From:
 Munster, Vincent (NIH/NIAID) [E]

 Sent:
 Sun, 2 Feb 2020 08:33:11 -0700

To: Dr VAN KERKHOVE, Maria; Gerber, Susan I. (CDC/DDID/NCIRD/DVD); Malik Peiris; Abdullah Assiri; Young-Ki Choi; Tong, Suxiang (Sue) (CDC/DDID/NCIRD/DVD); Thornburg, Natalie

(CDC/DDID/NCIRD/DVD); Tamin, Azaibi (CDC/DDID/NCIRD/DVD); Ghazi Kayali; 오명돈;

(b) (6)

Cc: Letko, Michael (NIH/NIAID) [F]; van Doremalen, Neeltje (NIH/NIAID) [E]

Subject: Re: MERS-CoV strain comparison manuscript

Sounds good, will add some language about the meeting,

Cheers,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: "VAN KERKHOVE, Maria" < (b)(6)Date: Saturday, February 1, 2020 at 1:52 PM (b) (6) "Gerber, Susan I. To: ' (b) (6) < (CDC/DDID/NCIRD/DVD)" < (b) (6) Abdullah Assiri (b) (6) Malik Peiris < (b) (6) Young-Ki Choi < (b) (6) "Tong, Suxiang (Sue) (CDC/DDID/NCIRD/DVD)" < (b) (6) "Tamin, (b) (6) Natalie Thornburg < Azaibi (CDC/DDID/NCIRD/DVD)" < (b) (6) Ghazi Kayali < (b) (6) (b) (6) " (b)(6)"Myoung-don" Oh" < (b) (6) < (b) (6) (b)(6)(b) (6) Neeltje van Doremalen Cc: Michael Letko < (b) (6)

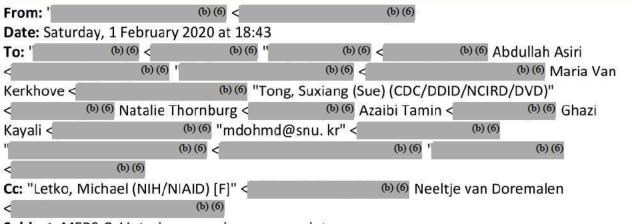
Subject: Re: MERS-CoV strain comparison manuscript

Dear Vincent and colleagues,

Many thanks for this outstanding work. May I kindly request that you include the background information about the WHO meeting held in Hong Kong in 2017 where the importance of these studies and the "ask" for this study was discussed in the introduction? I think its really important to mention this meeting, following the 2015 Korean outbreak.

I will need to submit for clearance on my end as well, but it could go really quickly once I have a revised draft.

Thanks so much, Maria



Subject: MERS-CoV strain comparison manuscript

Dear collaborators,

Please find attached the manuscript on the stability and strain comparison of MERS-CoV. I tried to be as inclusive as possible and include everyone who made a significant contribution to this manuscript. If however you feel I might have overlooked someone, please reach out and I'll add this person to the manuscript.

Also, for some of the co-authors from the HKU, Korean and CDC labs I don't have the email, so please distribute the draft to these people.

I know that most of you are involved in the 2019-NCoV outbreak and are extremely busy, but I think this work is an important collaborative effort (also with regards of the new coronavirus outbreak) and we are hoping to submit in ~14 days to ensure rapid dissemination of this research.

Kind regards,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: Munster, Vincent (NIH/NIAID) [E]
Sent: Sat, 1 Feb 2020 10:42:59 -0700

To: Gerber, Susan I. (CDC/DDID/NCIRD/DVD); Malik Peiris; Abdullah Assiri; Young-Ki

Choi; VAN KERKHOVE, Maria; Tong, Suxiang (Sue) (CDC/DDID/NCIRD/DVD); Thornburg, Natalie

(CDC/DDID/NCIRD/DVD); Tamin, Azaibi (CDC/DDID/NCIRD/DVD); Ghazi Kayali; 오명돈;

(b) (6) (b) (6)

Cc: Letko, Michael (NIH/NIAID) [F]; van Doremalen, Neeltje (NIH/NIAID) [E]

Subject: MERS-CoV strain comparison manuscript

Attachments: 1\_24\_20 - Pathogenesis and stability of diverse MERS-CoV strains\_VM\_ML .docx

Importance: High

#### Dear collaborators,

Please find attached the manuscript on the stability and strain comparison of MERS-CoV. I tried to be as inclusive as possible and include everyone who made a significant contribution to this manuscript. If however you feel I might have overlooked someone, please reach out and I'll add this person to the manuscript.

Also, for some of the co-authors from the HKU, Korean and CDC labs | don't have the email, so please distribute the draft to these people.

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Kind regards,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

# Surface-aerosol stability and pathogenicity of diverse MERS-CoV strains from 2012 - 2018

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#### Abstract

Middle East Respiratory Syndrome coronavirus (MERS-CoV) was first detected in the human population in 2012 and has continued to cause human cases in the Middle East as a result of frequent spillover from dromedary camels to humans and subsequent nosocomial transmission. MERS-CoV strains from different geographic regions and human or dromedary camel origin exhibit genetic variation in all open reading frames, including nonsynonymous mutations and deletions. While some of these MERS-CoV variants have been characterized at the molecular level, it is still unclear how viral variation influences pathogenicity and environmental stability. Here we compare the environmental stability, replication kinetics and pathogenicity of several diverse strains of MERS-CoV. We show that MERS-CoV remained infectious for 3 hours within aerosols and over 48 hours on surfaces. In addition, both copper and silver surfaces reduced the viability of MERS-CoV compared to either polypropylene or stainless steel. While most of the MERS-CoV strains performed similarly in our tests, one camel-derived isolate had significantly reduced environmental surface stability, losing infectivity within 24-hours while at the same time exhibiting markedly increased replication kinetics, whereas another was significantly different in pathogenicity. Taken together, these findings underscore the importance of continual surveillance in humans and camels together with genetic and phenotypic characterization of novel MERS-CoV strains. It highlights the relative stability of MERS-CoV in aerosols and fomites, suggesting their importance in nosocomial transmission. In addition, it shows that the ongoing, natural mutation of MERS-CoV results in different viral phenotypes

#### Introduction

Middle East Respiratory Syndrome Coronavirus (MERS-CoV) was first discovered in 2012 and continues to cause outbreaks in the Middle East as a result of frequent spillover from dromedary camels to humans. MERS-CoV has a mortality rate of ~35% and has spread to 27 countries (1, 2). While dromedary camels have been shown to be the immediate animal reservoir, phylogenetic analysis has shown that humans are a dead-end host (3). Approximately 41% of MERS-CoV cases in the Kingdom of Saudi Arabia (KSA) are primary, resulting from direct camel-to-human transmission (4). To date, MERS-CoV has been detected in camels in Burkina Faso, Egypt, Ethiopia, Jordan, Kenya, Morocco, Nigeria, Saudi Arabia, Senegal, Sudan, Tunisia, and Uganda (5-13). While MERS-CoV has been isolated from camels in Africa, there are no reports of zoonotic transmission to humans, unlike what has been observed in the Middle East (9).

Human-to-human transmission of MERS-CoV has been reported and accounts for 59% of cases in KSA. Human-to-human transmission is inefficient and primarily occurs in hospital settings and within households. (14). The exact route of transmission between humans however, is currently still unclear. It is possible that direct contact with infected individuals, as well as fomite and aerosol transmission all collectively contribute to viral transmission. Epidemiological studies have mapped indirect patient contact within hospitals, providing evidence for aerosol and hospital-worker mediated spread (15-18). The largest outbreak of MERS-CoV outside of the Middle East occurred in South Korea. A single traveler from the Middle East brought MERS-CoV to South Korea, resulting in 185 subsequent infections (19).

Coronaviruses are the largest non-segmented RNA-based viruses identified, with genome sizes averaging around 30kB. Even though coronavirus polymerase has a proofreading function, coronaviruses within the same species are polymorphic. A recent study found approximately 99% nucleotide similarity as well as small deletions in nonstructural proteins

between various isolates collected in the Middle East and North Africa (20). While this variation may seem minimal, 1% is equivalent to 300 nucleotide changes in the 30kB genome. Indeed, many of these changes are nonsynonymous and are distributed throughout the viral genome. As previously shown, single amino acid changes in the viral genome can result in profoundly varying phenotypes in viral replication (21). Additionally, one study has aimed to functionally characterize some of these MERS-CoV strain differences, with a particular focus on ORF deletions, and found significant effects in the virus' ability to antagonize host innate immune pathways, translating to viral attenuation in an animal model (20). Given that MERS-CoV continues to cause outbreaks and evolve, these findings underscore the importance of characterizing how MERS-CoV genetic variation alters viral replication, pathogenicity and stability.

Here we expand on previous work from others by testing a broad panel of viral isolates collected from both humans and camels, representing every major geographic region with MERS-CoV outbreaks and spanning from early to contemporary outbreaks. Because MERS-CoV spreads within households and hospitals, we characterized and compared viral phenotypes with immediate implications for public health. We focused on environmental stability both in aerosols as well as surface stability on common materials found in hospitals, replication kinetics in immortalized human cell lines and primary human airway epithelial cultures as well as pathogenicity in a transgenic mouse model our lab previously developed to test vaccine efficacy (22).

#### Methods

# Ethical approval

Animal experiment approval was obtained by the Institutional Animal Care and Use Committee (IACUC) at Rocky Mountain Laboratories. All animal experiments were executed in an Association for Assessment and Accreditation of Laboratory Animal

Care (AALAC)-approved facility, following the guidelines in NIH Guide for the Care and Use of Laboratory Animals, Animal Welfare Act, United States Department of Agriculture and United States Public Health Service Policy on Humane Care and Use of Laboratory Animals. The Institutional Biosafety Committee (IBC) approved work with MERS-CoV strains under BSL3 conditions. Sample inactivation was performed according to IBC-approved standard operating procedures.

# MERS-CoV stock propagation

MERS-CoV strains were obtained from different collaborators and passaged once in VeroE6 cells in DMEM (Sigma Aldrich) supplemented with 2% fetal bovine serum (Fisher Scientific), 1 mM L-glutamine (Thermo Fischer), 50 U/ml penicillin (Thermo Fischer) and 50 μg/ml streptomycin (Thermo Fischer). Virus stocks were clarified by centrifugation and frozen at -80°C. Virus titrations were performed by endpoint titration in VeroE6 cells inoculated with tenfold serial dilutions of virus. Cytopathic effect was scored at D5 and TCID<sub>50</sub> was calculated from four replicates by the Spearman-Karber method (23).

# Sequencing stocks

All experiments, through second-strand cDNA synthesis, were performed in a BSLII cabinet for safety considerations. MERS-CoV samples were treated with RiboZero H/M/R rRNA (Illumina, San Diego, CA) depletion mix following the manufacturer's instructions. After Ampure RNACleanXP (Beckman Coulter, Brea, CA) purification, the enriched RNA was eluted and assessed on a BioAnalyzer RNA Pico

Chip (Agilent Technologies, Santa Clara, CA). These samples were then used to prepare second-strand cDNA, following the Truseq Stranded mRNA Library Preparation Guide, Revision E., (Illumina, San Diego, CA). To remove any remaining positive-strand RNA, samples were treated with RiboShredder RNase Blend. After AMpure XP purification (Beckman Coulter, Brea, CA), samples were analyzed on a RNA Pico chip to confirm RNA removal and the ends were adenylated following manufacturer's recommendations. Final libraries were visualized on a BioAnalyzer DNA1000 chip (Agilent Technologies, Santa Clara, CA) and quantified using KAPA Library Quant Kit (Illumina) Universal qPCR Mix (Kapa Biosystems, Wilmington, MA) on a CFX96 Real-Time System (BioRad, Hercules, CA). Libraries were pooled together in equimolar concentrations and sequenced on the MiSeq (Illumina, Inc, San Diego, CA) using on-board cluster generation and 2 x 250 paired-end sequencing. The cluster density was at 454k/mm2 per lane resulting in 8.7 Million reads passing filter per run with an average 85% > Q30.

# **Phylogenetics**

All available MERS-CoV genome sequences were downloaded from GenBank and curated to remove sequences that were not independently sampled. The GenBank MERS-CoV sequences were aligned with the consensus sequences for MERS-CoV isolates used in this study using the MAFFT v. 7.388 plugin (24) in Geneious Prime. The phylogenetic tree was inferred using the maximum likelihood method under the GTR + gamma model of nucleotide substitution with 1000 bootstrap replicates implemented with PhyML version 3.3.20190321.

Stability of MERS-CoV on surface and in aerosols

Four different surfaces were evaluated: polypropylene (ePlastics), AISI 304 alloy stainless steel (Metal Remnants), copper (99.9%) (Metal Remnants) and silver (99.9%) (Sigma-Aldrich). Discs with a radius of 15 mm were cut out, sterilized and placed in 24-well plates. Each disc received 50 µl of MERS-CoV at a titer of 10<sup>5</sup> TCID<sub>50</sub>/mL. At appropriate times, 1 mL of DMEM was added to the well, aliquoted and stored at -80°C. All samples were titrated on VeroE6 cells.

