildlife-origin viral zoonoses, including SARS-CoV, Nipah and Hendra virus, Avian influenza and novel viruses from bats. I have successfully managed teams of virologists, field biologists, mathematical modelers, veterinarians, epidemiologists, laboratorians and anthropologists. Much of the groundwork for the current proposal has developed from my previous collaborative research with each member of the team assembled in the current R01 renewal proposal.

1. 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.
2. Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL, and **Daszak P*** (2008). Global trends in emerging infectious diseases. **Nature** 451:990-993
3. Olival KJ*, Hosseini PR, Zambrana-Torrel C, Ross N, Bogich TL, **Daszak P*** (2017). Host and viral traits predict zoonotic spillover from mammals. **Nature** 546, 646–650.
4. Carroll D, **Daszak P***, Wolfe ND, Gao GF, Morel C, Morzaria S, Pablos-Méndez A, Tomori O, Mazet JAK (2018). The global virome project. **Science** 359: 872-874.

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

B. Positions and Honors**Positions and Employment**

- 1993 -98 Senior Faculty Research Scientist, Kingston University UK
 1998 Guest Researcher, Centers for Disease Control and Prevention (CDC)
 1999 -01 Faculty Research Scientist, University of Georgia
 2001 - Sr. Adjunct Faculty, Columbia University
 2001 - 09 Executive Director, Consortium for Conservation Medicine, EcoHealth Alliance, New York
 2009 - President & Chief Scientist, EcoHealth Alliance New York

Other Experience and Professional Membership

- 2003 - 7 NIH: ad hoc member, ZRG1 IDM-G 90 (2003-5) ZRG1 IRAP-Q (2005-7)
 2004 - Editorial Board, *Conserv. Biol.*
 2005 NIAID: Steering Committee, workshop on virus-host shifts & emergence of new pathogens
 2010 - Editor-in-Chief, *EcoHealth*; Member of IOM Forum on Microbial Threats; External Advisory Board, DHS and Kansas State Univ. Ctr. of Excellence for Emerg. & Zoonotic Animal Diseases (CEEZAD)
 2011 Steering Committee, NIAID Workshop on Arboviruses
 2014 - Member NRC Advisory Committee to advise the US Global Change Research Program (USGCRP)
 2015 - Member of Supervisory Board, One Health Platform; Editorial Board *One Health*
 2016 - Member, WHO Expert group on Public Health Emergency Disease Prioritization
 2016 - Member, Core Steering Committee & Co-Chair, Science & Technol WG, Global Virome Project
 2017 External Review Committee, CSIRO Health & Biosecurity Business Unit
 2017 - Chair, Forum on Microbial Threats, National Academies of Science, Engineering & Medicine

Honors

- 1999 Meritorious service award, CDC
 2000 CSIRO silver medal for collaborative research
 2002 Honored by the naming of a new species of centipede, *Cryptops daszaki* (*J Nat Hist* 36: 76-106)
 2003 6th Annual Lecturer, Medicine & Humanities, Texas A&M
 2007 Finalist, Director's Pioneer Award
 2008 Presidential Lecturer, University of Montana
 2012 Elected member of the Cosmos Club, Washington DC
 2013 Honored by the naming of a new parasite species, *Isospora daszaki* (*Parasit. Res.* 111:1463-1466)
 2013 Hsu-Li Distinguished Lectureship in International Epidemiology, Univ. Iowa
 2015 Robert Leader Endowed Lecture in Food Safety, Michigan State Univ.
 2018 - Member, National Institute of Medicine (NAM), USA.

C. Contribution to Science

1. Research on the bat origins of emerging viruses. A range high impact emerging viruses appear to have bat reservoirs (e.g. SARS-CoV, EBOV, NiV, HeV, MERS-CoV, SADS-CoV). As PI on four prior R01s, my work has helped demonstrate the bat-origin for some of these (SARS-CoV, SADS-CoV), analyze the drivers of emergence and risk factors for spillover. Collaborating with virologists in China, we have isolated and characterized SARS-like CoVs from bats that use the same human host cell receptor (ACE-2) as SARS-CoV. This work provides critical reagents and resources that have helped advance understanding of virus-host binding and may contribute to vaccine development. My other work identified factors underlying the emergence of NiV from *Pteropus* bats in Malaysia and Bangladesh; that MERS-CoV likely originated in bats; that SADS-CoV originates in bats; and that bats harbor a significantly higher proportion of zoonoses than all other mammalian groups after correcting for reporting biases.

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

- a. Pulliam JRC, Epstein JH, Dushoff J, Rahman SA, Bunning M, HERG, Jamaluddin AA, Hyatt AD, Field HE, Dobson AP & **Daszak P*** and the Henipavirus Ecology Research Group (HERG). (2012). Agricultural intensification, priming for persistence, and the emergence of Nipah virus: a lethal bat-borne zoonosis. **J Roy Soc Interface** 9:89-101
- b. Ge X-Y, Li J-L, Yang X-L, Chmura AA, Zhu G, Epstein JH, Mazet JK, Hu B, Zhang W, Peng C, Zhang Y-J, Luo C-M, Tan B, Wang N, Zhu Y, Crameri G, Zhang S-Y, Wang L-F, **Daszak P***, Shi Z-L* (2013). Isolation and characterization of a bat SARS-like Coronavirus that uses the ACE2 receptor. **Nature** 503: 535-538.
- c. Memish ZA, Mishra N, Olival KJ, Fagbo SF, Kapoor V, Epstein JH, Al Hakeem R, Durosinloun A, Al Asmari M, Islam A, Kapoor A, Briese T, **Daszak P**, Al Rabeeah A, Lipkin WI. (2013). Middle East respiratory syndrome coronavirus in bats, Saudi Arabia. **EID** 19(11): 1819-1823.
- d. Zhou P, Fan H, Lan T, Yang X-L, Shi W-F, Zhang W, Zhu Y, Zhang Y-W, Xie Q-M, Mani S, Zheng X-S, Li B, Li J-M, Guo H, Pei G-Q, An X-P, Chen J-W, Zhou L, Mai K-J, Wu Z-X, Li D, Anderson DE, Zhang L-B, Li S-Y, Mi Z-Q, He T-T, Cong F, Fuo P-J, Huang R, Luo Y, Liu X-L, Chen J, Huang Y, Sun Q, Zhang X-L-L, Wang Y-Y, Xing S-Z, Chen Y-S, Sun Y, Li J, **Daszak P***, Wang L-F*, Shi Z-L*, Tong Y-G*, Ma J-Y* (2018). Fatal Swine Acute Diarrhea Syndrome caused by an HKU2-related Coronavirus of Bat Origin. **Nature** 556: 255-258.

2. Analyzing the process of disease emergence. Emerging infectious diseases are a significant threat to global health. However, their emergence is sporadic, complex, and seemingly unpredictable. In the early 2000s I started to use analytical approaches to see if there are patterns in disease emergence, and if these are predictable. By collating a database of all known prior EID events, identifying their point origins, and correcting for reporting biases, I published the first ever predictive 'hotspots' maps of where disease emergence is most likely. Under various grants that I have led, or been a co-investigator on, I have published spatial analyses of the drivers of disease spread, and strategies to predict pandemic emergence.

- a. Kilpatrick AM, Chmura AA, Gibbons DW, Fleischer RC, Marra PP & **Daszak P** (2006). Predicting the global spread of H5N1 avian influenza. **PNAS** 103: 19368-19373.
- b. Morse SS, Mazet JAK, Woolhouse M, Parrish CR, Carroll D, Karesh WB, Zambrana-Torrel C, Lipkin WI, **Daszak P*** (2012). Prediction and prevention of the next pandemic zoonosis. **Lancet** 380:1956-1965.
- c. **Daszak P***, Zambrana-Torrel C, Bogich TL, Fernandez M, Epstein JH, Murray KA, Hamilton H (2013). Interdisciplinary approaches to understanding disease emergence: The past, present and future drivers of Nipah virus emergence. **PNAS** 110: 3681-3688
- d. Allen T, Murray KA, Zambrana-Torrel C, Morse SS, Rondinini C, Di Marco M, Breit N, Olival KJ, **Daszak P*** (2017). Global hotspots and correlates of emerging zoonotic diseases. **Nature Comm** 8: 1124

3. Studies of wildlife disease ecology to understand emerging zoonoses. The majority of EIDs are zoonotic, with the majority of these originating in wildlife. In the 1990s, new collaborations among ecologists and medical researchers began to show that understanding disease dynamics in wildlife can allow better forecasting of disease risk in people. I reviewed this field in a paper in *Science* in 2000 and in a more recent paper in *Nature* on the links among biodiversity and health. During the last two decades, I have led collaborative research programs on how the ecology of specific wildlife-origin zoonoses can help explain patterns of risk to people. This includes my work in 4 R01s and as EHA institutional lead for USAID-EPT-PREDICT, and Chief of Party for USAID-IDEEAL. This work has led to strategies to estimate the diversity of yet-to-be discovered viruses, and a program to identify them (the Global Virome Project).

