Understanding the Risk of Bat Coronavirus Emergence

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Abstract

Understanding the Risk of Bat Coronavirus Emergence Novel zoonotic, bat-origin CoVs are a significant threat to global health and food security, as the cause of SARS in China in 2002, the ongoing outbreak of MERS, and of a newly emerged Swine Acute Diarrhea Syndrome in China. In a previous R01 we found that bats in southern China harbor an extraordinary diversity of SARSr-CoVs, some of which can use human ACE2 to enter cells, infect humanized mouse models causing SARS-like illness, and evade available therapies or vaccines. We found that people living close to bat habitats are the primary risk groups for spillover, that at one site diverse SARSr-CoVs exist that contain every genetic element of the SARS-CoV genome, and identified serological evidence of human exposure among people living nearby. These findings have led to 18 published peer-reviewed papers, including two papers in Nature, and a review in Cell. Yet salient questions remain on the origin, diversity, capacity to cause illness, and risk of spillover of these viruses. In this R01 renewal we will address these issues through 3 specific aims:

Aim 1. Characterize the diversity and distribution of high spillover-risk SARSr-CoVs in bats in southern China. We will use phylogeographic and viral discovery curve analyses to target additional bat sample collection and molecular CoV screening to fill in gaps in our previous sampling and fully characterize natural SARSr-CoV diversity in southern China. We will sequence receptor binding domains (spike proteins) to identify viruses with the highest potential for spillover which we will include in our experimental investigations (Aim 3).

Aim 2. Community, and clinic-based syndromic, surveillance to capture SARSr-CoV spillover, routes of exposure and potential public health consequences. We will conduct biological-behavioral surveillance in high-risk populations, with known bat contact, in community and clinical settings to 1) identify risk factors for serological and PCR evidence of bat SARSr-CoVs; & 2) assess possible health effects of SARSr-CoVs infection in people. We will analyze bat-CoV serology against human-wildlife contact and exposure data to quantify risk factors and health impacts of SARSr-CoV spillover.

Aim 3. In vitro and in vivo characterization of SARSr-CoV spillover risk, coupled with spatial and phylogenetic analyses to identify the regions and viruses of public health concern. We will use S protein sequence data, infectious clone technology, in vitro and in vivo infection experiments and analysis of receptor binding to test the hypothesis that % divergence thresholds in S protein sequences predict spillover potential. We will combine these data with bat host distribution, viral

diversity and phylogeny, human survey of risk behaviors and illness, and serology to identify SARSr-CoV spillover risk hotspots across southern China. Together these data and analyses will be critical for the future development of public health interventions and enhanced surveillance to prevent the re-emergence of SARS or the emergence of a novel SARSr-CoV.

Public Health Relevance

Daszak, Peter 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.

Funding Agency

Agency	National Institute of Health (NIH)
Institute	National Institute of Allergy and Infectious Diseases (NIAID)
Type	Research Project (R01)
Project #	2R01AI110964-06
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Program Officer	Stemmy, Erik J
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Project End	2020-04-24
Budget Start	2019-07-24
Budget End	2020-04-24
Support Year	6
Fiscal Year	2019
Total Cost	
Indirect Cost	

Institution

Name	Ecohealth Alliance, Inc.
Department	
Type	
DUNS #	077090066
City	New York

State	NY
Country	United States
Zip Code	10001

Related projects

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NIH 2018 R01 AI	Understanding the Risk of Bat Coronavirus Emergence Daszak, Peter / Ecohealth Alliance, Inc.	
NIH 2017 R01 AI	Understanding the Risk of Bat Coronavirus Emergence Daszak, Peter / Ecohealth Alliance, Inc.	$597,112
NIH 2016 R01 AI	Understanding the Risk of Bat Coronavirus Emergence Daszak, Peter / Ecohealth Alliance, Inc.	
NIH 2015 R01 AI	Understanding the Risk of Bat Coronavirus Emergence Daszak, Peter / Ecohealth Alliance, Inc.	$630,445
NIH 2014 R01 AI	Understanding the Risk of Bat Coronavirus Emergence Daszak, Peter / Ecohealth Alliance, Inc.	$666,442

Publications

Luo, Chu-Ming; Wang, Ning; Yang, Xing-Lou et al. **(2018)** Discovery of Novel Bat Coronaviruses in South China That Use the Same Receptor as Middle East Respiratory Syndrome Coronavirus. J Virol 92:

Luo, Yun; Li, Bei; Jiang, Ren-Di et al. **(2018)** Longitudinal Surveillance of Betacoronaviruses in Fruit Bats in Yunnan Province, China During 2009-2016. Virol Sin 33:87-95

Zhou, Peng; Fan, Hang; Lan, Tian et al. **(2018)** Fatal swine acute diarrhoea syndrome caused by an HKU2-related coronavirus of bat origin. Nature 556:255-258

Wu, Zhiqiang; Lu, Liang; Du, Jiang et al. **(2018)** Comparative analysis of rodent and small mammal viromes to better understand the wildlife origin of emerging infectious diseases. Microbiome 6:178

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Hu, Ben; Zeng, Lei-Ping; Yang, Xing-Lou et al. **(2017)** Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insights into the origin of SARS coronavirus. PLoS Pathog 13:e1006698

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Thanks for the COVID-9/11, Dr. Frankenstein. Looks like your monster is out of the lab. Many scientists warned against this type of gain of function research.

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Berk
a year ago edited

I wonder if "We will use [...] infectious clone technology, in vitro and in vivo infection experiments" means making modified viruses? The budget dates and when the Wuhan lab was running job ads seems to fit with the arrival of covid in the vicinity of the lab. Complete coincidence of course but I'm still curious.

^ | ⌄ Reply

> **Lisa Hudson** ➦ Berk
> 9 months ago
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> There is no such thing as a coincidence.
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It's like this guy predicted the high likelihood of the coronavirus epidemic!e

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> Or started it through his funding of the wuhan virology labs...where they've taken bats from nature that have these viruses and brought them to wuhan!!!
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Stop the Fear Mongering . Unless you have specific FACTS, that can be independently validated, This "disqussion" is nothing but propagating rumours, distrust, xenophobia, lies, tribal bullsht, and does absolutely nothing to help.

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