Virus stability in aerosols was determined as described previously (25). Briefly, the collison nebulizer used to produce aerosols was loaded with 10<sup>6.5</sup> TCID<sub>50</sub>/ml of MERS-CoV in DMEM containing 2% FBS. Aerosols were maintained in the Goldberg drum and samples were collected at 0-, 30-, 60-, 120- and 180-minutes post aerosolization by passing air at 6L/min for 30 seconds from the drum through a 47mm gelatin filter (Sartorius). Filters were dissolved in 10 mL of DMEM containing 10% FBS and stored at -80°C. All samples were titrated on VeroE6 cells.

# Replication of MERS-CoV strains in vitro

VeroE6 cells were plated in 6-well plates and inoculated with an MOI of 0.01. Supernatant samples were obtained at 8, 24, 48 and 72 hours post infection (h.p.i.). Human airway epithelium inserts (HAE, Epithelix) were maintained as specified by manufacturer. HAEs were washed with 200 µl of phosphate-buffered saline for 30 minutes, followed by inoculation with MERS-CoV at an MOI of 0.1. Samples were obtained at 8, 24, 48, 72, and 96 h.p.i.

### Animal experiments

Transgenic *balb/c* mice expressing human DPP4 were inoculated intranasally (I.N.) with 10<sup>3</sup> TCID<sub>50</sub> MERS-CoV. Mice were weighed and oropharyngeal swabs were taken daily. At D3, four mice were euthanized, and lung tissue was harvested. The remaining six mice were monitored for survival. Mice were euthanized upon presence of severe disease signs (e.g. hunched posture, lack of movement) or >20% of weight loss.

RNA extraction and quantitative reverse-transcription polymerase chain reaction

Tissues were homogenized and RNA was extracted using the RNeasy method (Qiagen) according to the manufacturer's instructions. Swabs were added to 1 mL of DMEM, vortexed, and 140 µl was utilized for RNA extraction using the QiaAmp Viral RNA kit on the QIAxtractor. MERS-CoV viral RNA was detected via the UpE MERS-CoV assay (26) using the Rotor-GeneTM probe kit (Qiagen). MERS-CoV dilutions with known genome copies were run in parallel to allow calculation of genome copies in samples.

# Histology and immunohistochemistry

Necropsies and tissue sampling were performed according to IBC-approved protocols. Lungs were perfused with 10% formalin and processed for histologic review. Harvested tissues were fixed for a minimum of seven days in 10% neutral-buffered formalin and then embedded in paraffin. Tissues were processed using a VIP-6 Tissue Tek, (Sakura Finetek, USA) tissue processor and embedded in Ultraffin paraffin polymer (Cancer

Diagnostics, Durham, NC). Samples were sectioned at 5 μm, and resulting slides were stained with hematoxylin and eosin. Specific anti-CoV immunoreactivity was detected using MERS-CoV nucleocapsid protein rabbit antibody (Sino Biological Inc.) at a 1:4000. The tissues were processed for immunohistochemistry using the Discovery ULTRA automated IHC/ISH staining instrument (Ventana Medical Systems) with a Discovery ChromoMap DAB (Ventana Medical Systems) kit, scanned with the Aperio ScanScope AT2 (Aperio Technologies, Inc.) and the entire section analyzed with the ImageScope Positive Pixel Count algorithm (version 9.1). All tissue slides were evaluated by a board-certified veterinary anatomic pathologist.

# Statistical analyses

All analyses were done using GraphPad Prism version 7.05 for Windows. All strains were compared to EMC/12. Linear regression was determined for the mean value of three runs per virus. Statistical significance was determined using ordinary one-way ANOVA followed by Bonferonni's multiple comparisons test or a two-way unpaired student's t-test.

#### Results

Stability of different MERS-CoV strains in aerosols or as fomites

We utilized eight different MERS-CoV strains in the current study. Five strains were isolated from human cases and three strains were isolated from dromedary camels. Strains were isolated between 2012 and 2018, and originated from the Middle East (5), Africa (2) or South Korea (1) (*Table*). All originally obtained viruses were

passaged once in VeroE6 cells. Virus stocks were sequenced on the MiSeq. Mutations compared to the published sequence are detailed in table S1.

Available full-length MERS-CoV sequences were downloaded from Genbank. A phylogenetic maximum likelihood tree was constructed of the GenBank MERS-CoV sequences and the consensus sequences for the MERS-CoV isolates. The investigated MERS-CoV strains were distributed throughout the phylogenetic tree (*Figure 1*) and thus represent a broad sample of known genetic variation within currently circulating MERS-CoV strains.

Stability of MERS-CoV strains was determined in aerosols as well as in fomites.

We investigated the stability of MERS-CoV as fomites on four different surfaces:

polypropylene, stainless-steel, copper and silver. These surfaces were chosen as they represent commonly encountered surfaces in hospital environments or could function as a virocidal.

Back-titrations of all virus strains showed comparable starting virus titers. Stability of MERS-CoV on polypropylene and stainless-steel surfaces was similar to results previously reported for MERS-CoV stability on surfaces (27), except for strain C/KSA/13. Infectious virus titers of C/KSA/13 were significantly lower compared to EMC/12 on polypropylene (0, 1, and 24hrs) and stainless-steel surfaces (0, 24, and 48hrs). In contrast, infectious virus titers were low for all strains on copper and silver surfaces at 24hrs. Linear regression was calculated for the first 24hrs for each surface, and loss of infectious virus was significantly higher on copper and silver surfaces than on polypropylene and stainless-steel surfaces (-0.11576, -0.08744, -0.0529, and -0.0469 respectively) (*Figure 2A*).

All MERS-CoV strains were aerosolized in a Goldberg drum, samples were taken at 0, 30, 60, 120 and 180 min post aerosolization and titrated. No significant differences in linear regression of loss of infectious virus in aerosols was detected between strains (EMC/12 = -0.00419; U/14 = -0.00781; KSA/15 = -0.00594; SK/15 = -0.00682; KSA/18 = -0.00527; C/KSA/13 = -0.00639; C/E/13 = -0.00671; C/BF/15 = -0.00477). For all MERS-CoV strains, infectious virus could still be detected at 180 minutes post aerosolization (*Figure 2B*).

In vitro replication of different MERS-CoV strains

Growth of all strains was then compared in two different *in vitro* cell systems:

VeroE6 cells and HAE cultures. All strains were compared to the reference strain

EMC/12 using a two-tailed unpaired Student's t-test. At 48 hpi, C/KSA/13 and KSA/15

grew to significantly higher titers than EMC/12 in VeroE6 cells. At 72 hpi, C/KSA/13 and

C/BF/15 grew to significantly lower titers than EMC/12 in HAE cultures. No other

significant differences were observed in either VeroE6 cells or HAE cultures. While not always stasticially significant, all camel-derived viruses had reduced replication kinetics as compared to EMC/12 in HAE cells at 24-72 hpi (*Figure 3*).

Disease progression of different MERS-CoV strains in hDPP4 transgenic mice

MERS-CoV enters cells expressing the receptor: human dipeptidyl peptidase IV (hDPP4). Our lab previously developed transgenic mice expressing hDPP4 to test MERS-CoV vaccine efficacy (22). Ten mice per group were inoculated I.N. with 10<sup>3</sup> TCID<sub>50</sub> MERS-CoV per mouse. Mice started to lose weight on D2 to D5. Body weight kept decreasing for all groups, except for the mice inoculated with C/BF/15: only one

mouse continued to lose weight (*Figure 4A*). This was accompanied by similar signs of disease across all groups; ruffled coat, increased breathing rate, reluctance to move, and hunched posture. No such signs were observed for mice inoculated with C/BF/15 that did not lose weight. Survivors were only found in the group inoculated with SK/15 (1 out of 6) and the group inoculated with C/BF/15 (5 out of 6). Average time to death was similar for all groups, excluding C/BF/15 (EMC/12 = 7.33; U/14 = 6.5; KSA/15 = 7; SK/15 = 7.6; KSA/18 = 7.67; C/KSA/13 = 7.5; C/E/13 = 8) (*Figure 4B*).

Oral swabs were taken at D1 to D7 post inoculation and viral RNA was measured via qRT-PCR. The total amount of viral shedding was determined per group. No significant differences were found in the amount of shedding between different groups (*Figure 4C-D*). Viral RNA and mRNA was then measured via qRT-PCR in lung tissue obtained from four animals per group at D3. Genomic RNA was significantly lower in lung tissue of mice inoculated with SK/15, C/E/15 and C/BF/15. mRNA was only significantly lower in lung tissue of mice inoculated with C/BF/15 (*Figure 4E-F*).

Lung pathology was then examined by a board-certified veterinary pathologist blinded to study group allocation. No differences in pathology were observed. Animals rarely showed pulmonary pathology at D3, however animals that had lesions showed only a minimal and random lymphocytic infiltrate. Immunohistochemistry detecting MERS-CoV antigen was expressed rarely or randomly scattered in pulmonary tissue type I and II pneumocytes and not located in areas of inflammation. Morphometric analysis of pulmonary tissue with immunoreactivity revealed no significant difference between groups (*Figure 4G*).

#### Discussion

The respiratory nature of MERS-CoV, in combination with its high mortality rate and frequent spillover from dromedary camels, pose this virus as a potential threat to global health. The ongoing endemic in the Middle East and subsequent discovery of MERS-CoV in camel herds across Africa has resulted in a wealth of available genetic data for various viral strains and isolates. Critically, a small number of studies have now shown how genetic variation in MERS-CoV drastically affects viral phenotypes such as replication kinetics and pathogenicity. These findings highlight the need for MERS-CoV surveillance and, importantly, assess new strains as they are isolated for changes which may increase spread, transmission and pathogenicity. In this study, we assessed several viral phenotypes as they relate to public health, in an attempt to better inform public health policy making with regards to MERS-CoV. We assembled a panel of diverse MERS-CoV viral isolates (*Table 1, Figure 1*). Because MERS-CoV frequently spills over into the human population, we chose to include both human- and camelderived strains.

Nosocomial spread is at the center of MERS-CoV outbreaks. Therefore, we first assessed the stability of the virus on various surface material types commonly found in hospitals (polypropylene and stainless steel) as well as materials with potential antiviral and well-known antimicrobial properties (silver and copper) (28, 29). Regardless of the surface material tested, C/KSA/13 was the least stable over time and fell below detectable levels by 24 hours (*Figure 2A*). Surprisingly, all virus strains tested had notably reduced stability when left on copper and silver surfaces, with the copper surface proving most effective at reducing viral titers (*Figure 2A*, *right panels*). While

copper and silver are generally appreciated for their antibacterial properties, copper has recently been shown to also have antiviral properties against influenza A H1N1 (30-32). The exact mechanism of copper's antiviral properties is still unclear, but may be related to the formation of hydroxyl radicals by copper ions when in aqueous solution (32). Silver-based nanoparticles have been shown to be antiviral for human immunodeficiency virus-1 (33), herpes simplex virus 2 (34), hepatitis B virus (35), respiratory syncytial virus (36), and monkey pox virus (37). Regardless of the mechanism, taking advantage of the antiviral properties of copper and silver could be a relatively straightforward method to decrease nosocomial transmission. Indeed, both silver and copper can be used for coating medical tools (38), and commonly touched items such as bed rails, door handles and intravenous poles (39). These findings may be more broadly applicable to other coronaviruses, such as the recently emerging 2019-nCoV in Wuhan, China. Further research should be invested in determining coronavirus susceptibility to copper-mediated inactivation.

MERS-CoV infects the lower respiratory tract in humans, and while the exact route of transmission has not been proven in a laboratory setting, it is likely to occur through aerosols and fomites (40). Studies have suggested that a hospital air-handling system may have contributed to nosocomial spread during the 2015 MERS-CoV outbreak in South Korea (16, 40) and our group has previously shown that the virus can remain viable suspended in air for up to 10 minutes (27). We therefore tested aerosol stability over time of our various strains in a Goldberg drum and observed that all viruses remained viable for a minimum of 180 minutes with on average about a log reduction in viral titer observed within the collected aerosols (*Figure 2B*). Even though

we did not observe major differences in this experiment, strain stability is an important phenotype to continue monitoring, as mutations in viral capsid proteins have been shown to enhance environmental stability of bacteriophages, Dengue virus, and transmissible gastroenteritis virus (41-43). Because MERS-CoV isolates contain polymorphisms throughout the entire viral genome, including the structural proteins that form virions, it is still possible mutations may arise that influence overall virus particle stability. C/KSA/13, which showed reduced stability on surfaces compared to EMC/12, contains polymorphisms in Orf1b, spike, and the virion matrix protein and exhibited the least environmental stability. If and how genetic variations may influence MERS-CoV stability warrants further research. With both SARS-CoV and MERS-CoV aerosol generating procedures have been directly implicated nosocomial virus transmission events and it is therefore important that we study the stability of the virus within aerosols and deposited on surfaces of this important group of pathogens to be able to compare this to the recently emerging 2019-nCoV.