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

- a. **Daszak P***, Cunningham AA, Hyatt AD (2000). Emerging infectious diseases of wildlife - threats to biodiversity and human health. **Science** 287: 443-449
- b. 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.
- c. Anthony SJ, Epstein JH, Murray KA, Navarrete-Macias I, Zambrana-Torrel 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**, Lipkin WI. (2013). A strategy to estimate unknown viral diversity in mammals. **MBio** 4(5): e00598-13.

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

USAID Emerging Pandemic Threats Mazet (PI) 10/01/14 – 09/30/19
 PREDICT-2

The goal of this work is to conduct surveillance for novel pathogens in wildlife, livestock and people; characterize human risk behavior; analyze EID risk; and design interventions in >20 countries
 Role: PI on Subcontract

1R01 AI110964 Daszak (PI) 06/01/14 – 05/31/19
 Understanding the Risk of Bat Coronavirus Emergence

The goal of this work is to conduct ecological and virological studies on bats in China that harbor SARS-like coronaviruses, and conduct behavioral risk surveys and testing in people, with a goal of identifying risk factors for further spillover of SARS-like CoVs, and help identify the likely drivers of the SARS-CoV outbreak in 2003.
 Role: PI

USAID 1414374 (RDMA, Thailand) Daszak (CoP) 10/01/13 - 03/30/19
 Infectious Disease Emergence and Economics of Altered Landscapes (IDEEAL)

The goal of this cooperative agreement is to analyze how land use change affects disease risk in SE Asia, and how economic costs of disease can be used to develop novel intervention policies.
 Role: Chief of Party

Completed Research Support

NSF DEB 1414374 Perrings (PI) 10/15/14 - 04/14/18

US-UK Collab: Risks of Animal and Plant Infectious Diseases through Trade (RAPID Trade)
 The goal of this NSF-NIH-USDA EEID award, joint with a UK BBSRC grant is to analyze and model how policy changes to trade affect emerging disease risk globally
 Role: Co-Investigator

HDTRA1 Allen (PI) 04/15/15 - 04/14/17

Global Rapid Identification of undiagnosed EID Events
 The goal of this project was to design software that can be used in the DoD biosurveillance ecosystem (BSVE) to rapidly diagnose novel EID events.
 Role: Co-Investigator

1R01GM100471 (NIGMS) Perrings (PI) 09/15/11-06/30/15

MASpread: Modeling Anthropogenic Effects in the Spread of Infectious Disease
 The goal of this project was to develop novel approaches to modeling and analyzing disease spread and the social decisions involved in control
 Role: Co-Investigator

NSF Daszak (PI) 07/01/10-06/30/15

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

EcoHealthNet - a Research Coordination Network

Funding for student exchange and workshops to fuse veterinary science, ecology and human medical sciences

Role: PI

USAID Emerging Pandemic Threats Mazet (PI) 10/01/09 – 09/30/14
 PREDICT-1

The goal of this work was to conduct surveillance for novel pathogens in wildlife, livestock and people in developing countries

Role: PI on Subcontract

2 R01TW005869 Daszak (PI) 09/01/08 – 08/31/13

The Ecology, Emergence and Pandemic Potential of Nipah virus in Bangladesh

This project involved mathematical modeling and fieldwork on 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

The goal of this work was to organize a workshop among NIH, NSF, leading US and Chinese scientists to discuss potential for a jointly funded NIH-NSF-China funding mechanism

Role: PI

1 R01AI079231 (NIAID) Daszak (PI) 09/18/08 – 08/31/13

Risk of viral emergence from bats.

The goal was to model hotspots for bat viral diversity, identify & characterize new bat viruses & understand their pathology

Role: PI

NSF BCS 0826779 Daszak (PI) 10/01/08 – 03/31/12

AOC - HSD – Collaborative Research: Human-related factors affecting emerging infectious diseases

The goal of this work was 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

Supplemental funding: Predicting the risk of global H5N1 spread

This project involved 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

Predicting spatial variation in West Nile virus transmission

The goal was to study interaction among WNV vector, reservoir host populations across an urban-to-rural gradient.

Role: Co-PI

R01 TW05869 (Fogarty Intl. Ctr.) Daszak (PI) 08/01/02 - 05/31/07

Anthropogenic change & emerging zoonotic paramyxoviruses

The goal was to identify the cause of emergence of Nipah and Hendra viruses in Malaysia and Australia.

Role: PI

NSF HSD 0525216 Daszak (PI) 10/15/05 - 10/14/06

Collaborative Research: Socio-Economic and Environmental Drivers of Emerging Diseases

The goal of this work was to analyze patterns of disease emergence globally leading to development of a global hotspots map of disease emergence.

Role: PI

BIOGRAPHICAL SKETCH

NAME Zhengli Shi	POSITION TITLE Co-Investigator		
eRA COMMONS USER NAME (credential, e.g., agency login) (b) (6)			
EDUCATION/TRAINING			
INSTITUTION AND LOCATION	DEGREE	MM/YY	FIELD OF STUDY
Department of Biology, Wuhan University, China	BS	1987	Genetics
Wuhan Inst. Virol., Chinese Acad. Sci., China	MS	1990	Virology
University Montpellier II, Montpellier, France	Ph.D.	2000	Virology

A. Personal Statement

I have been working on the discovery and characterization of novel viruses from bats and other wildlife since 2004. This included the discovery that Chinese horseshoe bats are the natural reservoir of SARSr-CoVs and the likely origin of SARS-CoV. My group then isolated SARSr-CoVs from bats sharing high homology with human SARS-CoV and demonstrated their interspecies transmission risk, largely confirming bats as the source of SARs. My lab has carried out systematic studies on the epidemiology, genetic evolution, interspecies infection mechanism and pathogenesis of a series of bat-borne emerging viruses including SARSr-CoV, MERS-CoV, EBOV and others. This work has involved collaboration on all other scientists on this R01 renewal proposal, in particular Drs. Daszak and Linfa Wang, who I have collaborated with since 2003, publishing 2 papers in *Nature* and one in *Science* together on our bat-virus work, as well as dozens of others. Recently, this collaborative team discovered that an outbreak of fatal Swine Acute Diarrhea Syndrome in southern China that killed more than 24,000 piglets was caused by spillover of bat HKU2-related coronaviruses. In this proposed work, my group will be responsible for CoV testing in bat samples, serological testing in human samples, and virus characterization work such as cell entry analysis and receptor identification.

B. Positions and Honors.

Positions and Employment

1990 - 93	Research assistant, Wuhan Institute of Virology, Chinese Academy of Sciences, China
1993 - 95	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

2011 -	Director, Center for Emerging Infectious Diseases, Wuhan Inst. Virology, Chinese Acad. Sci.
2013 -	Director, BSL-3 laboratory at Wuhan Institute of Virology, Chinese Acad. Sci.
2014 -	Director, Committee of Biosafety, Wuhan Institute of Virology, Chinese Acad. Sci.
2014 -	Director, CAS Key Laboratory of Special Pathogens and Biosafety
2015 -	Vice Director, BSL-4 laboratory, Wuhan Institute of Virology, Chinese Acad. Sci.
2016 - 18	Associate Editor of <i>Virology Journal</i>
2017 - 19	Editorial Board of <i>Virology</i>
2017-2019	Editor in Chief, <i>Virologica Sinica</i>

Honors

- 2003 Natural Science Award (the Second Prize) of Hubei Province, China.
 2004 Outstanding supervisor of graduate student of Hubei Province, China.
 2006 Outstanding scientist of the Chinese Academy of Sciences.
 2006 Outstanding Research Article on Natural Science (the First Prize), Hubei Province, China
 2014 Young and Middle-aged Scholar with Distinguished Contribution in Hubei Province, China
 2014 Outstanding Research Article on Natural Science (the Grand Prize), Hubei Province, China
 2016 Palm Knight Medal for Education, Government of the Republic of France
 2017 Natural Science Award (the First Prize) of Hubei Province, China.