We tested viral replication kinetics of our virus panel in both VeroE6 cells as well as primary HAE cells (*Figure 3*). All virus isolates came up to similar titers on the VeroE6 cells by 72 hours, however KSA/15 and C/KSA/13 had a higher titer than EMC/12 by 48 hours post infection. Albeit not significant, C/BF/15 has a lower viral titer than EMC/12 at 48 and 72 hpi. These results are in good agreement with a previous study showing that C/BF/15 has impaired replication (20). In primary HAE cultures, all camel-derived viral isolates had reduced replication kinetics compared to EMC/12 (*Figure 3B*). Taken together, these data suggest MERS-CoV may adapt in humans after transmission from camels.

Last, we tested our panel of viruses in a transgenic hDPP4 mouse model (22). We have previously shown that MERS-CoV replicates in type I and II pneumocytes within in the lower respiratory tract of this animal model (22). While MERS-CoV disease progression does not involve the central nervous system in humans, this small animal model is suitable for vaccine candidate testing, with animal survival or viral-induced death as a binary readout for vaccine efficacy. With the exception of C/BF/15 and SK/15, all strains tested were uniformly lethal in these animals, resulting in similar weight loss profiles and histopathology scores (*Figure 4*). MERS-CoV C/BF/15 contains a deletion in open reading frame 4b (ORF4b), which has been shown in a similar mouse model, to result in impaired suppression of the host interferon response and increased type I and type III interferon signaling (20). Taken together, these results pave the way for testing MERS-CoV vaccine candidates for broadly neutralizing potential in this animal model.

Our results with MERS-CoV C/KSA/13 demonstrate a potential tradeoff between environmental surface stability and replication kinetics. Notably, this is a camel derived isolate, and we did not observe similar phenotypic relationships for the other strains tested. Ideally, future studies should be done with camel-derived viruses and more closely related human-derived viruses to see what, if any, adaptations occur after zoonosis. Our viral stability results suggest copper should be incorporated more in hospital settings, particularly in areas of high contact between hospital workers and MERS patients, such as door handles, bed rails, and medical tools. Overall, we observed a range of stability, replication and pathogenesis phenotypes between

different MERS-CoV isolates, underscoring the importance of continued surveillance of this virus.

#### References

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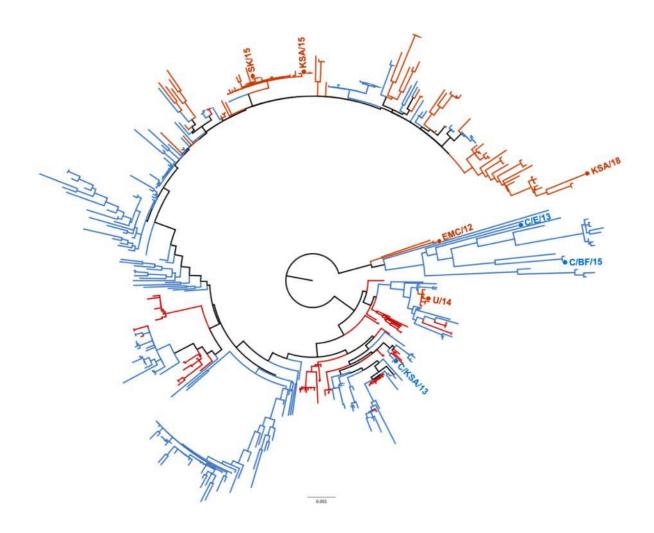
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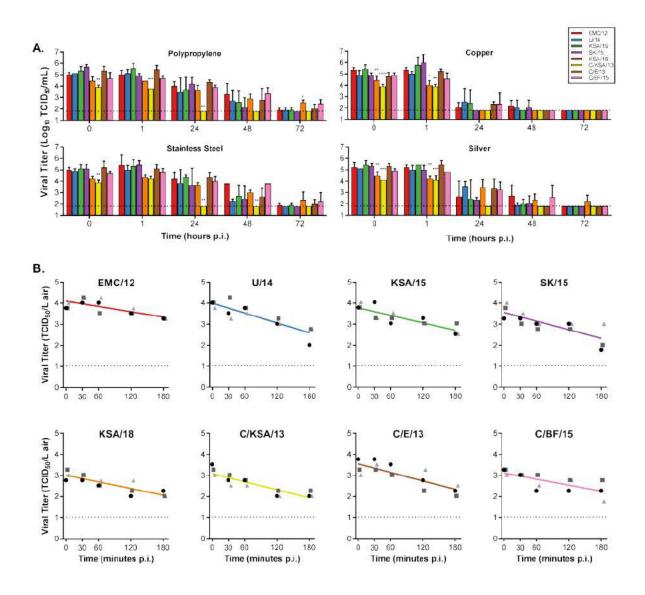
# **Tables and Figures**

Table 1. Details of MERS-CoV strains used in current study.

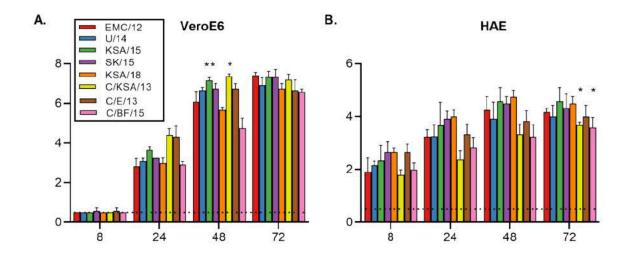
Name	Host	Year	Location	Full name	Access number	SNPs
EMC/12	Human	2012	KSA	HCoV-EMC/2012	JX869059	C6172T; C24059T; C24499A; G27162A
U/14	Human	2014	USA	Hu/Florida/USA-2/Saudi Arabia/2014	KP223131	None
KSA/15	Human	2015	KSA	Hu/Hofuf/KSA-11002/2015	KY688120	None
SK/15	Human	2015	South Korea	Hu/Korea/Seoul/177-3/2015	KX034100	C2149A; A6884G; T9566C; G10155T; A11376T; C14162T;C23041T; C26189T
KSA/18	Human	2018	KSA	Hu/Saudi Arabia/3015600912/2018	MN723544	C21149A; G22366A; C25009T
C/KSA/13	Camel	2013	KSA	Camel/Saudi Arabia/KFU- HKU1/2013	KJ650297	C25207T; C27875T
C/E/13	Camel	2013	Egypt	Camel/Egypt/NRCE/HKU270/2013	KJ477103	T16306C; C24100T; 26880T
C/BF/15	Camel	2015	Burkina Faso	Camel/Burkina Faso/CIRAD- HKU785/2015	MG923471	M29358C



**Figure 1. Phylogenetic tree of MERS-CoV strains.** Maximum likelihood tree of 446 full MERS-CoV genomes showing distribution of isolates used in this study. Human-derived MERS-CoV isolates used in this study are highlighted in red, camel-derived MERS-CoV isolates are highlighted in blue. Phylogenetic tree reconstructed with PhyML and rooted at the midpoint.



**Figure 2. Stability of MERS-CoV strains on surfaces and in aerosols.** A.) 50 μl of MERS-CoV was spread on surface, either polypropylene, stainless steel, copper or silver. 1 mL of DMEM was added at T=0, 1, 24, 48 or 72 hours and titrated. B.) MERS-CoV containing aerosols were sprayed into the Goldberg drum, and samples were taken at T=0, 30, 60, 120 and 180 minutes and titrated. Linear regression was calculated per virus and displayed in the graph as a line. A-B.) Statistically significant differences between EMC/12 and other strains were calculated using an unpaired Student's two-tailed t-test corrected for multiple comparisons via Bonferroni. Dotted line = limit of detection; p-values = \*<0.05; \*\*<0.01.\*\*\*\*



**Figure 3. Virus replication in VeroE6 and human airway epithelium.** Vero E6 cells (A) or HAE cultures (B) were infected with an MOI of 0.01 or 0.1 respectively, and samples of supernatant were obtained at 8, 24, 48 and 72 h.p.i. and titrated. Statistically significant differences as compared to the prototypical strain, EMC12, were calculated using an unpaired two-tailed Student's t-test. Dotted line = limit of detection; p-values = \*<0.05; \*\*<0.01, \*\*\*<0.001

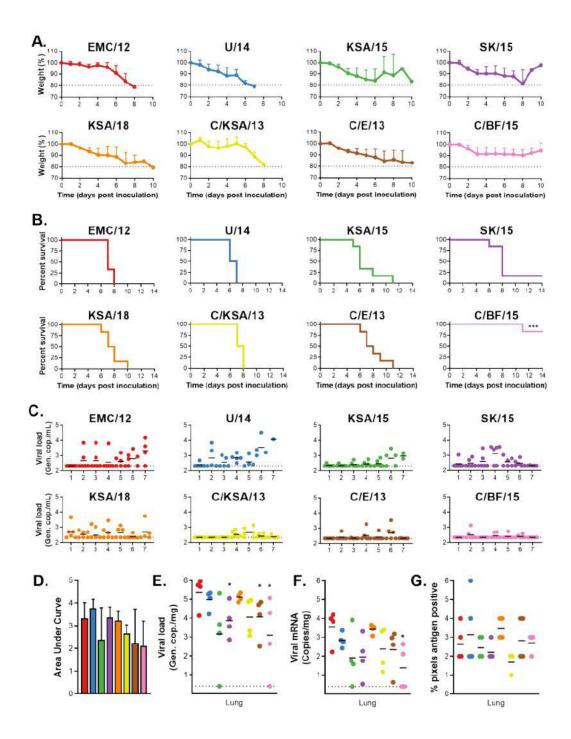


Figure 4. In vivo replication of different MERS-CoV strains. hDPP4 mice were inoculated I.N. with 10<sup>3</sup> TCID<sub>50</sub> MERS-CoV. Four mice were euthanized on D3, and the remaining 6 mice were monitored for survival. A.) Relative weight loss of hDPP4 mice. B.) Survival of hDPP4 mice. C.) Oropharyngeal shedding of MERS-CoV as measured via UpE qRT-PCR. D.) Area under the curve of oropharyngeal MERS-CoV shedding per virus strain. E.) Viral load in lung tissue obtained from mice euthanized at D3. F.) Viral mRNA load in lung tissue obtained from mice euthanized at D3. G.) Lung tissue were stained for MERS-CoV antigen and % of positive

pixels was quantified. Statistical significance was compared using an unpaired two-tailed Student's t-test. P-value = \*<0.05.

Table S1. SNPs in strains used in study compared to published sequences. Numbering based on published sequence.

Name	Access #	SNPs
EMC/12	JX869059	C6172T; C24059T; C24499A; G27162A
U/14	KP223131	None
KSA/15	KY688120	None
SK/15	KX034100	C2149A; A6884G; T9566C; G10155T; A11376T; C14162T; C23041T; C26189T
KSA/18	MN723544	C21149A; G22366A; C25009T
C/KSA/13	KJ650297	C25207T; C27875T
C/E/13	KJ477103	T16306C; C24100T; 26880T
C/BF/15	MG923471	M29358C

From: Munster, Vincent (NIH/NIAID) [E]
Sent: Wed, 29 Jan 2020 09:07:12 +0000

To: Ausraful Islam

Cc: (b) (6) Emily Gurley

Subject: Re: Best bat samples for corona virus

We have also seen coronaviruses in oral samples,

Do you have the assay to run them? If not we can provide you guys with updated primer and probes (we updated the original nested per to include the novel chinese bat coronaviruses). We also made synthetics RNA controls. You have to be a bit carefull with these tests as they are very prone to contamination.

Cheers,

Vincent

On Jan 29, 2020, at 02:06, Ausraful Islam < (b) (6) wrote:

Hi Vincent,

We are planning to test some bat fecal samples for coronavirus. Are there any other samples we should collect and test?

**Thanks** 

Rajib

Ausraful Islam, DVM, MS, MPH Assistant Scientist, Programme for Emerging Infections, Infectious Diseases Division, <image001.png>

Mobile: (b) (6)

Phone: (b) (6) Ext: (b) (6)

Skype: islam\_ausraf Web: www.icddrb.org

Munster, Vincent (NIH/NIAID) [E] From: Sent: Tue, 28 Jan 2020 16:41:29 +0000 To: (b) (6) Plowright, Raina; Mandy Todd; Manuel Ruiz Aravena; Dan Crowley; Caylee Cc: Falvo; Maureen Kessler; Devin Jones Subject: Re: BLOODSMEARS Fine with me! Cheers, Vincent (b) (6) wrote: On Jan 28, 2020, at 10:12, Alison Peel < Sure - fine with me. Vincent - can you please confirm that you've seen this discussion before we ship? Thanks Ali On Tue, 28 Jan 2020 at 19:33, Plowright, Raina < (b) (6) wrote: Can you please include the blood smears in package to RML? Can you package them separately so Trent can bring them to MSU when he next come to Bozeman? It will take us a couple of months to get CDC permission to bring samples directly to MSU. The slides should already be decontaminated. Sent from my iPhone On Jan 28, 2020, at 9:28 AM, Alison Peel < (b) (6) wrote:

Hi all,

As you all know, our last shipped was rejected at the border and shipped back to us. We are preparing to re-ship and I wanted to clarify what the plans were with shipping blood smears.

I know Vincent is keen to reduce the number of samples coming through RML, because of the decontamination processes that samples have to go through. We have discussed MSU getting CDC permits so we can ship things like this directly to MSU, but I don't know what the timeline is for this.

So, Question for Vincent and Raina (in consultation with others): Should we include blood slides in our next shipment to RML or hold off until the permits are in place to ship directly to MSU?

Thanks Ali From: Plowright, Raina

**Sent:** Tue, 28 Jan 2020 09:09:13 +0000 **To:** Munster, Vincent (NIH/NIAID) [E]

Cc: Bushmaker, Trenton (NIH/NIAID) [E]; Mandy Todd; Alison Peel; Kwe Claude,

Yinda (NIH/NIAID) [F]

Subject: Re: Shipping list Dec-2019

Thanks for the update Ali and Vincent.

Vincent, Can Emily's team send samples and you guys store until ready to screen? Unfortunately the Bangladesh and Australia samples will be on a similar schedule.

Sent from my iPhone

On Jan 28, 2020, at 2:57 PM, Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote:

Hi Raina,

As mentioned previously we are under quite a lot of work pressure, including work for hector and Jamie, (b) (4) etc.

This in addition to a currently rapidly increasing coronavirus outbreak.

Not everything can be a priority, so be mindful of this. And again, it would be good if we continue the discussion on sampling and numbers as we still seem to be getting >3000's of samples?, while we should be moving to the next phase of the program?

Regards,

Vincent

On Jan 28, 2020, at 04:37, Plowright, Raina < (b) (6) wrote:

Hi from Bangladesh!

I'm not finding the last email in the chain so excuse the leapfrog back in the conversation chain – also limiting email recipients.

(b) (4)

I don't think I heard from Mandy and Ali about Australian shipment plan but I apologize if I've missed emails on this.

What I need is an update on timing from the Australians and an update from Vincent on capacity to handle samples right now.

Thanks all,

Raina

From: "Bushmaker, Tre	nton (NIH/NIAID) [F	1" <	(b) (6)
Date: Tuesday, January			
To: Mandy Todd <		(b) (6) "Plowright, Raina"	
<	(b) (6)	(b) (6) <	(b) (6)
Cc: Manuel Ruiz Araver	na <	(b) (6) "Munster, \	/incent (NIH/NIAID) [E]"
<	(b) (6) "Rynda-Apple	e, Agnieszka" <	(b) (6)
"Kwe Claude, Yinda (NI	H/NIAID) [F]" <	(b) (6)	
Subject: RE: Shipping lis	st Dec-2019		

Mandy,

I'm starting to think you have a camera on me... the package arrived 30 minutes ago.

During the shipment we had a few issues:

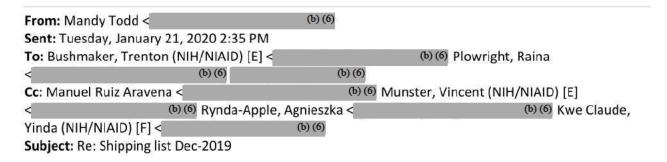
- 1. They PROMISED delivery by Jan 17<sup>th</sup>. Today is the 21<sup>st</sup>. I would've liked to skip the US holiday(20<sup>th</sup>) was the only special request.
- 2. They go through a contractor in the US who:
  - a. I did not have a phone number for so I couldn't call them for a updates.
  - b. Only work 8-5 hours.
  - c. Had issues with customs in Denver but they figured it out.
- 3. Promised delivery on Wednesday (22<sup>nd</sup>) but instead it just arrived today (randomly one day earlier).

#### Good things:

- 1. Dry ice looked good. No temperature probe however.
- 2. The cost is  $^{1,300}$  for one box that would hold  $^{10}$  boxes.

I would stick with the devil we know but what do you think?

-Trent



Hi Trent,

Has your shipment with SFS Pharma arrived and if so, any feedback on the experience?

Mandy Todd
Senior Technical Officer
Environmental Futures Research Institute
N78_2.11 Sir Samuel Griffith Building
Griffith University
Nathan, QLD 4111
Extension: (b) (6).
Phone: (b) (6)
Mobile: (b) (6)
<image001.png></image001.png>
From: Mandy Todd < (b) (6)

Great thanks Trent, please let us know how it goes. WC were meeting to discuss the failed shipment this afternoon so I'm expecting to hear an update shortly.

Kind regards,

Kind regards,

Mandy Todd

Senior Technical Officer

Environmental Futures Research Institute
N78\_2.11 Sir Samuel Griffith Building
Griffith University
Nathan, QLD 4111

Extension: (b) (6)
Phone: (b) (6)
Mobile: (b) (6)

<image001.png>

From: Bushmaker, Trent	on (NIH/NIAID) [E]		(b) (6)	
Sent: Tuesday, 14 Janua	ry 2020 2:58 AM			
To: Plowright, Raina <		(b) (6)	(b) (6) <	(b) (6)
Cc: Mandy Todd	(	b) (6) Manuel Ruiz A	Aravena	
<	(b) (б) Munster, V	incent (NIH/NIAID	) [E] <	(b) (6)
Rynda-Apple, Agnieszka	<	(b) (6) Kwe	Claude, Yinda (NIH/NIA	(ID) [F]
<	(b) (6)			
Subject: RE: Shipping lis	t Dec-2019			

I am doing a shipment of cells from Geelong today or tomorrow via SFS pharma so we can use it as a test shipment. It should be here by the end of the week.

### -Trent

```
From: Plowright, Raina < (b) (6)

Sent: Friday, January 10, 2020 2:40 PM

To: Bushmaker, Trenton (NIH/NIAID) [E] (b) (6)

Cc: Mandy Todd < (b) (6) (b) (6) Kwe Claude, Yinda (NIH/NIAID) [F] < (b) (6) Manuel Ruiz Aravena < (b) (6)

Munster, Vincent (NIH/NIAID) [E] < (b) (6) Rynda-Apple, Agnieszka < (b) (6)

Subject: Re: Shipping list Dec-2019
```

## Hi All,

We have a few projects that are being held up by delay in shipment, so if WC is a problem, let's discuss other solutions so we can get some critical samples here.

I hope WC are nice guys about this!

On Jan 9, 2020, at 7:38 PM, Bushmaker, Trenton (NIH/NIAID) [E]	(b) (6) wrote:
Mandy, Thank you for the update. We should be good for shipping whenever. As always, let me know if you from me.	need something
Just a quick FYI, I am going to be in Congo ~March 15-April 6th. Doesn't mean you can't ship but ju you a heads up.	st wanted to give
-Trent	
From: "Mandy Todd" < (b) (6)  Date: Thursday, January 9, 2020 at 4:12:24 PM  To: "Bushmaker, Trenton (NIH/NIAID) [E]" < (b) (6) ' (b) (6)  Cc: "Kwe Claude, Yinda (NIH/NIAID) [F]" < (b) (6) "Manuel Ruiz Aravena"  (b) (6) "Munster, Vincent (NIH/NIAID) [E]" (b) (6) "  (b) (6) "Rynda-Apple, Agnieszka" < (b) (6) "  Subject: Re: Shipping list Dec-2019	Plowright, Raina"
Hi Trent,	
Thanks for checking in on this and the offer of help. I need to speak with Ali but my thoughts were that we wouldn't send the shipmen have sorted out with World Courier how the failed shipment will be paid for. Wor still completing an internal investigation into how they approved the erroneous p however I will prod them a little and see if they have any updates for me.	ld Courier is
Kind regards, Mandy Todd	
Senior Technical Officer Environmental Futures Research Institute N78_2.11 Sir Samuel Griffith Building Griffith University Nathan, QLD 4111	
Extension: (b) (6)  Phone: (b) (6)  Mobile: (b) (6) <outlook-dpseifau.png></outlook-dpseifau.png>	

From: Bushmaker, Trenton (NIH/NIAID) [E] < (b) (6) Sent: Wednesday, 8 January 2020 4:55 AM (b)(6)(b) (6) < (b) (6) To: Mandy Todd < Cc: Kwe Claude, Yinda (NIH/NIAID) [F] < (b) (6) Manuel Ruiz Aravena (b) (6) Munster, Vincent (NIH/NIAID) [E] < (b) (6) Plowright, Raina < (b) (6) Rynda-Apple, Agnieszka (b) (6) Subject: RE: Shipping list Dec-2019 Hello and Happy 2020, Could you update us on what is happening/planning with the re-shipment of samples? Do you need any help from my end? Hope you are well.

-Trent

Trenton Bushmaker
Biologist, Virus Ecology Unit
Rocky Mountain Laboratories
903 South 4th Street
Hamilton, MT 59840
Phone: (b) (6)
Email: (b) (6)

From: Alison Peel (b) (6)

Sent: Thursday, December 12, 2019 1:25 PM

To: Bushmaker, Trenton (NIH/NIAID) [E] (b) (6)

Cc: Kwe Claude, Yinda (NIH/NIAID) [F] < (b) (6) Mandy Todd

< (b) (6) Manuel Ruiz Aravena < (b) (6) Munster,

Vincent (NIH/NIAID) [E] < (b) (6) Plowright, Raina < (b) (6)

Rynda-Apple, Agnieszka < (b) (6)

Subject: Re: Shipping list Dec-2019

Thanks very much Trent, this is really helpful. I think Mandy will follow up with them today (she's been juggling this from the field this week).

We had looked into using SFS pharma previously and they are certainly a lot cheaper. If they are an approved courier for you guys, we'd certainly be interested in trying them. Let me know how you find them with your next shipment

Thanks again, Ali

On Fri, 13 Dec 2019 at 2:09 am, Bushmaker, Trenton (NIH/NIAID) [E] < (b) (6) wrote:

Ali,

I fully agree with assumption. For other shipments we send the brokerage team at World Courier the finial paper work beforehand. They approve the paper work and then, and only then the shipment is sent. I would send them an email to explaining we expect no additional charges for the samples to be reshipped to RML.

I have just looked back into my notes and we have only had one shipment sent back because of customs issues but it was via DHL, not World Courier.

On another note, I am working on a shipment of cells from Australia via SFS pharma. I will let you know how this goes, this might be an option. We can use it as a test shipment.

Sad situation....

-Trent

From: Alison Peel < (b) (6)

Sent: Wednesday, December 11, 2019 9:40 PM

To: Plowright, Raina (b) (6)

Cc: Mandy Todd < (b) (6) Bushmaker, Trenton (NIH/NIAID) [E]

< (b) (6) Manuel Ruiz Aravena < (b) (6) Munster,

Vincent (NIH/NIAID) [E] < (b) (6) Rynda-Apple, Agnieszka

< (b) (6) Kwe Claude, Yinda (NIH/NIAID) [F] < (b) (6)

Subject: Re: Shipping list Dec-2019

Thanks Raina.

Mandy and Manuel are the most meticulous people I know, so it seems like we've been given poor advice here.

Trent - my assumption is that, as part of their service, WC should be checking the documents for the shipment and this is part of why they are so expensive. So, I feel like they have some responsibility here. Is this your understanding, have you previously had situations like this?

Cheers

Ali

On Thu, 12 Dec 2019 at 14:26, Plowright, Raina < (b) (6) wrote:

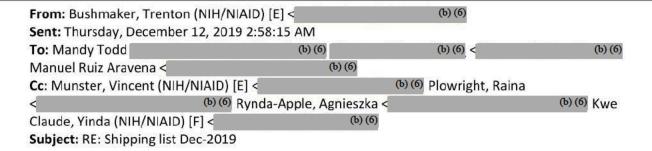
I'm so sorry to hear this, given how much work you and Ali and Manuel have done to get it to where it is. I hope the samples are in good condition. Can you troubleshoot the issues and turn it around again? Raina

On Dec 11, 2019, at 9:16 PM, Mandy Todd < (b) (6) wrote:

Hi all,

Unfortunately World Courier have just notified me that the shipment has been rejected by the USFWS and will be returned to us. Please let me know if you'd like to see the rejection notice.

## Mandy



Thank you Mandy. I will discuss this the brokerage team when they call. Keep me updated if you hear anything.

## -Trent

```
From: Mandy Todd < (b) (6)

Sent: Wednesday, December 11, 2019 9:50 AM

To: Bushmaker, Trenton (NIH/NIAID) [E] < (b) (6) Manuel
Ruiz Aravena < (b) (6)

Cc: Munster, Vincent (NIH/NIAID) [E] < (b) (6) Plowright, Raina

< (b) (6) Rynda-Apple, Agnieszka < (b) (6) Kwe

Claude, Yinda (NIH/NIAID) [F] < (b) (6)

Subject: Re: Shipping list Dec-2019
```

Thanks Trent. World Courier have responded and say that the "Cites was stamped by Australian quarantine prior to export" and that it is not possible to export without customs clearance, but we used three permits the WTA's email referred to only one of the permits so it's possible that one was missed.

Kind regards Mandy Todd

```
From: Bushmaker, Trenton (NIH/NIAID) [E] < (b) (6)

Sent: Thursday, December 12, 2019 2:26:23 AM

To: Mandy Todd < (b) (6) (b) (6)

Manuel Ruiz Aravena < (b) (6)

Cc: Munster, Vincent (NIH/NIAID) [E] < (b) (6) Plowright, Raina < (b) (6) Rynda-Apple, Agnieszka < (b) (6) Kwe

Claude, Yinda (NIH/NIAID) [F] < (b) (6)

Subject: RE: Shipping list Dec-2019
```

## Mandy,

I called World Courier to see if I can do anything on my end. The customs brokerage team should be calling me back very soon to discuss.