C. Selected peer-reviewed publications most relevant to the current application

* = Co-corresponding or first author

Li W*, Shi Z*, Yu M, Ren W, Smith C, Epstein HJ, Wang H, Crameri G, Hu Z, Zhang H, Zhang J, Mceachern J, Field H, Daszak P, Eaton TB, Zhang S, Wang LF (2005). Bats are natural reservoirs of SARS-like coronaviruses. **Science**, 310: 676-679.

Ren W, Qu X, Li W, Han Z, Yu M, Zhang S, Wang LF, 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.

Yuan J, Hon CC, Li Y, Wang D, Xu G, Zhang H, Zhou P, Poon LM, Lam TT, Leung FC. 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.

Ge XY, Li JL, Yang X-L, Chmura AA, Zhu G, Epstein JH, Mazet JK, Hu B, Zhang W, Peng C, Zhang YJ, Luo CM, Tan B, Wang N, Zhu Y, Crameri G, Zhang SY, Wang LF, Daszak P*, Shi Z* (2013). Isolation and characterization of a bat SARS-like Coronavirus that uses the ACE2 receptor. **Nature** 503: 535-538.

Menachery VD, Yount BL, Debbink K, Agnihothram S, Gralinski LE, Plante JA, Graham RL, Scobey T, Ge XY, Donaldson EF, Randell SH, Lanzavecchia A, Marasco WA, Shi Z*, Baric RS* (2015). A SARS-like cluster of circulating bat coronaviruses shows potential for human emergence. **Nature Medicine**, 21:1508-1513.

Yang XL, Hu B, Wang B, Wang MN, Zhang Q, Zhang W, Wu LJ, Ge XY, Zhang YZ, Daszak P, Wang LF*, Shi Z* (2016). Isolation and Characterization of a Novel Bat Coronavirus Closely Related to the Direct Progenitor of Severe Acute Respiratory Syndrome Coronavirus. **Journal of Virology**, 90: 3253-3256.

Zeng L, Ge X, Peng C, Yang X, Tan B, Gao Y, Chen J, Chmura AA, Daszak P*, Shi Z* (2016) Bat Severe Acute Respiratory Syndrome-Like Coronavirus WIV1 Encodes an Extra Accessory Protein, ORFX, Involved in Modulation of the Host Immune Response. **Journal of Virology**, 90(14): 6573–6582.

Hu B, Zeng LP, Yang XL, Ge XY, Zhang W, Li B, Xie JZ, Shen XR, Zhang YZ, Wang N, Luo DS, Zheng XS, Wang MN, Daszak P, Wang LF, Cui J*, Shi Z* (2017). Discovery of A Rich Gene Pool of Bat SARS-related Coronaviruses Provides New Insights into the Origin of SARS Coronavirus. **PLOS Pathogens**, 13(11): e1006698.

Zhou P, Fan H, Lan T, Yang XL, Shi WF, Zhang W, Zhu Y, Zhang YW, Xie QM, Mani S, Zheng XS, Li B, Li JM, Guo H, Pei GQ, An XP, Chen JW, Zhou L, Mai KJ, Wu ZX, Li D, Anderson D, Zhang LB, Li SY, Mi ZQ, He TT, Cong F, Guo PJ, Huang R, Luo Y, Liu XL, Chen J, Huang Y, Sun Q, Zhang XLL, Wang YY, Xing SZ, Chen YS, Sun Y, Li J, Daszak P, Wang LF, Shi Z, Tong YG, Ma JY (2018) Fatal swine acute diarrhea syndrome caused by an HKU-2 related coronavirus of bat origin. **Nature**, 556: 255-258.

Luo CM, Wang N, Yang XL, Liu HZ, Zhang W, Li B, Hu B, Peng C, Geng QB, Zhu G, Li F*, Shi Z* (2018). Discovery of Novel Bat Coronaviruses in South China That Use the Same Receptor as Middle East Respiratory Syndrome Coronavirus. **Journal of Virology**, 92 (13): e00116-18.

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

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.

Yuan J, Zhang Y, Li J, Zhang Y, Wang LF*, Shi Z* (2012). Serological evidence of ebolavirus infection in bats, China. **Virology Journal**, 9: 236.

Yang XL, Zhang YZ, Jiang RD, Guo H, Zhang W, Li B, Wang N, Wang L, Waruhiu C, Zhou JH, Li SY, Daszak P, Wang LF*, Shi Z* (2017). Genetically Diverse Filoviruses in *Rousettus* and *Eonycteris* spp. Bats, China, 2009 and 2015. **Emerging Infectious Diseases**, 23(3):482-486.

Zeng LP, Ge XY, Peng C, Tai WB, Jiang SB, Du LY*, Shi Z* (2017). Cross-neutralization of SARS coronavirus-specific antibodies against bat SARS-like coronaviruses. **Science China Life Sciences**, 60(12):1399-1402.

Wang N, Li SY, Yang XL, Huang, HM, Zhang YJ, Guo H, Luo CM, Miller M, Zhu G, Chmura AA, Hagan E, Zhou JH, Zhang YZ, Wang LF, Daszak P*, Shi Z* (2018). Serological Evidence of Bat SARS-Related Coronavirus Infection in Humans, China. **Virologica Sinica**, 33(1):104-107.

D. Research Support
Ongoing Research Support

[Redacted] (b) (4)

Geographical distribution and genetic variation of pathogens in Africa
Role: PI

31770175 National Natural Science Foundation of China 01/01/2018-12/31/2021
Evolution mechanism of the adation of bat SARS-related coronaviruses to host receptor molecules and the risk of interspecies infection
Role: PI

[Redacted] (b) (4)

Genetic evolution and transmission mechanism of important bat-borne viruses
Role: PI

R01 AI110964 Daszak (PI) 06/01/14-05/31/19
Understanding Risk of Bat Coronaviruses
The goal of this study is to analyze the risk of coronavirus spillover from bats to humans in Southern China
Role: Co-Investigator

Emerging Pandemic Threat Program, USAID Mazet (PI) 10/01/14-09/30/19
PREDICT 2
The goal of this project is to create and implement a global virus surveillance system in animals and humans and analyze spillover risk.
Role: China Country Coordinator

Completed Research Support

[Redacted] (b) (4)

Metagenomic analysis of bat intestinal viruses
Role: PI

[Redacted] (b) (4)

Mechanism of interspecies transmission of zoonotic viruses

Role: Co-PI

(b) (4)
Genetic diversity, identification and pathogenesis of bat viruses


(b) (4)

BIOGRAPHICAL SKETCH

NAME Kevin J. Olival	POSITION TITLE Co-Investigator		
eRA COMMONS USER NAME (b) (6)			
EDUCATION/TRAINING			
INSTITUTION AND LOCATION	DEGREE	MM/YY	FIELD OF STUDY
Colorado State University, Fort Collins, CO	BS	05/1997	Biology
Columbia University, New York, NY	MA	10/2003	Conservation Biology
Columbia University, New York, NY	PhD	05/2008	Ecology & Evolution
American Museum of Natural History, New York	Post Doc	08/2009	Molecular Parasitology
NIH Fogarty US Global Health Fellow, New York	Post Doc	08/2011	EIDs

A. Personal Statement

The goal of this proposal is to understand the current and future threat of bat-borne coronavirus spillover in Southern China, by identifying which viruses, host species, and human behaviors are associated with the highest risk of CoV exposure. Specifically, we will use a combination of targeted bat sampling, human behavioral risk analyses, mathematical modeling, and phylogenetic and molecular methods to test several hypotheses related to zoonotic spillover risk of β -CoVs, with specific attention paid towards SARSr-CoVs. My research experience over the last 16 years on bat-borne disease evolution, ecology, dynamics, population genetics, and viral discovery is strongly complementary to these aims. Our current proposal builds upon the findings of an ongoing NIAID R01 grant (ending 5/31/19), for which I was a co-investigator. Prior to this I coordinated research efforts under a NIAID award (2011-2016), investigating the risk of viral emergence from bats. This included sample collection and testing of thousands of bats from 8 countries globally. As an NIH Fogarty Global Health Post-Doc Fellow, I gained invaluable experience working internationally with a project focused on the ecology and evolution of Nipah virus in Bangladesh. My work over the last decade includes leading field investigations and bat viral surveillance in a wide range of countries, including: Bangladesh, Cambodia, India, Indonesia, Malaysia, Thailand, Philippines, Saudi Arabia, Georgia, Jordan, and Turkey. Discoveries include the first viral isolation of Nipah virus from the large flying fox in Malaysia; evidence of MERS-CoV in bats in Saudi Arabia; and the first serological evidence of Ebola Zaire virus in bats in Asia. I currently serve as the Modeling & Analytics coordinator under the USAID PREDICT-2 project, working with a team of analyst to develop new approaches to predict and prevent zoonoses. As part of this effort, I developed a new approach that combines phylogenetic, ecological, and life-history traits to predict viral diversity, host range, and spillover potential, leading to a recent first author paper in *Nature*.

1.  (b) (4)
2. Memish ZA, Mishra N, Olival KJ, Fagbo SF, Kapoor V, Epstein JH, AlHakeem R, Al Asmari M, Islam A, Kapoor A, Briese T, Daszak P, Al Rabeeah AA, Lipkin WI. (2013). Middle East Respiratory Syndrome Coronavirus in Bats, Saudi Arabia. **Emerging Infectious Diseases**. 19(11): 1819-1823.
3. Olival KJ*, Hosseini P, Zambra-Torrellio C, Ross N, Bogich T, Daszak P*. (2017). Host and viral traits predict zoonotic spillover from mammals. **Nature** 546(7660): 646-650.

*corresponding author

B. Positions and Honors

Positions and Employment

1999 - 02 Research Associate, Kewalo Marine Laboratory, University of Hawaii
 2003 - 07 US Environmental Protection Agency STAR Fellow
 2006 - 13 Instructor, Columbia University Secondary School Summer Program
 2010 - 15 Senior Research Scientist, EcoHealth Alliance
 2015 - 17 Associate Vice President for Research, EcoHealth Alliance
 2009 - Visiting Scientist, American Museum of Natural History
 2009 - Adjunct Faculty, Earth Institute Center for Environmental Sustainability, Columbia University
 2017 - Vice President for Research, EcoHealth Alliance

Other Experience and Professional Memberships

1998 - 00 Member, AAAS
 2000 - 02 Mentor, NSF Undergraduate Mentoring in Environmental Biology (UMEB), University of Hawaii
 2003 - 05 Member, American Society of Mammalogists
 2005 - 06 Member, New York Academy of Sciences
 2011 - Scientific Steering Committee Member, Southeast Asian Bat Conservation Research Unit
 2011 - Scientific Advisory Board Member, Lube Bat Conservancy, FL
 2011 - Scientific Advisor, Bat Conservation International
 2011 - Review Editor, EcoHealth
 2015 - US White-Nose Syndrome Stakeholder Committee and Communications Committee Member
 2015 - Island and Seas, Board Member
 2017 - DoD DTRA: Steering Committee Member, Bat One Health Research Network

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 EPA STAR Fellowship Award
 2008 PhD *with Distinction*, Columbia University
 2013 Plenary talk on bat virus modeling at 11th Annual ASM Biodefense and EID Research Meeting
 2013-14 Institute of Medicine, Forum on Microbial Threats. Invited speaker, briefings on MERS-CoV and Emerging Viral Diseases
 2016 Plenary Speaker, NYC Medtech conference – Global Virome Project
 2017-18 Three papers awarded the InCites Highly Cited Paper™ designation (top 1% in field) for Immunology and Microbiology

C. Contribution to Science

1. Viral Discovery and Characterization in Bats


A large body of my research has focused on understanding the distribution and diversity of viruses in wildlife populations to better understand the ecological risk of viral emergence. This includes the first use of species accumulation curves to estimate viral diversity using data from longitudinal surveillance of fruit bats in Bangladesh, and a large meta-analysis of viral prevalence in bats to optimize discovery strategies. Two field studies highlighted below include a broad geographic survey of bat coronaviruses in Thailand, and the first isolation and full genome characterization of Nipah virus from the large flying fox in Malaysia.

- a. Rahman SA, Hassan SS, Olival KJ, Mohamed M, Chang L-Y, Hassan L, Saad NM, Shohaimi SA, Mamat ZC, Naim MS, Epstein JH, Suri AS, Field HE, Daszak P and HERG. (2010). Characterization of Nipah virus from Naturally Infected *Pteropus vampyrus* Bats, Malaysia. **Emerging Infectious Disease** 16(12): 1990-1993.

- b. Anthony SJ, Epstein JH, Murray KA, Navarrete-Macias I, Zambrana-Torrel CM, Solovyov A, Ojeda-Flores R, Arrigo NC, Islam A, Khan SA, Hosseini P, Bogich TL, Olival KJ, Sanchez-Leon MD, Karesh WB, Goldstein T, Luby SP, Morse SS, Mazet JAK, Daszak P, Lipkin WI. (2013). A Strategy To Estimate Unknown Viral Diversity in Mammals. **Mbio**. 4(5): e00598-13.
- c. Wacharapluesadee S, Duengkae P, Rodparn A, Kaewpom T, Maneeorn P, Kanchanasaka B, Yinsakmongkon S, Sittidetboripat N, Chareesaen C, Khlangsap N, Pidthong A, Leadprathom K, Ghai S, Epstein JH, Daszak P, Olival KJ, Blair PJ, Callahan MV, Hemachudha T. (2015). Diversity of Coronavirus in Bats from Eastern Thailand. **Virology Journal** 12:57.
- d. Young CC and Olival KJ*. (2016). Optimizing Viral Discovery in Bats. **PLOS ONE** 11(2): e0149237.

2. Serological Surveillance

Bats are believed to harbor a unique and large diversity of viruses, including a number of pathogens that pose a risk to human health (e.g. Ebola, Nipah, SARS-CoV). I have been involved with field and laboratory investigations of several bat-borne pathogens that pose the greatest risk to humans over the years, including Filoviruses, Henipaviruses, and SARS and MERS-related Coronaviruses. Collection and analysis of serological data was critical to each of these studies. Using serological and PCR data we discovered that bats are reservoirs of Ebola Reston virus in the Philippines. Extensive, proactive surveillance of wild bat and primate populations in Thailand for Ebola viruses importantly showed that several suspected species are likely *not* important reservoirs. The work in Thailand was predicated by my own investigations in Bangladesh where we discovered the first evidence for Ebola Zaire virus infection in a wildlife species outside of Africa – changing our paradigm as to where these viruses can be found globally. Lastly, I have been involved with extensive work to identify the natural reservoir host of Reston virus in Philippines that included both molecular and serological findings.

- a. Olival KJ*, Islam A, Yu M, Anthony SJ, Epstein JH, Khan SA, Khan SU, Crameri G, Wang LF, Lipkin WI, Luby SP, and Daszak P. (2013). Ebolavirus Antibodies in Fruit Bats, Bangladesh. **Emerging Infectious Diseases** 19(2): 270-273.
- b. Wacharapluesadee S, Olival KJ, Kanchanasaka B, Duengkae P, Kaewchot S, Srongmongkol P, Ieamsaard G, Maneeorn P, Sittidetboripat N, Kaewpom T, Petcharat S, Yingsakmongkon S, Rollin PE, Towner JS, Hemachudha T. (2015). Surveillance for Ebola Virus in Wildlife, Thailand. **Emerging Infectious Diseases** 21(12): 2271-2273.
- c. Jayme S, Yu M, Jong Cd, Olival KJ, Tagtag A, Hughes T, Foord A, Marsh G, Crameri G, Epstein JH, Santos I, Catbagan D, Lim M, Benigno C, Wang L, Daszak P, Field H, Newman S. (2015). Molecular evidence of Ebola Reston virus infection in Philippine bats. **Virology Journal**. 12(1): 107.
- d.  (b) (4)

3. Modeling Disease Emergence and Spillover Risk

I have used my applied ecology background working with analyses of wildlife and their pathogens to develop new models to improve our global understanding of zoonotic spillover and disease circulation. In addition to my previously mentioned *Nature* paper, this includes studies that examined the environmental drivers of bat virus spillover to humans, cross-species transmission among bat species, spatial analysis of emerging zoonotic disease hotspots, and host-specific determinants of fungal infection in bats. These modeling approaches explicitly use data from PCR- and serology-based field studies, combined with an understanding of wildlife biology and ecology, to assess the environmental and demographic drivers of disease transmission -- bridging the gap between field investigations and modeling transmission risk.