However, it is does not look good because of the "export documentation was not endorsed by an Australian Border Force official" what they said also. WC said the package might have to be sent back because of this.

If you have any updates or emails from Australian customs please forward.

#### -Trent

Trenton Bushmaker
Biologist, Virus Ecology Unit
Rocky Mountain Laboratories
903 South 4th Street
Hamilton, MT 59840
Phone: (b) (6)
Email: (b) (6)

From: Mandy Todd <	(b) (6)		
Sent: Tuesday, December 10, 2019 10:	39 PM		
To: Bushmaker, Trenton (NIH/NIAID) [I	E] <	(b) (6)	(b) (6) Manuel
Ruiz Aravena <	(b) (6)		
Cc: Munster, Vincent (NIH/NIAID) [E] <		(b) (б) Plowright, Raina	
< (b) (6) Ryn	da-Apple, Agnieszka	<	(b) (6) Kwe
Claude, Yinda (NIH/NIAID) [F] <	(b) (6)		
Subject: Re: Shipping list Dec-2019			

Hi all,

I've just received an email from the Australian department that issues the CITES permits (the WTA), they advise they have received a request from the US Fish and Wildlife Service regarding two problems with the documentation. The first problem is that the specimen export records that accompany the copy of the permit had lines in them which were handwritten. The last couple of times the WTA has issued me permits the specimen export records have been incomplete/not on watermarked paper, etc. I had them re-issued but they still didn't have the lines in them so I wrote them myself, unaware that it was a requirement for them to be printed.

The second problem is that the export documentation was not endorsed by an Australian Border Force official, which leads me to believe that the samples didn't clear Australian customs. I have emailed World Courier seeking clarification on this.

The WTA representative has advised the USFWS that the samples are in fact authorised under the permits, however the final decision will be with the USFWS.

Kind regards, Mandy Todd

### Senior Technical Officer

Environmental Futures Research Institute N78\_2.11 Sir Samuel Griffith Building Griffith University Nathan, QLD 4111

Extension: (b) (6)

Phone: (b) (6)

Mobile: (b) (6)

From: Bushmaker, Trenton (NIH/NIAID) [E] < (b) (6)

Sent: Tuesday, 10 December 2019 3:07 AM

To: (b) (6) < (b) (6) Manuel Ruiz Aravena

< (b) (6) Mandy Todd < (b) (6)

Cc: Munster, Vincent (NIH/NIAID) [E] < (b) (6) Plowright, Raina

< (b) (6) Rynda-Apple, Agnieszka < (b) (6) Kwe

Claude, Yinda (NIH/NIAID) [F] < (b) (6)

Subject: RE: Shipping list Dec-2019

Update as 12/9/2019 at 10am Mountain Time:

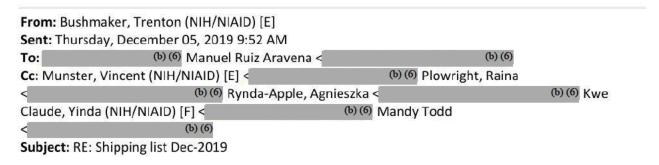
Still not cleared USDA, I will call them this afternoon to push a little bit. WC said deliver still should be Tuesday morning. I will update everyone this afternoon.

-Trent

Update as of 12/6/2019 at 1:30pm Mountain Time...

We are looking at delivery of the AUS samples early next week. They have not clear customs. I will monitor the situation over the weekend and update if something changes.

-Trent



Update as of 12/5/2019 at 10am Mountain time....

I have attached the email for World Courier this morning. I have giving them a call and the estimated customs clearance & delivery is this Saturday (7<sup>th</sup>). Everything is looking good!

Let me know if you have questions.

-Trent

```
From: Alison Peel < (b) (6)

Sent: Monday, December 02, 2019 5:06 PM

To: Bushmaker, Trenton (NIH/NIAID) [E] < (b) (6)

Cc: Manuel Ruiz Aravena < (b) (6) Munster, Vincent (NIH/NIAID) [E] < (b) (6) Plowright, Raina < (b) (6) Rynda-Apple, Agnieszka < (b) (6) Mandy Todd < (b) (6)

Subject Roy Shipping list Dog 2010
```

Subject: Re: Shipping list Dec-2019

Hi Trent,

Thanks for that. Yep - I agree that there a high level of mutual respect on both sides, and I think basically it just comes down to so many things going on and it being hard to keep track of everything -, especially across multiple email threads. No blame in any direction, and no need to apologise:) If we can get requests/instructions off emails and into written protocols, then I think it will be smoother sailing from then:)

Cheers

Ali

On Tue, 3 Dec 2019 at 10:00, Bushmaker, Trenton (NIH/NIAID) [E] < 6) (6) wrote: Ali,

Kwe and/or me should be around 16<sup>th</sup> if we required the meeting, just processing (b) (4) Vincent will be in Brazzaville, Congo during this time but might have some availability depending on internet access.

I just want to support Vincent's comments that nothing was directed specifically at your team. Hope you know we think your crew is awesome for getting these samples out in great condition.

My apologies to Manuel and you for any miscommunication that I may have caused. Will be better next shipment.

-Trent

Hi all,

Hi everyone,

On Tue, 3 Dec 2019 at 06:51, Alison Peel <

(b) (6) From: Alison Peel < Sent: Monday, December 02, 2019 4:21 PM (b) (6) To: Manuel Ruiz Aravena < (b) (6) Munster, Vincent (NIH/NIAID) [E] Cc: Plowright, Raina < (b) (6) Rynda-Apple, Agnieszka < (b) (6) Bushmaker, Trenton (NIH/NIAID) [E] < (b) (6) Kwe Claude, Yinda (NIH/NIAID) [F] (b) (6) Mandy Todd < (b)(6)Subject: Re: Shipping list Dec-2019 Hi all, Perhaps we should aim to work through all this on a zoom call and modify the protocol on the spot? Would Monday 16th December (afternoon-US)/Tuesday 17th December (morning-Aus) work for everyone? Cheers Ali

To expand on Manuel's points, yes, the lists of sample numbers weren't finalised til just before the shipment, but I think all the different sample types were included in that original email, so I think that's the time that we need to be having the discussions about sample types.

Since Manuel will be leaving in a few weeks, it would be great to clarify a stepwise protocol for future shipments - including who at RML should be cc'd about shipments, how far in advance and with what level of detail (accounting for the fact that the actual numbers of samples may vary slightly in the week prior to shipment). We can also add a step into the protocol about confirming whether samples should be sent to RML or elsewhere (if permits allow).

Thanks everyone :)

Cheers

Ali

On Tue, 3 Dec 2019 at 06:12, Manuel Ruiz Aravena

(b) (6) wrote:

My apologies Trent for the delay sending the final shipping list. I didn't want to send a list of samples that was changing in length and sample positions until last minute for different
contingencies including the (b) (4
In addition, we
had the final permits during the last week, therefore numbers could have changed until that
moment (b) (4)
If you are flexible with last minute changes we could
share future lists as they are in progress, but this could involve, anyway, that the final list could be available just a few days before the shipment occurs or even as now, when the boxes are leaving Griffith.
So, to move forward, is there any specific timeframe in which receiving the list of samples would make things smoother in your end? (we would add this to our protocols for sample requests and shipment)
About the list format that could have been confusing with the preliminary lists, finally for this shipment I managed to put a few lines of R code to merge data and change formats from ours to the one you use at RML which would make things easier for future shipments.
I personally apologize for any inconveniences, I know how much effort sample management requires, and I hope this didn't make things too complicated in your end.
Please, let me know what needs to be fixed in the list and I would do it today.
Cheers, M
PS: I'll check the bill # once I get to the office and send it to you.
From: Plowright, Raina < (b) (6)
Sent: Tuesday, 3 December 2019 5:35 AM
To: Munster, Vincent (NIH/NIAID) [E] < (b) (6)
Cc: Alison Peel < (b) (6) Rynda-Apple, Agnieszka < (b) (6)
Bushmaker, Trenton (NIH/NIAID) [E] < (b) (6) Kwe Claude, Yinda (NIH/NIAID) [F]
< (b) (6) Mandy Todd < (b) (6) Manuel Ruiz Aravena
(b) (6)
Subject: Re: Shipping list Dec-2019
We would have to get a CDC import permit for slides. We can do this if you need but I don't have a staff

On Dec 2, 2019, at 12:32 PM, Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote:

member capable of this kind of thing, so I would have to do all of the paperwork. We can discuss by

phone.

Hi Raina,

We just figured out that (b) (4) so it would be good to have an idea what to do with these?

Thanks for all the help, especially Ali who has been very responsive. Just making sure thate everyone is aware, that there is a huge effort involved in both the front end (Oz) and back-end (RML), so it would be good that end users of samples are aware of this and that last-minute changes in shipping lists or "new" sample types can cause some confusion / sorting out,

Cheers,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: "Plowright, Raina" < (b) (6)

Date: Monday, December 2, 2019 at 12:25 PM

To: Alison Peel < (b) (6)

Cc: " (b) (6) < (b) (6) Trenton Bushmaker

< (b) (6) "Kwe Claude, Yinda (NIH/NIAID) [F]"

< (b) (6) Mandy Todd < (b) (6) Manuel Ruiz

Aravena < (b) (6)

Subject: Re: Shipping list Dec-2019

We have no import permit for (b) (4) (CDC suggested we go through RML) so slides would have to go through RML. Dan Becker was leading this part of the project but hasn't stayed involved since he left and there is no clear leader on the slides to ensure all protocols are adhered to. We really need a single 'sample tsar' to ensure all samples are cared for under the best protocols, but I think we have been understaffed in this respect and so it is messy, but everyone is stepping up and everyone is doing more than their best effort to pull it off (especially Manuel—thanks Manuel!). Thanks team for the enormous effort to get the samples away.

Raina

On Dec 2, 2019, at 12:15 PM, Alison Peel < (b) (6) wrote:

Thanks Vincent for the reminder and clarification on that. Similarly, it's quite a task on our end to get the shipments away, with requests (and last minute requests) from many people, changes to shipment lists

(b) (4) when results come in from Kwe, and many many layers of permits, agreements and approvals across multiple institutions. All good though, we can continue to refine the process.

I had it in my mind that MSU didn't have all the required import permits, but if they are obtained, then that would be much easier.

Raina- who is our best point of contact at MSU re import permits?

**Thanks** 

Ali

On Tue, 3 Dec 2019 at 5:07 am, Munster, Vincent (NIH/NIAID) [E] < 6) 6) wrote: Thanks Ali,

This info most have been "lost" then on this end. Thanks for replying so quickly, it is quite the task with multiple shipments coming on to make sure that everything runs smoothly. Just as a reminder that this is nothing directed specifically at your team, we'll have the same scrutiny with (b) (4)

Just want to make sure, that once they are at RML, they can only be released following RML established procedures. So anything which can be routed around RML to MSU is easier for us (as every inactivation will take-up significant time of the people here).

Cheers,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: Alison Peel <	(b) (6)		
Reply-To: "	(b) (6) <	(b) (6)	
Date: Monday, Decem	ber 2, 2019 at 11:59 AM		
To: "	(b) (6) <	(b) (6)	
Cc: Trenton Bushmake	er <	(b) (6) "Kwe Claude, Yinda (N	IH/NIAID) [F]"
<	(b) (6) Mandy Todd <	(b) (6)	Manuel Ruiz
Aravena <	(b) (6) "Plo	wright, Raina" <	(b) (6)
Subject: Por Shipping	ist Doc 2010		

Subject: Re: Snipping list Dec-2019

Hi all,

Still early here, so I or Manuel can respond more in full later on but I just wanted to say that we emailed details of the samples in this shipment on November 1st and had a discussion with Trent about the slides and the clots at that time. The slides were not sent on dry ice- just a regular box.

We should have sent the final list prior to shipment, but we did send this draft list well in advance and answered any questions posed by Trent. Let us know what else we can do for next time.

Cheers

Ali

On Tue, 3 Dec 2019 at 4:48 am, Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote: Hi Manuel,

You might want to consider sending the slides directly to MSU? That would make it a little bit easier from our end. If Raina can discuss this with their local IRB, if these are not considered infectious than there is no need for a CDC import permit. Also, these will not have to be shipped using a cold-chain. So they could be shipped using a regular package rather than a very expensive dry-ice shipment.

As Trent said, make sure these things are discussed well ahead of time, this would facilitate a better logistics from our end,

cheers

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

Hello,

Thank you for packing list, however Manuel I will talk with you individually because we need to have a few things to fixed on the packing list. I just want to reiterate that I need this packing list <u>before the samples are shipped</u>. This way we can discuss any discrepancies beforehand. This will delay the processing of samples and the results to you guys.

<u>Most important for now</u>....! will need the House Airway bill# and the Job# if you are still sending it via World Courier. I will need to track the package, we have had issues of them sending packages to different locations and via odd routes of travel.

Let me know if you have questions. Thank you again for sending the samples, can't wait to find something!