- a. Brierley L, Vonhof MJ, Olival KJ, Daszak P, Jones KE. (2016). Quantifying global drivers of zoonotic bat viruses: a process-based perspective. **American Naturalist** 187: E53-64
- b. Willoughby AR, Phelps K, PREDICT Consortium, Olival KJ*. (2017). "A Comparative Analysis of Viral Richness and Viral Sharing in Cave-Roosting Bats". **Diversity** 9 (35).
- c. Allen T, Murray KA, Zambrana-Torrel C, Morse SS, Rondinini C, Di Marco M, Breit N, Olival KJ, Daszak P. (2017). Global hotspots and correlates of emerging zoonotic diseases. **Nature Communications**. 8(1124): 1-10
- d. Verant ML, Bohuski EA, Richgels KLD, Olival KJ, Epstein JH, and Blehert DS. (2018). Determinants of *Pseudogymnoascus destructans* within bat hibernacula: implications for surveillance and management of white-nose syndrome. **Journal of Applied Ecology** 55: 820-829.

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

HDTRA11710064	Olival (PI)	10/02/17-10/01/22
Understanding the Risk of Bat-Borne Zoonotic Disease Emergence in Western Asia		
The goal of this project is to characterize pathogen diversity, strengthen zoonotic disease surveillance capacity, and test key hypotheses about the risk of bat-borne zoonotic disease emergence in Western Asia.		
Role: PI		
R01 AI110964	Daszak (PI)	06/01/14-05/31/19
Understanding Risk of Bat Coronaviruses		
The goal of this study is to analyze the risk of coronavirus spillover from bats to humans in Southern China		
Role: co-PI		
Emerging Pandemic Threat Program, USAID	Mazet (PI)	10/01/14-09/30/19
PREDICT 2		
The goal of this project is to create and implement a global virus surveillance system in animals and humans and analyze spillover risk.		
Role: Modeling and Analytics Coordinator; Country lead for Indonesia, South Sudan, and Thailand.		

Completed Research Support

Emerging Pandemic Threat Program, USAID	Mazet (PI)	10/01/09-09/30/14
PREDICT		
The goal of this project was to conduct zoonotic virus surveillance in wildlife in 20 countries, and modeling hotspots and drivers for disease emergence.		
Role: Key Personnel: Modeling Team; Country lead for Thailand and Indonesia		
Service Award, US Fish and Wildlife	Epstein (PI)	09/01/12-09/30/14
Characterization of Climatic Parameters within Bat Hibernacula, their Influence on Environmental Loads of <i>Geomyces destructans</i> , and Implications for the Migration of White-Nose Syndrome in Bats.		
The goal of this project was to identify environmental and other factors that influence the progression and severity of White Nose Syndrome in bats.		
Role: co-PI		
R01 AI079231	Daszak (PI)	09/18/08-08/31/13

Risk of viral emergence from bats

Modeled hotspots for viral diversity and emergence in bats, discovery of new viruses, and in vitro test of infectiousness for novel pathogens.

Role: Key Personnel: led project implementation, study design, and phylogenetic modeling

Endangered Species grant, USGS

Russell, Vonhof, and Olival (PI)

06/18/12-06/17/13

Genetic Approaches to Defining Taxonomic and conservation Units for the Hawaiian Hoary Bat

The goal of this project was to determine the phylogenetic position and conservation genetic units for endangered hoary bats.

Role: co-PI

3R01 TW005869-06S1

Daszak (PI)

09/01/09 – 8/31/11

NIH Fogarty Ecology of Infectious Diseases ARRA award

The goal of this project was to conduct Nipah virus surveillance in wild bat populations and use genetic methods to understand viral circulation in Bangladesh.

Role: Fogarty US Global Health Fellow

BIOGRAPHICAL SKETCH

NAME Ralph Steven Baric	POSITION TITLE Co-Investigator
eRA COMMONS USER NAME (b) (6)	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	MM/YY	FIELD OF STUDY
North Carolina State University, Raleigh, NC	BS	1977	Zoology
North Carolina State University, Raleigh, NC	Ph.D.	1982	Microbiology
University of Southern CA, School of Med, (Los Angeles, CA)	Post-Doc	1986	Microbiology

A. Personal Statement: The Baric laboratory uses genetic, biochemical, molecular and immunologic approaches to study the molecular mechanisms regulating viral evolution, virus immunity, virus-host interactions and vaccine mediated protective immunity using coronaviruses (CoV), noroviruses and flaviviruses (Dengue) as models. SARS-CoV and MERS-CoV are used as models to address fundamental questions in genetics, structure-function analyses, entry and cross species transmission, fidelity regulation, host susceptibility allele mapping, pathogenesis as well as therapeutic design and testing. Synthetic genomics and reverse genetics are used to create a panel of CoV molecular cDNA clones for SARS-CoV, SARS-like bat coronaviruses (SL-CoV), MERS-CoV, several human coronavirus, Dengue 1-4 and Zika virus. The Baric laboratory has developed key animal models of human disease, including SARS-CoV and SL-CoV pathogenesis in young and aged mice, and CRISPR gene edited mice encoding permissive mutations in the murine dipeptidyl peptidase receptor, making the animals permissive for MERS-CoV infection and disease.

The Baric laboratory has longstanding expertise in CoV evolution and emergence, replication, virus-receptor interactions, genetics, animal model development and pathogenesis. Not only has the Baric laboratory made fundamental breakthroughs in all aspects of CoV genetics, biology and immunology, but it has designed, developed and tested small molecule inhibitors and vaccines against emerging CoVs. Our group has collaborated with Drs. Daszak, Shi and Wang on SARS-CoVs for the past 3 years, and this R01 is a natural development of this collaboration.

Qualifications by Publication: : >314 total publications, >120 since 2013, H-index: 84.

<http://www.ncbi.nlm.nih.gov/sites/myncbi/ralph.baric.1/bibliography/40583903/public/?sort=date&direction=ascending>.

Key Manuscripts

1. Sheahan TP, Sims AC, Graham RL, Menachery VD, Gralinski LE, Case JB, Leist SR, Pyrc K, Feng JY, Trantcheva I, Bannister R, Park Y, Babusis D, Clarke MO, Mackman RL, Spahn JE, Palmiotti CA, Siegel D, Ray AS, Cihlar T, Jordan R, Denison MR, Baric RS (2017). Broad-spectrum antiviral GS-5734 inhibits both epidemic and zoonotic coronaviruses. **Science Translational Medicine**, 9(396). eaal3653. PMC5567817.
2. Scobey T, Yount BL, Sims AC, Donaldson EF, Agnihothram SS, Menachery VD, Graham RL, Swanstrom J, Bove PF, Kim JD, Grego S, Randell SH, Baric RS (2013). Reverse genetics with a full-length infectious cDNA of the Middle East respiratory syndrome coronavirus. **Proceedings of the National Academy of the Sciences**, 110(40):16157-62. PMC3791741.
3. Menachery, VD, Yount, BL, Debbink, K, Agnihothram, S., Gralinski, LE, Plante, JA, Graham, RL, Scobey T, Ge SY, Donaldson EF, Randell SH, Lanzavecchia A, Marasco WA, Shi Z, Baric RS (2015). A SARS-like cluster of circulating bat coronaviruses shows potential for human emergence. **Nature Medicine**, Nov 9. doi: 10.1038/nm.3985. [Epub ahead of print]. PMID:26552008.

4. Cockrell AS, Yount BL, Scobey T, Jensen K, Douglas M, Beall A, Tang XC, Marasco WA, Heise MT, Baric RS (2016). A Mouse Model for MERS Coronavirus Induced Severe Respiratory Distress Syndrome. **Nature Microbiology**, 2:16226. PMC5578707.

B. Positions and Honors.

Employment Experience:


- 1986-92 Assistant Professor, Department of Parasitology and Laboratory Practice and Department of Epidemiology, University of North Carolina (UNC), Chapel Hill, NC
- 1992-2001 Associate Professor, Departments of Epidemiology and Microbiology & Immunology, UNC Chapel Hill
- 2001- Professor, Departments of Epidemiology and Microbiology and Immunology, UNC Chapel Hill

Selected Awards/Honors:

- 2018 US Natl. Acad. Sci. "China-US Workshop on Challenges of Emerging Infections, Laboratory Safety and Global Health Security, Jan 2018, Galveston, Tx.
- 2015 US Natl. Acad. Sci./UK Royal Society Workshop: Sackler Scientific Forum on the Trends in Synthetic Biology and Gain of Function and Regulatory Implications, U.K.
- 2015 US Natl. Acad. Sci. "China-U.S. Workshop on the Challenges of Emerging Infections, Laboratory Safety, and Global Health Security" September 28-30 in Beijing, China
- 2015 MERS-CoV Stakeholders Workshop, invited panelist, NIH
- 2014 National Academy of Sciences: Working Group on Risks and Benefits of Gain of Function Research
- 2005-15 Review Board, *J. Virology*
- 2008-15 Senior Editor, *Plos Pathogens*
- 2008 US Natl. Acad. Sci. Working Group: Gene Sequence Methods for Classification of Select Agents
- 2007-08 Associate Editor, *Plos Pathogens*
- 2005-09 Permanent Member, NIH VirB Study Section
- 2003 Finalist/Runner-up, World Technology Award
- 1989-94 Established Investigator: American Heart Association
- 1984-86 Harvey Weaver Scholar, National Multiple Sclerosis Society

C. Contributions to Virology: The Baric laboratory has made significant contributions to our understanding of all aspects of CoV biology, including: i) CoV genetics and reverse genetics for SARS-CoV, MHV, MERS-CoV, HCoV NL63, PEDV, TGEV, bat SARS-like CoV (SL-CoV), BtCoV HKU-5 and others, ii) demonstration of proof-reading activities in the CoV genome, iii) identification and characterization of bat SL-CoV with pre-pandemic potential, iii) coronavirus transcription mechanisms, iv) mechanisms of interferon antagonism and interferon stimulated gene expression control, v) virus host susceptibility allele mapping, vi) epitope mapping of human monoclonal antibodies, vii) identification of broad spectrum human monoclonal antibodies against SARS-CoV and MERS-CoV, viii) mouse models of human disease (MERS-CoV and SARS-CoV), ix) aging and emerging coronavirus vaccine efficacy, and x) live and attenuated vaccine design in young and aged animal models of human disease. The Baric laboratory has also made major contributions to norovirus immunology and flavivirus reverse genetics and the human immune responses after infection.

Some representative major contributions outside and within the CoV field include:

1.  (b) (4)
2. Gralinski LE, Ferris MT, Aylor DL, Whitmore AC, Green R, Frieman MB, Deming D, Menachery VD, Miller DR, Buus RJ, Bell TA, Churchill GA, Threadgill DW, Katze MG, McMillan L, Valdar W, Heise MT, Pardo-Manuel de Villena F, Baric RS (2015) Genome Wide Identification of SARS-CoV Susceptibility Loci Using the Collaborative Cross. **PLOS Genetics**, 11(10): e1005504. PMID:26452100.
3. Lindesmith L, Moe C, Marionneau S, Ruvoen N, Jiang X, Lindblad L, Stewart P, LePendou J, Baric R (2003). Human susceptibility and resistance to Norwalk virus infection. **Nature Medicine**, 9(5):548-53. PMID:12692541.

- Lindesmith LC, Donaldson EF, Lobue AD, Cannon JL, Zheng DP, Vinje J, Baric RS (2008). Mechanisms of GII.4 norovirus persistence in human populations. **PLOS Medicine**, 5(2):e31. PMC2235898.

C.1. Coronavirus Pathogenesis and Virus Immunity. Our group has studied the role of virus-immune interactions in coronavirus and other emerging virus pathogenesis mechanisms.

- Rasmussen AL, Okumura A, Ferris MT, Green R, Feldmann F, Kelly SM, Scott DP, Safronetz D, Haddock E, LaCasse R, Thomas MJ, Sova P, Carter VS, Weiss JM, Miller DR, Shaw GD, Korth MJ, Heise MT, Baric RS, de Villena FP, Feldmann H, Katze MG (2014). Host genetic diversity enables Ebola hemorrhagic fever pathogenesis and resistance. **Science**, 2014 346(6212):987-91. PMC4241145.
- Gralinski LE, Sheahan TP, Morrison TE, Menachery VD, Jensen K, Leist SR, Whitmore A, Heise MT, Baric RS (2018). Complement Activation Contributes to Severe Acute Respiratory Syndrome Coronavirus Pathogenesis. **mBio**, 9(5). e01753-18. PMC6178621.
- Menachery VD, Einfeld AJ, Schäfer A, Josset L, Sims AC, Proll S, Fan S, Li C, Neumann G, Tilton SC, Chang J, Gralinski LE, Long C, Green R, Williams CM, Weiss J, Matzke MM, Webb-Robertson BJ, Schepmoes AA, Shukla AK, Metz TO, Smith RD, Waters KM, Katze MG, Kawaoka Y, Baric RS (2014). Pathogenic influenza viruses and coronaviruses utilize similar and contrasting approaches to control interferon-stimulated gene responses. **mBio**, 5(3): e01174-14. PMC4030454.
- Graham RL, Becker MM, Eckerle LD, Bolles M, Denison MR, Baric RS (2012). A live, impaired-fidelity coronavirus vaccine protects in an aged, immunocompromised mouse model of lethal disease. **Nature Medicine**, 18(12):1820-6. PMCID: PMC3518599.

C.2. Coronavirus Innate Immunity/Animal Models. The Baric laboratory group has studied CoV host range expansion using experimental evolution and SARS-CoV, MERS-CoV, civet SL-CoV, bat SL-CoV, and bat CoV HKU5 as models. This includes synthetic reconstruction of civet and bat CoV from *in silico* sequence, the first reported recovery of recombinant bat viruses, and characterization of host range phenotypes *in vitro* and *in vivo*. Applications of experimental evolution have focused on molecular mechanisms associated with virus-receptor interactions in viral persistence, virus innate immune interactions, and increased virulence in mice.

- Agnihotram S, Yount BL, Donaldson EF, Huynh J, Menachery VD, Gralinski LE, Graham RL, Becker MM, Tomar S, Scobey TD, Osswald HL, Whitmore A, Gopal R, Ghosh AK, Mesecar A, Zambon M, Heise M, Denison MR, Baric RS (2014). A mouse model for Betacoronavirus subgroup 2c using a bat coronavirus strain HKU5 variant. **mBio**, 5(2): e00047-14. PMC3977350.
- Sheahan T, Rockx B, Donaldson E, Corti D, Baric R (2008). Pathways of cross-species transmission of synthetically reconstructed zoonotic severe acute respiratory syndrome coronavirus. **Journal of Virology**, 82(17):8721-32. PMC2519660
- Becker MM, Graham RL, Donaldson EF, Rockx B, Sims AC, Sheahan T, Pickles RJ, Corti D, Johnston RE, Baric R*, Denison MR* (2008). Synthetic recombinant bat SARS-like coronavirus is infectious in cultured cells and in mice. **Proceedings of the National Academy of the Sciences**, 105(50):19944-9. PMC2588415. (* = co-first authors)
- Menachery VD, Schäfer A, Burnum-Johnson KE, Mitchell HD, Einfeld AJ, Walters KB, Nicora CD, Purvine SO, Casey CP, Monroe ME, Weitz KK, Stratton KG, Webb-Robertson BM, Gralinski LE, Metz TO, Smith RD, Waters KM, Sims AC, Kawaoka Y, Baric RS (2018). MERS-CoV and H5N1 influenza virus antagonize antigen presentation by altering the epigenetic landscape. **Proceedings of the National Academy of the Sciences**, 115(5): E1012-E1021. PMID: 29339515.

C.3. Virus Genetic Platforms. The Baric laboratory has pioneered reverse genetic analyses of CoVs and DENVs. Several CoV infectious cDNA clones are available in the lab, including SARS-CoV, MERS-CoV, conventional human and model CoVs, and several bat CoVs with pandemic potential. The availability of these genetic platforms allows for detailed studies into the role of viral genes in pathogenesis, innate immune antiviral immunity, vaccine performance and design, virus-receptor interactions, entry and virus evolution.

- Yount B, Curtis K, Fritz L, Hensley L, Jahrling P, Prentice E, Denison M, Geisbert T, Baric RS (2003). Reverse Genetics with a full length infectious cDNA for the SARS Coronavirus. **Proceedings of the National Academy of the Sciences**, 100(22): 12995-13000. PMCID: PMC240733.