-Trent

Trenton Bushmaker Biologist, Virus Ecology Unit

Rocky Mou	ntain Laboratories
903 South	4th Street
Hamilton, I	MT 59840
Phone:	(b) (6)
Email:	(b) (6)

From: Manuel Ruiz	Aravena <	(b) (6)	
Sent: Sunday, Decer	mber 01, 2019 9:56 PM		
To: Bushmaker, Tren	nton (NIH/NIAID) [E] <	(b) (6)	
Cc:	(b) (6) Munster, Vincent	(NIH/NIAID) [E] <	(b) (6) Kwe Claude,
Yinda (NIH/NIAID) [F	]<	(b) (6) Plowright, Raina <	(b) (6)
Mandy Todd <	(b) (6)		
Subject: Shipping lis	t Dec-2019		
Hi Trent,			

Samples are on their way to RML!

I attach the list of samples.

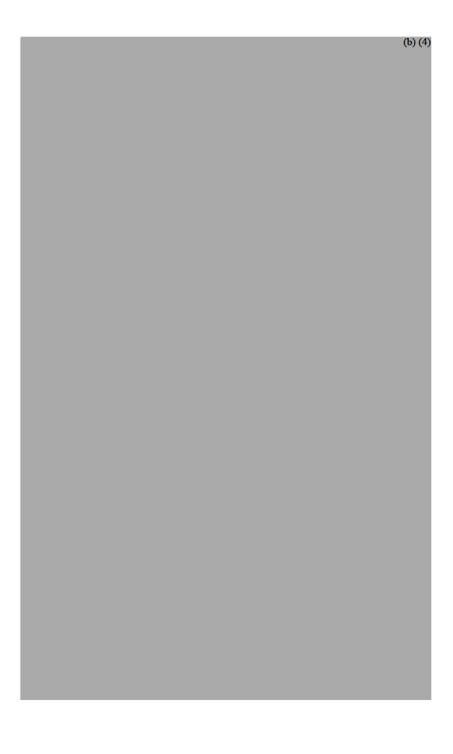
Samples are packed in a way that whole boxes can be transfer to MSU without moving samples among them.

(b) (4) for Vicky's experiments are in Box AUS\_155 (Locations F01 to F04)

Details of content and destinations are below.

Regards, Manuel





From: Plowright, Raina

Sent:Tue, 28 Jan 2020 08:57:10 +0000To:Munster, Vincent (NIH/NIAID) [E]Subject:Automatic reply: Shipping list Dec-2019

I will be traveling internationally until (b) (6) and will be in (b) (6) If you do not hear from me shortly and you expect a reply, please resend your email after I return.

From: Plowright, Raina

**Sent:** Tue, 28 Jan 2020 04:36:41 +0000

To: Bushmaker, Trenton (NIH/NIAID) [E]; Mandy Todd; Alison Peel
Cc: Munster, Vincent (NIH/NIAID) [E]; Kwe Claude, Yinda (NIH/NIAID) [F]

Subject: Re: Shipping list Dec-2019

## Hi from Bangladesh!

I'm not finding the last email in the chain so excuse the leapfrog back in the conversation chain – also limiting email recipients.

(b) (4)

I don't think I heard from Mandy and Ali about Australian shipment plan but I apologize if I've missed emails on this.

What I need is an update on timing from the Australians and an update from Vincent on capacity to handle samples right now.

Thanks all,

Raina

#### Mandy,

I'm starting to think you have a camera on me... the package arrived 30 minutes ago.

During the shipment we had a few issues:

- They PROMISED delivery by Jan 17<sup>th</sup>. Today is the 21<sup>st</sup>. I would've liked to skip the US holiday(20<sup>th</sup>) was the only special request.
- 2. They go through a contractor in the US who:
  - a. I did not have a phone number for so I couldn't call them for a updates.
  - b. Only work 8-5 hours.
  - c. Had issues with customs in Denver but they figured it out.
- 3. Promised delivery on Wednesday (22<sup>nd</sup>) but instead it just arrived today (randomly one day earlier).

#### Good things:

- 1. Dry ice looked good. No temperature probe however.
- 2. The cost is ~\$1,300 for one box that would hold ~(10) boxes.

I would stick with the devil we know but what do you think?

From: Mandy Todd <	(b) (6)	
Sent: Tuesday, January 21, 2020 2:35 PM		
To: Bushmaker, Trenton (NIH/NIAID) [E] <		6) 6) Plowright, Raina
(b) (6)	(b) (6)	
Cc: Manuel Ruiz Aravena <	(b) (6)	Munster, Vincent (NIH/NIAID) [E]
(b) (6) Rynda-Apple, Ag	nieszka <	(b) (6) Kwe Claude,
Yinda (NIH/NIAID) [F] <	(b) (6)	
Subject: Re: Shipping list Dec-2019		
Hi Trent,		
Has your shipment with SFS Pharma arrive	d and if so. a	any feedback on the experience?
, , , , , , , , , , , , , , , , , , ,		,
Kind regards,		
rema regards,		
Mandy Todd		
Senior Technical Officer		
er e onem e are are		
Environmental Futures Research Institute		
N78_2.11 Sir Samuel Griffith Building		
1476_2.11 Sil Samael Griffian Danding		
Griffith University		
Nathan, QLD 4111		
Extension: (b) (6)		
Extension. (970)		
Phone: (b) (6)		
Mobile: (b) (6)		





From: Mandy Todd <		(b) (6)	
Sent: Tuesday, 14 Janua	ary 2020 2:51 PM		
To: Bushmaker, Trento	n (NIH/NIAID) [E] <		(b) (6) Plowright, Raina
<	(b) (6)	(b) (6) <	(b) (6)
Cc: Manuel Ruiz Araver	na <	(b) (б) Muns	ster, Vincent (NIH/NIAID) [E]
<	(b) (6) Rynda-Apple, A	Ignieszka <	(b) (6) Kwe Claude,
Yinda (NIH/NIAID) [F] <		(b) (6)	
Subject: Re: Shipping lis	st Dec-2019		

Great thanks Trent, please let us know how it goes. WC were meeting to discuss the failed shipment this afternoon so I'm expecting to hear an update shortly.

Kind regards,

Mandy Todd

## Senior Technical Officer

Environmental Futures Research Institute

N78\_2.11 Sir Samuel Griffith Building

Griffith University

Extension: (b) (6)

Phone: (b) (6)

Mobile: (b) (6)





Subject: RE: Shipping list Dec-2019

I am doing a shipment of cells from Geelong today or tomorrow via SFS pharma so we can use it as a test shipment. It should be here by the end of the week.

-Trent

From: Plowright, Raina < (b) (6)

Sent: Friday, January 10, 2020 2:40 PM

To: Bushmaker, Trenton (NIH/NIAID) [I Cc: Mandy Todd < (NIH/NIAID) [F] <	(b) (6) (b) (6) Manuel Ruiz Ara	(b) (6) (b) (6) Kwe Claude, Yii	nda (b) (6)
Munster, Vincent (NIH/NIAID) [E] < (b) (6)  Subject: Re: Shipping list Dec-2019	A CONTROL OF THE SECTION AND A CONTROL OF THE	Rynda-Apple, Agnieszka	(6) (6)
Hi All, We have a few projects that are being other solutions so we can get some cri I hope WC are nice guys about this! Raina		ment, so if WC is a problem	n, let's discuss
On Jan 9, 2020, at 7:38 PM, Bushmake	r, Trenton (NIH/NIAID)	[E] <	(b) (6) wrote:
Mandy, Thank you for the update. We should be go from me.	ood for shipping whenever.	As always, let me know if you	need something
Just a quick FYI, I am going to be in Congo you a heads up.	~March 15-April 6th. Doe	sn't mean you can't ship but jus	st wanted to give
-Trent			
	(b) (	(b) (6) (b) (6)  (6) "Manuel Ruiz Aravena"  < <u>vincent.munster@nih.gov</u> >, "l	Plowright, Raina
Hi Trent,			
Thanks for checking in on this and to but my thou have sorted out with World Courier still completing an internal investigation however I will prod them a little and	ughts were that we wo r how the failed shipn ation into how they a	ouldn't send the shipment nent will be paid for. Worl pproved the erroneous pa	ld Courier is
Kind regards, Mandy Todd			

# Senior Technical Officer

Environmental Futures Research Institute N78\_2.11 Sir Samuel Griffith Building Griffith University Nathan, QLD 4111

Extension: (b) (6)
Phone: (b) (6)
Mobile: (b) (6)

<Outlook-dpseifau.png>

Cc: Kwe Claude, Yinda (NIH/NIAID) [F] <

Vincent (NIH/NIAID) [E] <

Rynda-Apple, Agnieszka <

Subject: Re: Shipping list Dec-2019

	a constitution in the constitution in			
From: Bushmaker, Trent	on (NIH/NIAID) [E	[]<	(b) (6)	
Sent: Wednesday, 8 Janu	uary 2020 4:55 AN	И		
To: Mandy Todd <		(b) (6)	(b) (6) <	(b) (6)
Cc: Kwe Claude, Yinda (N	IIH/NIAID) [F] <		(b) (6) Manuel Ruiz Ara	ivena
<	(b) (6) Munste	er, Vincent (NIH/	NIAID) [E] <	(b) (6)
Plowright, Raina <		(b) (6) Rynda	-Apple, Agnieszka	
<	(b) (6)			
Subject: RE: Shipping list	Dec-2019			
Hello and Happy 2020,				
Could you update us on	what is happening	g/planning with	the re-shipment of sample	s? Do you need any
help from my end?	15.5			
Hope you are well.				
-Trent				
Trenton Bushmaker				
Biologist, Virus Ecology U	Jnit			
Rocky Mountain Laborat	ories			
903 South 4th Street				
Hamilton, MT 59840				
Phone: (b) (6)				
Email:	(b) (6)			
From: Alison Peel <	(b) (	6)		
Sent: Thursday, Decemb	er 12, 2019 1:25	PM		
To: Bushmaker, Trenton	(NIH/NIAID) [E]		(b) (6)	

(b) (6) Manuel Ruiz Aravena <

(b) (6) Mandy Todd

(b) (6) Plowright, Raina <

(b) (6)

(b) (6) Munster,

(b) (6)

Thanks very much Trent, this is really helpful. I think Mandy will follow up with them today (she's been juggling this from the field this week).

We had looked into using SFS pharma previously and they are certainly a lot cheaper. If they are an approved courier for you guys, we'd certainly be interested in trying them. Let me know how you find them with your next shipment

Thanks again,

Ali

On Fri, 13 Dec 2019 at 2:09 am, Bushmaker, Trenton (NIH/NIAID) [E] < (b) (6) wrote:

Ali,

I fully agree with assumption. For other shipments we send the brokerage team at World Courier the finial paper work beforehand. They approve the paper work and then, and only then the shipment is sent. I would send them an email to explaining we expect no additional charges for the samples to be reshipped to RML.

I have just looked back into my notes and we have only had one shipment sent back because of customs issues but it was via DHL, not World Courier.

On another note, I am working on a shipment of cells from Australia via SFS pharma. I will let you know how this goes, this might be an option. We can use it as a test shipment.

Sad situation....

-Trent

From: Alison Peel < (b) (6)

Sent: Wednesday, December 11, 2019 9:40 PM

To: Plowright, Raina < (b) (6)

Cc: Mandy Todd < (b) (6) Bushmaker, Trenton (NIH/NIAID) [E]

< (b) (6) Manuel Ruiz Aravena < (b) (6) Munster,

Vincent (NIH/NIAID) [E] < (b) (6) Rynda-Apple, Agnieszka

< (b) (6) Kwe Claude, Yinda (NIH/NIAID) [F] < (b) (6)

Subject: Re: Shipping list Dec-2019

, ...

Thanks Raina.

Mandy and Manuel are the most meticulous people I know, so it seems like we've been given poor advice here.

Trent - my assumption is that, as part of their service, WC should be checking the documents for the shipment and this is part of why they are so expensive. So, I feel like they have some responsibility here. Is this your understanding, have you previously had situations like this?

Cheers

Ali

On Thu, 12 Dec 2019 at 14:26, Plowright, Raina < (b) (6) wrote: I'm so sorry to hear this, given how much work you and Ali and Manuel have done to get it to where it is. I hope the samples are in good condition. Can you troubleshoot the issues and turn it around again?

On Dec 11, 2019, at 9:16 PM, Mandy Todd < (b) (6) wrote:

Hi all,

Raina

Unfortunately World Courier have just notified me that the shipment has been rejected by the USFWS and will be returned to us. Please let me know if you'd like to see the rejection notice.

## Mandy

From: Bushmaker, Trenton (NIH/NIAID) [E] < (b) (6)

Sent: Thursday, December 12, 2019 2:58:15 AM

To: Mandy Todd < (b) (6) (b) (6) < (b) (6)

Manuel Ruiz Aravena < (b) (6)

Cc: Munster, Vincent (NIH/NIAID) [E] < (b) (6) Plowright, Raina

< (b) (6) Rynda-Apple, Agnieszka < (b) (6) Kwe

Claude, Yinda (NIH/NIAID) [F] < (b) (6)

Subject: RE: Shipping list Dec-2019

Thank you Mandy. I will discuss this the brokerage team when they call. Keep me updated if you hear anything.