2. Rockx B, Sheahan T, Donaldson E, Harkema J, Sims A, Heise M, Pickles R, Cameron M, Kelvin D, [Baric R](#) (2007). Synthetic reconstruction of zoonotic and early human severe acute respiratory syndrome coronavirus isolates that produce fatal disease in aged mice. **Journal of Virology** 81(14):7410-23. PMC1933338.
3. Widman DG, Young E, Yount BL, Plante KS, Gallichotte EN, Carbaugh DL, Peck KM, Plante J, Swanstrom J, Heise MT, Lazear HM, [Baric RS](#) (2017). A Reverse Genetics Platform that Spans the Zika Virus Family Tree. **mBio**, 8(2): e02014-16. PMC5340872
4. Donaldson EF, Yount B, Sims AC, Burkett S, Pickles RJ, [Baric RS](#) (2008). Systematic assembly of a full-length infectious clone of human coronavirus NL63. **Journal of Virology**, 82(23):11948-57. PMC2583659.

C4. Virus Vaccine Design and Antiviral Immunotherapy. Viruses are major causes of morbidity and mortality globally. The Baric laboratory has used structure-guided immunogen design and epitope exchange to build multivalent immunogens to increase vaccine breadth and diagnostic potential.

1. Deming DJ, Sheahan T, Heise M, Yount B, Davis N, Sims A, Suthar M, Whitmore JH, Pickles R, West A, Donaldson E, Curtis K, Johnston, RE, [Baric RS](#) (2006). Vaccine efficacy in senescent mice challenged with recombinant SARS-CoV bearing epidemic and zoonotic spike variants. **PLOS Medicine**, 3(12): e525 PMID: PMC1716185.
2. Tang XC, Agnihothram SS, Jiao Y, Stanhope J, Graham RL, Peterson EC, Avnir Y, Tallarico AS, Sheehan J, Zhu Q, [Baric RS](#), Marasco WA (2014). Identification of human neutralizing antibodies against MERS-CoV and their role in virus adaptive evolution. **Proceedings of the National Academy of the Sciences**, 111(19):E2018-26. PMC4024880
3. Lindesmith LC, Ferris MT, Mullan CW, Ferreira J, Debbink K, Swanstrom J, Richardson C, Goodwin RR, Baehner F, Mendelman PM, Bargatze RF, [Baric RS](#) (2015). Broad blockade antibody responses in human volunteers after immunization with a multivalent norovirus VLP candidate vaccine: immunological analyses from a phase I clinical trial. **PLOS Medicine**, 12(3):e1001807 PMC4371888.
4. Bolles M, Deming D, Long K, Agnihothram S, Whitmore A, Ferris M, Funkhouser W, Gralinski L, Totura A, Heise M, [Baric RS](#) (2011). A double-inactivated severe acute respiratory syndrome coronavirus vaccine provides incomplete protection in mice and induces increased eosinophilic proinflammatory pulmonary response upon challenge. **Journal of Virology**, 85(23):12201-15. PMC3209347

D. Research Support.

U19 AI 100625 Baric/Heise (MPI) 09/01/17-08/31/22

Systems Immunogenetics of Biodefense Pathogens in the Collaborative Cross

The Collaborative Cross is a mouse resource for study of complex genetic interactions in diverse populations, to identify novel polymorphic genes regulating immune responses to SARS, influenza and WNV, analyze genetic underpinning of immune phenotypes in mice and humans, and generate panels of genetically defined mice to probe polymorphic gene control of immune responses against a pathogens or other immune stimuli.

R01 AI108197 Denison/Baric (MPI) 05/01/18-04/30/23

Determinants of Coronavirus Fidelity in Replication and Pathogenesis

Experiments in this aim will test the hypothesis that nsp14 functions in maintaining high replication fidelity and viral RNA synthesis are coupled and that targeted engineered mutations across nsp14 alter: a) RNA fidelity outcomes; b) sensitivity to nucleoside mutagens and polymerase inhibitors; c) sensitivity to innate immunity.

HHSN2722010000191-HHSN27200003 Baric (PI) 09/30/17-03/31/24

MERS-CoV Mouse Model for Vaccine & Therapeutic Testing (Task Order A57)

Use generation of transgenic mice and modifications to the MERS-CoV genome to identify a mouse model for MERS-CoV that recapitulates human disease phenotypes for evaluating vaccine platforms and therapeutics.

U19 AI 109680 Whitley (PI) 03/01/14-02/28/19

Antiviral Drug Discovery and Development Center

The specific aims of the proposal will identify small molecule inhibitors of CoV fidelity and RNA capping, define their mechanism of action, and determine their efficacy against SARS-CoV and across CoV families using in vivo mouse models of acute and persistent CoV disease. Role: Co-Investigator

- U19 AI 109761 Lipkin (PI) 03/01/14-02/28/19
 Diagnostic and Prognostic Biomarkers for Severe Viral Disease
 The goal is to develop new platform technologies that use functional genomics as diagnostic and prognostic indicators of severe end stage lung disease, systemic and enteric diseases following virus infection, including coronaviruses, flaviviruses and noroviruses. Role: Project Leader
- R01 AI110700 Baric (PI) 04/20/15-03/31/20
 Mechanisms of MERS-CoV Entry, Cross-species Transmission and Pathogenesis
 The overall goal is to build a comprehensive understanding of the molecular mechanisms guiding group 2c CoV receptor recognition, entry and pathogenesis.
- (b) (4) Baric (PI) (b) (4)
 Breadth of Blockade Antibody Responses Following Norovirus Vaccination.
 (b) (4) and UNC will collaborate to evaluate the breadth of the antibody blockade response following norovirus vaccination in various human volunteer populations.
- P01 AI106695 Harris (PI) 07/1/2015-6/30/20
 Protective immunity following dengue virus natural infections and vaccination
 Project 2: Aravinda deSilva and Ralph S. Baric (Co-PI).
 The goal is to identify natural correlates of protective immunity following natural infection and or vaccination.
 Role: Co-Investigator
- R01-AI125198 de Silva (PI) 05/01/16 – 04/30/21
 Preclinical assays to predict dengue vaccine efficacy
 We use samples from DENV tetravalent Sanofi Pasteur vaccine clinical trials to identify mechanisms and correlates of protective immunity or breakthrough infections in vaccinees. Role: Co-investigator.
- R01 1AI132178 Baric/Sheahan(MPI) 08/15/17-8/14/22
 Broad-spectrum antiviral GS-5734 to treat MERS-CoV and related emerging CoV.
 The goal of this proposal is collaborate with Gilead Inc. and obtain GS-5734 preclinical data for IND development and translational studies, all designed to move the therapeutic into human trials.
- (b) (4) Breuer (PI) (b) (4)
 Why do Norovirus pandemics occur and how can we control them?
 The program uses hospital and community cohorts of NoV infected individuals to ask fundamental questions into the molecular and evolutionary epidemiology of human NoV infections, focusing on the GII.4 strains, leading to new models of virus emergence and disease prevention. Role: Co-Investigator:
- R01 AI 089728 Li (PI) 07/01/16-06/30/21
 University of Minnesota/NIAID
 Receptor recognition and cell entry of coronaviruses
 The program studies receptor usage and cell entry mechanisms of emerging coronaviruses, focused on PEDV, MHV and SARS-like Coronaviruses. Role: Co-Investigator
- R21 AI135682 Georgiou (PI) 04/01/18-03/30/20
 UT Austin/NIAID
 Molecular Analysis of Serum Antibody Constituents in Zika Virus Infection.
 The goal of this application is to identify antibodies that make up the serologic repertoire after Zikv infection of naive and DENV preimmune individuals. Role: Co-investigator.
- R21 AI137887 Moorman/Heise (MPI) 02/05/18-01/31/20
 NIH/NIAID \$150,000
 Molecular Characterization of Functional RNA Structures in the ZikV genome
 The goal of this project is to study the RNA Structure of Zika virus. Proposed studies will identify new viral virulence determinants that can be targeted to generate safer and more effective Zika virus vaccines and therapeutics. Role: Co-Investigator.

BIOGRAPHICAL SKETCH

NAME Noam Ross	POSITION TITLE Co-Investigator
eRA COMMONS USER NAME (b) (6)	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	MM/YY	FIELD OF STUDY
Brown University (US)	BS	05/2006	Environmental Sci.
University of California-Davis, (US)	PhD	09/2015	Ecology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	MM/YYYY	FIELD OF STUDY
Brown University, Providence, RI	BS	05/2006	Environmental Science
University of California-Davis, Davis, CA	Ph.D	09/2015	Ecology

A. Personal Statement

The goal of our proposal is to identify and quantify the drivers of bat-borne coronavirus spillover in Southern China, by identifying which host traits, viral characteristics, and human behaviors are associated with the highest risk of CoV exposure. This will require statistical and mathematical modeling approaches that can integrate the separate ecological, evolutionary, and behavioral processes into a robust framework. My background in quantitative disease ecology makes me a natural fit to work on the statistical and mathematical aspects of this project. My research has consisted of developing both statistical and theoretical models for emerging diseases in both plants, mammals, and humans. I have developed dynamic models of diseases such as MERS and Ebola virus in wildlife populations in order to support targeting field surveillance, and applied predictive empirical and mechanistic modeling techniques to the study of Nipah virus emergence and circulation in bats. My statistical work has included analysis of survey-based evidence of new disease emergence in Uganda, global predictive models of anthrax emergence, and large-scale macroecological patterns in host-virus associations which captured previously unmodeled heterogeneity in disease burden. Importantly, this work included the creation of methods and open-source tools for simulating, fitting, and performing optimization using such models, ensuring that I will be able to support the creation of robust and reproducible statistical models this project.

- Olival KJ, Hosseini PR, Zambrana-Torrel C, Ross N, Bogich TL, Daszak P (2017). Host and viral traits predict zoonotic spillover from mammals. **Nature** 546: 646–650
- Salerno J, Ross N, Ghai R, Mahero M, Travis DA, Gillespie TR, Hartter J (2017) Human-wildlife interactions predict febrile illness in park landscapes of western Uganda. **EcoHealth** 14(4):675-690.
- Carlson CJ, Kracalik I, Ross N, Alexander K, Hugh-Jones ME, Fegan M, Elkin B, Epp T, Shury T, Bagirova M, Getz WM, Blackburn JK (2018) The global distribution of *Bacillus anthracis* and associated anthrax risk to humans, livestock, and wildlife. **Nature Microbiology** In Review.

B. Positions and Honors**Positions and Employment**

2006 Contract Market Researcher: Energy Efficient Products Initiative, Wal-Mart, Providence, RI
2006 - 07 Analyst, Environmental Markets and Performance, GreenOrder, New York, NY

- 2007 - 09 Senior Analyst, Environmental Markets and Performance, GreenOrder, New York, NY
2010 - 15 Graduate Researcher, University of California-Davis
2015 - 17 Disease Ecologist, EcoHealth Alliance, New York, NY
2017 - Senior Research Scientist, EcoHealth Alliance, New York, NY

Other Experience and Professional Memberships

- 2012 - 13 Member, NSF IGERT.org advisory board
2012 - 15 Founder and Organizer, Davis R Users' Group
2013 - Member, Ecological Society of America
2014 - Contributor and reviewer, ROpenSci
2014 - Meeting Session Organizer, Ecological Society of America
2015 - Instructor, Software Carpentry Foundation
2015 - Instructor, Data Carpentry Foundation
2015 - Associate Editor, ROpenSci
2016 - Member, R Epidemics Consortium

Reviewer: *Ecology Letters*, *Theoretical Ecology*, *EcoHealth*, *Conservation Letters*, *Biological Reviews*, *Journal of Open Source Software*

Awards and Fellowships

- 2010 NSF IGERT Traineeship in Rapid Environmental Change
2010 UC Davis Graduate Ecology Fellowship
2012 Don Dahlsten Memorial Grant, California Forest Pest Council
2012 NSF IGERT Bridge Fellowship

C. Contribution to Science

1. **Modeling Dynamics of Heterogeneity:** I have worked on both theoretical and applied approaches of dealing with heterogeneity when modeling ecological-epidemiological dynamics. This work focused on fungal disease epidemics using a framework traditionally used for parasites of stable populations in order to capture the role of individual variation in infection level. While the mathematical basis of these models for populations at or approximately at equilibrium is well established, their dynamic properties are less well known due to analytical intractability, and thus they are little-used in emerging diseases and epidemics. My work showed how and where these models diverged from other, traditional models in their dynamical properties, and identified statistical patterns that could be used to identify where these models are appropriate. I developed numerical tools for their simulation, modeling and control, which have been used in applied disease management studies.
 - a. Schreiber S, Ross N (2016) Individual-based Integral Projection Models: The role of size-structure on extinction risk and establishment success. **Methods in Ecology and Evolution**. <http://dx.doi.org/10.1111/2041-210X.12537>
 - b. Cobb RC, Ross N, Hayden JK, Eyre CA, Dodd RS, Frankel SJ, Garbelloto M, Rizzo DM (2018) Promise and pitfalls of endemic resistance when cultural resources are threatened by exotic tree pathogens. **Phytopathology**. <https://doi.org/10.1094/PHYTO-04-18-0142-R>
 - c. Cobb RC, Hartsough P, Ross N, Klein J, LaFever DH, Frankel SJ, Rizzo DM (2017) Resiliency or restoration: management of sudden oak death before and after outbreak. **Forest Phythophthoras**. <https://doi.org/10.5399/osu/fp.7.1.4021>
 - d. Ross N (2015). Disease with Multiple Infections: Population Structure, Dynamics, and Control. **University of California, Davis**. Dissertation.
2. **Modeling decision-making in complex systems:** A long-standing theme of my work has been linking ecological dynamics to social systems and decision-making under uncertainty. This has included determining whether statistical signals of ecological changes are sufficient to justify management changes in fisheries, and has recently extended to optimizing investment in disease surveillance and intervention.

- a) Machalaba C, Smith KM, Awada L, Berry K, Berthe F, Bouley TA, Bruce M, Abrahantes JC, Turabi EL, Feferholtz Y, Flynn L, Fournié G, Andre A, Grace D, Jonas O, Kimani T, Gall FL, Jose J, Peyre MM, Pinto J, Ross N, Rüegg SR, Salerno RH, Seifman R, Zambrana-Torrel C, Karesh WB. (2017) One Health Economics to confront disease threats. **Transactions of the Royal Society of Tropical Medicine and Hygiene** <https://doi.org/10.1093/trstmh/trx039>
- b) Boettiger C*, Ross N*, Hastings A (2013) Early Warning Signals: The Charted And Uncharted Territories. **Theoretical Ecology** <http://dx.doi.org/10.1007/s12080-013-0192-6> (*Co-equal authors)
- c) Fuller K, Kling D, Kroetz K, Ross N, Sanchirico JN (2013) Economics and Ecology of Open-Access Fisheries. In: Shogren JF (ed.) **Encyclopedia of Energy, Natural Resource, and Environmental Economics, Vol. 2** p.39-49. Amsterdam: Elsevier. <http://dx.doi.org/10.1016/B978-0-12-375067-9.00114-5>

3. Statistical software and reproducibility: As associate editor of the ROpenSci project, and a member of the Software Carpentry foundation, I develop, evaluate, and set standards and develop training materials for open-source statistical software overseeing the publication of over 30 scientific software packages in the past two years. I have also worked in the development and dissemination of tools for the use of nonlinear modeling methods.

- a. Ross N (2016) fasterize: high performance raster conversion for modern spatial data. <https://github.com/ecohealthalliance/fasterize>

b.  (b) (4)

c.  (b) (4)

- d. Ross N (2018) Nonlinear Modeling in R with GAMs: An Interactive Course. **DataCamp** <https://www.datacamp.com/courses/nonlinear-modeling-in-r-with-gams>

D. Research Support

Ongoing

USAID EPT PREDICT-2 Mazet (PI) 10/01/14 – 09/30/19
 Conducting surveillance for novel pathogens in wildlife, livestock and people; characterizing human risk behavior; modeling risk of novel disease emergence; identifying mitigation strategies
 Amount: \$35 Million subcontract from a \$100 Million award
 Role: Disease Ecologist

1R01AI110964 Daszak (PI) 06/01/14 – 05/31/19
 NIAID: Understanding the Risk of Bat Coronavirus Emergence
 Bat ecological, human risk behavioral and virological studies to understand the risk of bat coronavirus emergence
 Role: Key Personnel

HDTRA1-14-1-0029 Karesh (PI) 5/17/16 – 5/16/18
 Understanding Rift Valley Fever in Republic of South Africa
 Role: Key Personnel

Completed

W911NF-13-1-0305 Hastings (PI) 9/1/13-8/31/16
 Army Research Office Mathematical Sciences Core Program
 Dynamics at Intermediate Time Scales and Management of Ecological Populations

Role: Supported Graduate Student

EF-0622770 Rizzo (PI) 8/23/06-8/31/11

NSF Ecology of Infectious Disease Program

Collaborative Research: Sudden Oak Death: Feedback Between a Generalist Pathogen, Hosts, and Heterogeneous Environments at Multiple Spatial and Temporal Scales

Role: Supported Graduate Student