#### -Trent

From: Mandy Todd < (b) (6)

Sent: Wednesday, December 11, 2019 9:50 AM

To: Bushmaker, Trenton (NIH/NIAID) [E] < (b) (6) Manuel
Ruiz Aravena < (b) (6)

Cc: Munster, Vincent (NIH/NIAID) [E] < (b) (6) Plowright, Raina

< (b) (6) Rynda-Apple, Agnieszka < (b) (6) Kwe

Claude, Yinda (NIH/NIAID) [F] < (b) (6)

Subject: Re: Shipping list Dec-2019

Thanks Trent. World Courier have responded and say that the "Cites was stamped by Australian quarantine prior to export" and that it is not possible to export without customs clearance, but we used three permits the WTA's email referred to only one of the permits so it's possible that one was missed.

Kind regards Mandy Todd

From: Bushmaker, Trenton (NIH/N	NIAID) [E] <	(b) (6)		
Sent: Thursday, December 12, 20	19 2:26:23 AM			
To: Mandy Todd <	(b) (6)	(b) (6) <		(b) (6)
Manuel Ruiz Aravena <	(b) (6)			
Cc: Munster, Vincent (NIH/NIAID)	[E] <	(b) (6) Plowright, Raina		
(b) (6)	Rynda-Apple, Agnieszka <	WEST 072.2	(b) (6)	Kwe
Claude, Yinda (NIH/NIAID) [F] <	(b) (6)			
Subject: RE: Shipping list Dec-201	9			

Mandy,

I called World Courier to see if I can do anything on my end. The customs brokerage team should be calling me back very soon to discuss.

However, it is does not look good because of the "export documentation was not endorsed by an Australian Border Force official" what they said also. WC said the package might have to be sent back because of this.

If you have any updates or emails from Australian customs please forward.

-Trent

Trenton Bushmaker
Biologist, Virus Ecology Unit
Rocky Mountain Laboratories
903 South 4th Street
Hamilton, MT 59840
Phone: (b) (6)
Email: (b) (6)

```
From: Mandy Todd < (b) (6)

Sent: Tuesday, December 10, 2019 10:39 PM

To: Bushmaker, Trenton (NIH/NIAID) [E] < (b) (6) Manuel
Ruiz Aravena (b) (6)

Cc: Munster, Vincent (NIH/NIAID) [E] < (b) (6) Plowright, Raina

(b) (6) Rynda-Apple, Agnieszka < (b) (6) Kwe

Claude, Yinda (NIH/NIAID) [F] < (b) (6)

Subject: Re: Shipping list Dec-2019
```

Hi all,

I've just received an email from the Australian department that issues the CITES permits (the WTA), they advise they have received a request from the US Fish and Wildlife Service regarding two problems with the documentation. The first problem is that the specimen export records that accompany the copy of the permit had lines in them which were handwritten. The last couple of times the WTA has issued me permits the specimen export records have been incomplete/not on watermarked paper, etc. I had them re-issued but they still didn't have the lines in them so I wrote them myself, unaware that it was a requirement for them to be printed.

The second problem is that the export documentation was not endorsed by an Australian Border Force official, which leads me to believe that the samples didn't clear Australian customs. I have emailed World Courier seeking clarification on this.

The WTA representative has advised the USFWS that the samples are in fact authorised under the permits, however the final decision will be with the USFWS.

Kind regards, Mandy Todd

#### Senior Technical Officer

Environmental Futures Research Institute N78\_2.11 Sir Samuel Griffith Building Griffith University Nathan, QLD 4111

Extension: (b) (6)
Phone: (b) (6)
Mobile: (b) (6)

From: Bushmaker, Trenton (NIH/NIAID) [E] < (b) (6)

Sent: Tuesday, 10 December 2019 3:07 AM

To: (b) (6) < (b) (6) Manuel Ruiz Aravena

< (b) (6) Mandy Todd < (b) (6)

Cc: Munster, Vincent (NIH/NIAID) [E] < (b) (6) Plowright, Raina

< (b) (6) Rynda-Apple, Agnieszka < (b) (6) Kwe

Claude, Yinda (NIH/NIAID) [F] < (b) (6)

Subject: RE: Shipping list Dec-2019

Update as 12/9/2019 at 10am Mountain Time:

Still not cleared USDA, I will call them this afternoon to push a little bit. WC said deliver still should be Tuesday morning. I will update everyone this afternoon.

-Trent

Update as of 12/6/2019 at 1:30pm Mountain Time...

We are looking at delivery of the AUS samples early next week. They have not clear customs. I will monitor the situation over the weekend and update if something changes.

-Trent

Update as of 12/5/2019 at 10am Mountain time....

I have attached the email for World Courier this morning. I have giving them a call and the estimated customs clearance & delivery is this Saturday (7<sup>th</sup>). Everything is looking good!

Let me know if you have questions.

-Trent

```
From: Alison Peel < (b) (6)

Sent: Monday, December 02, 2019 5:06 PM

To: Bushmaker, Trenton (NIH/NIAID) [E] < (b) (6)

Cc: Manuel Ruiz Aravena < (b) (6) Munster, Vincent (NIH/NIAID) [E]

< (b) (6) Plowright, Raina < (b) (6) Rynda-Apple,

Agnieszka < (b) (6) Kwe Claude, Yinda (NIH/NIAID) [F]

< (b) (6) Mandy Todd < (b) (6)

Subject: Re: Shipping list Dec-2019
```

Hi Trent,

Thanks for that. Yep - I agree that there a high level of mutual respect on both sides, and I think basically it just comes down to so many things going on and it being hard to keep track of everything -, especially

across multiple email threads. No blame in any direction, and no need to apologise:) If we can get requests/instructions off emails and into written protocols, then I think it will be smoother sailing from then:)

Cheers

Ali

On Tue, 3 Dec 2019 at 10:00, Bushmaker, Trenton (NIH/NIAID) [E] < 6) (6) wrote: Ali,

Kwe and/or me should be around 16<sup>th</sup> if we required the meeting, just (b) (4)

Vincent will be in Brazzaville, Congo during this time but might have some availability depending on internet access.

I just want to support Vincent's comments that nothing was directed specifically at your team. Hope you know we think your crew is awesome for getting these samples out in great condition.

My apologies to Manuel and you for any miscommunication that I may have caused. Will be better next shipment.

-Trent

From: Alison Peel < (b) (6)

Sent: Monday, December 02, 2019 4:21 PM

To: Manuel Ruiz Aravena < (b) (6)

Cc: Plowright, Raina < (b) (6) Munster, Vincent (NIH/NIAID) [E]

< (b) (6) Rynda-Apple, Agnieszka < (b) (6) Bushmaker,

Trenton (NIH/NIAID) [E] < (b) (6) Kwe Claude, Yinda (NIH/NIAID) [F]

< (b) (6) Mandy Todd < (b) (6)

Subject: Re: Shipping list Dec-2019

Hi all,

Perhaps we should aim to work through all this on a zoom call and modify the protocol on the spot? Would Monday 16th December (afternoon-US)/Tuesday 17th December (morning-Aus) work for everyone?

Cheers

Ali

On Tue, 3 Dec 2019 at 06:51, Alison Peel < (b) (6) wrote: Hi all,

To expand on Manuel's points, yes, the lists of sample numbers weren't finalised til just before the shipment, but I think all the different sample types were included in that original email, so I think that's the time that we need to be having the discussions about sample types.

Since Manuel will be leaving in a few weeks, it would be great to clarify a stepwise protocol for future shipments - including who at RML should be cc'd about shipments, how far in advance and with what level of detail (accounting for the fact that the actual numbers of samples may vary slightly in the week

be sent to RML or elsewhere (if permits allow).
Thanks everyone :)
Cheers
Ali
On Tue, 3 Dec 2019 at 06:12, Manuel Ruiz Aravena < <a href="mailto:m.ruizaravena@griffith.edu.au">m.ruizaravena@griffith.edu.au</a> > wrote: Hi everyone,
My apologies Trent for the delay sending the final shipping list. I didn't want to send a list of samples that was changing in length and sample positions until last minute for different contingencies (b) (4)
In addition, we
had the final permits during the last week, therefore numbers could have changed until that moment (b) (4)
If you are flexible with last minute changes we could
share future lists as they are in progress, but this could involve, anyway, that the final list could be available just a few days before the shipment occurs or even as now, when the boxes are leaving Griffith.
So, to move forward, is there any specific timeframe in which receiving the list of samples would make things smoother in your end? (we would add this to our protocols for sample requests and shipment)
About the list format that could have been confusing with the preliminary lists, finally for this shipment I managed to put a few lines of R code to merge data and change formats from ours to the one you use at RML which would make things easier for future shipments.
I personally apologize for any inconveniences, I know how much effort sample management requires, and I hope this didn't make things too complicated in your end.
Please, let me know what needs to be fixed in the list and I would do it today.
Cheers, M
PS: I'll check the bill # once I get to the office and send it to you.
From: Plowright, Raina < (b) (6)
Sent: Tuesday, 3 December 2019 5:35 AM
To: Munster Vincent (NIH/NIAID) [F] < (b) (6)

prior to shipment). We can also add a step into the protocol about confirming whether samples should

Bushmaker, Trenton (NIH/NIAID) [E] < (b) (6) Kwe Claude, Yinda (NIH/NIAID) < (b) (6) Manuel Ruiz Aravena	101			
(b) (6) Manuel Ruiz Arayena	[F]			
(b) (6)				
Subject: Re: Shipping list Dec-2019				
We would have to get a CDC import permit for slides. We can do this if you need but I don't have a smember capable of this kind of thing, so I would have to do all of the paperwork. We can discuss by phone.				
On Dec 2, 2019, at 12:32 PM, Munster, Vincent (NIH/NIAID) [E] < 6) (6) wrote:				
Hi Raina,				
We just figured out that (b) (4)				
so it would be good to have an idea what to d	Ю			
with these?				
Thanks for all the help, especially Ali who has been very responsive. Just making sure thate everyone is aware, that there is a huge effort involved in both the front end (Oz) and back-end (RML), so it would be good that end users of samples are aware of this and that last-minute changes in shipping lists or "new" sample types can cause some confusion / sorting out,				
Cheers,				
Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH				
From: "Plowright, Raina" < (b) (6)				
Shahoda a abras and Arrivation — Arrivation — Arrivation of the said				
Date: Monday, December 2, 2019 at 12:25 PM				
Shahoda a abras and Arrivation — Arrivation — Arrivation of the said				

We have no import permit (b) (4) (CDC suggested we go through RML) so slides would have to go through RML. Dan Becker was leading this part of the project but hasn't stayed involved since he left and there is no clear leader on the slides to ensure all protocols are adhered to. We really need a single 'sample tsar' to ensure all samples are cared for under the best protocols, but I think we have been understaffed in this respect and so it is messy, but everyone is stepping up and everyone is doing

(b) (6) Manuel Ruiz

(b) (6) Mandy Todd <

Aravena <

Subject: Re: Shipping list Dec-2019

(b) (6)

more than their best effort to pull it off (especially Manuel—thanks Manuel!). Thanks team for the enormous effort to get the samples away.

Raina

On Dec 2, 2019, at 12:15 PM, Alison Peel < (b) (6) wrote:

Thanks Vincent for the reminder and clarification on that. Similarly, it's quite a task on our end to get the shipments away, with requests (and last minute requests) from many people, changes to shipment lists to 60 (4) when results come in from Kwe, and many many layers of permits, agreements and approvals across multiple institutions. All good though, we can continue to refine the process.

I had it in my mind that MSU didn't have all the required import permits, but if they are obtained, then that would be much easier.

Raina- who is our best point of contact at MSU re import permits?

Thanks Ali

On Tue, 3 Dec 2019 at 5:07 am, Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote: Thanks Ali,

This info most have been "lost" then on this end. Thanks for replying so quickly, it is quite the task with multiple shipments coming on to make sure that everything runs smoothly. Just as a reminder that this is nothing directed specifically at your team, we'll have the same scrutiny with the (b) (4)

Just want to make sure, that once they are at RML, they can only be released following RML established procedures. So anything which can be routed around RML to MSU is easier for us (as every inactivation will take-up significant time of the people here).

Cheers,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

Aravena < (b) (6) "Plowright, Raina" < (b) (6)

Subject: Re: Shipping list Dec-2019

Hi all,

Still early here, so I or Manuel can respond more in full later on but I just wanted to say that we emailed details of the samples in this shipment on November 1st and had a discussion with Trent about the slides and the clots at that time. The slides were not sent on dry ice- just a regular box.

We should have sent the final list prior to shipment, but we did send this draft list well in advance and answered any questions posed by Trent. Let us know what else we can do for next time.

Cheers

Ali

On Tue, 3 Dec 2019 at 4:48 am, Munster, Vincent (NIH/NIAID) [E] < 6) 6) wrote: Hi Manuel,

You might want to consider sending the slides directly to MSU? That would make it a little bit easier from our end. If Raina can discuss this with their local IRB, if these are not considered infectious than there is no need for a CDC import permit. Also, these will not have to be shipped using a cold-chain. So they could be shipped using a regular package rather than a very expensive dry-ice shipment.

As Trent said, make sure these things are discussed well ahead of time, this would facilitate a better logistics from our end,

cheers

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

```
From: Trenton Bushmaker < (b) (6)

Date: Monday, December 2, 2019 at 11:26 AM

To: Manuel Ruiz Aravena < (b) (6) Mandy Todd

< (b) (6) ( (b) (6) < (b) (6)

Cc: " (b) (6) < (b) (6) "Kwe Claude, Yinda (NIH/NIAID)

[F]" < (b) (6) "Plowright, Raina" < (b) (6)
```

Subject: RE: Shipping list Dec-2019

Hello,

Thank you for packing list, however Manuel I will talk with you individually because we need to have a few things to fixed on the packing list. I just want to reiterate that I need this packing list <u>before the</u>

<u>samples are shipped.</u> This way we can discuss any discrepancies beforehand. This will delay the processing of samples and the results to you guys.

<u>Most important for now</u>....! will need the House Airway bill# and the Job# if you are still sending it via World Courier. I will need to track the package, we have had issues of them sending packages to different locations and via odd routes of travel.

Let me know if you have questions. Thank you again for sending the samples, can't wait to find something!

#### -Trent

Trenton Bushmaker
Biologist, Virus Ecology Unit
Rocky Mountain Laboratories
903 South 4th Street
Hamilton, MT 59840
Phone: (b) (6)
Email: (b) (6)

Email: (b) (6)

From: Manuel Ruiz Aravena <	(b) (6)	
Sent: Sunday, December 01, 2019	9:56 PM	
To: Bushmaker, Trenton (NIH/NIA	AID) [E] (b) (6)	
Cc: (b) (6) Muns	ter, Vincent (NIH/NIAID) [E] <	(b) (6) Kwe Claude,
Yinda (NIH/NIAID) [F] <	(b) (6) Plowright, Raina <	(b) (6)
Mandy Todd <	(b) (6)	
Subject: Shipping list Dec-2019		

Hi Trent,

Samples are on their way to RML!

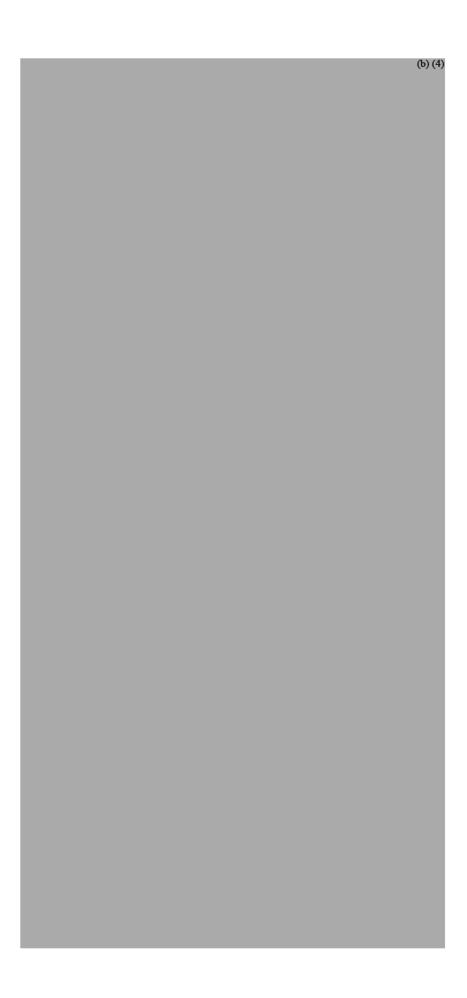
I attach the list of samples.

Samples are packed in a way that whole boxes can be transfer to MSU without moving samples among them.

(b) (4) for Vicky's experiments are in Box AUS\_155 (Locations F01 to F04)

Details of content and destinations are below.

Regards, Manuel



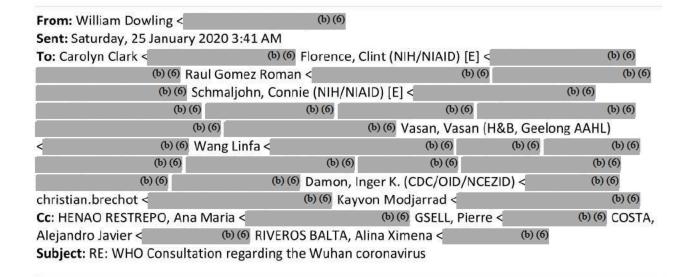
From: Wang Linfa Sent: Fri, 24 Jan 2020 19:48:49 +0000 William Dowling; Carolyn Clark; Florence, Clint (NIH/NIAID) [E]; Wolfraim, Larry (NIH/NIAID) [E]; Raul Gomez Roman; Carroll, Miles; Graham, Barney (NIH/VRC) [E]; Schmaljohn, Connie (NIH/NIAID) [E]; Holbrook, Michael (NIH/NIAID) [C]; Hensley, Lisa (NIH/NIAID) [E]; Baric, Ralph; Munster, Vincent (NIH/NIAID) [E]; (b)(6)(b) (6) Vasan, Vasan (b) (6) (H&B, Geelong AAHL); (b) (6) Damon, Inger K. (CDC/DDID/NCEZID/DHCPP); christian.brechot; Kayvon Modjarrad Cc: HENAO RESTREPO, Ana Maria; GSELL, Pierre; COSTA, Alejandro Javier; RIVEROS BALTA, Alina Ximena

RE: WHO Consultation regarding the Wuhan coronavirus

Got it. Thanks and talk soon

Subject:

Linfa (Lin-Fa) WANG, PhD FTSE
Professor & Director
Programme in Emerging Infectious Disease
Duke-NUS Medical School,
8 College Road, Singapore 169857
Tel: (b) (6)



#### Hello all

External Email -

I sent an outlook invite to everyone on this list. But if you did not get it, the call in information is below. Bill

## Join Skype Meeting

Trouble Joining? Try Skype Web App

### Join by phone

Sweden +46108885246,,	(b) (6) (Intility)
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US +13152940334, (b) (c	) (Intility)
US2 +13479604639, (b)	(6) (Intility)
Spain +34518889420, (	b) (6) (Intility)
France +33975183429,	(b) (6) (Intility)
Netherlands +31858887765	,, (b) (б) (Intility)
South Africa +27875509230	(b) (6) (Intility)
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English (United Kingdom)

English (United Kingdom)

Find a local number

Conference ID: (b) (6)
Forgot your dial-in PIN? Help

```
From: William Dowling
Sent: Thursday, January 23, 2020 10:40 PM
To: Carolyn Clark <
                                          (b) (6) Florence, Clint (NIH/NIAID) [E] <
                                                                                                        (b) (6)
                     (b) (6) Raul Gomez Roman <
                                                                             (b) (6)
                                                                                                           (b) (6)
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                      (b) (6) Schmaljohn, Connie (NIH/NIAID) [E] <
                                                                          (b) (6)
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Modjarrad <
                                                              (b) (6) GSELL, Pierre <
Cc: HENAO RESTREPO, Ana Maria <
                                                                                                  (b) (6) COSTA,
Alejandro Javier <
                                 (b) (6) RIVEROS BALTA, Alina Ximena <
                                                                                        (b) (6)
Subject: WHO Consultation regarding the Wuhan coronavirus
```

#### Hello all,

On behalf of the WHO R&D Blueprint team, I am writing to request your participation on a call tomorrow at 9 PM Central European time (which will be Saturday morning for some of you). The purpose of the call is to lend your expertise to coordination of WHO response efforts. To that end, we would like to discuss the current status of efforts to culture the Wuhan

coronavirus (or generate a recombinant virus); recent sequence data and modeling of the Spike protein; and potential next steps to assess cross reactivity with other coronaviruses. We realize that this is very short notice, but the situation is very dynamic. This would be an initial call with lengthier and more detailed calls in the near future.

Also, for those who have not seen them, I am attaching two reports on this topic that just came out and are highly relevant to the conversation.

Please let us know if you can make it. Call in details will be sent tomorrow.

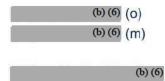
Thank you,

Bill Dowling (seconded to WHO)

#### William Dowling, PhD

Non-Clinical Vaccine Development Leader





1901 Pensylvania Ave, NW, Suite 1003, Washington, DC 20006 USA

#### www.cepi.net



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Important: This email is confidential and may be privileged. If you are not the intended recipient, please delete it and notify us immediate you should not copy or use it for any purpose, nor disclose its contents to any other person. Thank you.	ıly;

From: Wang Linfa

**Sent:** Fri, 24 Jan 2020 10:23:36 +0000

To: William Dowling

Cc: Carolyn Clark; Florence, Clint (NIH/NIAID) [E]; Wolfraim, Larry (NIH/NIAID) [E]; Raul Gomez Roman; Carroll, Miles; Graham, Barney (NIH/VRC) [E]; Schmaljohn, Connie (NIH/NIAID) [E];

Holbrook, Michael (NIH/NIAID) [C]; Hensley, Lisa (NIH/NIAID) [E]; Baric, Ralph; Munster, Vincent

 (NIH/NIAID) [E];
 (b) (6)
 (b) (6)
 Vasan, Vasan (H&B,

 Geelong AAHL);
 (b) (6)
 (b) (6)
 (b) (6)

 (b) (6)
 (b) (6)
 (b) (6)
 Damon, Inger

K. (CDC/DDID/NCEZID/DHCPP); (b) (6) Kayvon Modjarrad; HENAO RESTREPO,

Ana Maria; GSELL, Pierre; COSTA, Alejandro Javier; RIVEROS BALTA, Alina Ximena **Subject:** Re: WHO Consultation regarding the Wuhan coronavirus

Attachments: image004.png, image006.png, image008.png

Thanks for clarification!

Sent from my iPhone

On 24 Jan 2020, at 4:47 PM, William Dowling < (b) (6) wrote:

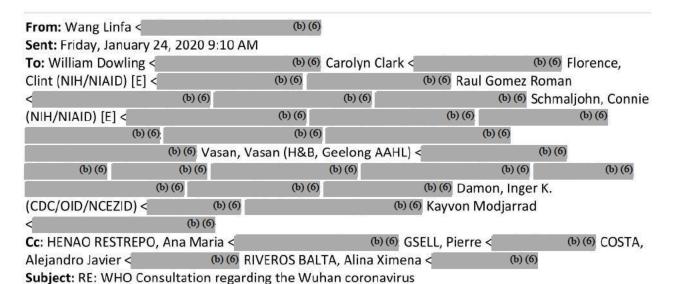
- External Email -

Dear Lin-Fa,

This is 9 PM Central Europe time on Friday Jan 24. I will be sending an outlook invite shortly with call -in details and agenda.

Thank you

Bill



Dear Bill,

Just to follow up with the exact timing of the meeting.

Do you mean 9 PM Central European time on Friday 24 Jan or Saturday 25 Jan as we received your email on Friday 24 Jan.

**Thanks** 

LF

Linfa (Lin-Fa) WANG, PhD FTSE
Professor & Director
Programme in Emerging Infectious Disease
Duke-NUS Medical School,
8 College Road, Singapore 169857
Tel: (b) (6)

From: William Dowling < (b) (6)

Sent: Friday, 24 January 2020 5:40 AM To: Carolyn Clark < (b) (6) Florence, Clint (NIH/NIAID) [E] < (b)(6)(b) (6) Raul Gomez Roman < (b)(6)(b)(6)(b) (6) Schmaljohn, Connie (NIH/NIAID) [E] < (b)(6)(b) (6) (b)(6)(b) (6) (b) (6) (b) (6) (b) (6) Vasan, Vasan (H&B, Geelong AAHL) (b) (6) Wang Linfa < (b) (6) (b) (6) (b)(6)(b) (6) (b) (6) (b) (6) (b) (6) (b) (6) (b) (6) Damon, Inger K. (CDC/OID/NCEZID) < (b)(6)(b) (6) Kayvon Modjarrad Cc: HENAO RESTREPO, Ana Maria < (b) (6) GSELL, Pierre < (b) (6) COSTA, (b) (6) RIVEROS BALTA, Alina Ximena < Alejandro Javier < (b)(6)

Subject: WHO Consultation regarding the Wuhan coronavirus

- External Email -

Hello all.

On behalf of the WHO R&D Blueprint team, I am writing to request your participation on a call tomorrow at 9 PM Central European time (which will be Saturday morning for some of you). The purpose of the call is to lend your expertise to coordination of WHO response efforts. To that end, we would like to discuss the current status of efforts to culture the Wuhan coronavirus (or generate a recombinant virus); recent sequence data and modeling of the Spike protein; and potential next steps to assess cross reactivity with other coronaviruses. We realize

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Please let us know if you can make it. Call in details will be sent tomorrow.

Thank you,

Bill Dowling (seconded to WHO)

#### William Dowling, PhD

Non-Clinical Vaccine Development Leader

<image004.png>



(b) (6)

1901 Pensylvania Ave, NW, Suite 1003, Washington, DC 20006 USA

#### www.cepi.net

<image006.png <image008.png
>

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From: Wang Linfa

Sent: Fri, 24 Jan 2020 08:09:39 +0000

To: William Dowling; Carolyn Clark; Florence, Clint (NIH/NIAID) [E]; Wolfraim, Larry (NIH/NIAID) [E]; Raul Gomez Roman; Carroll, Miles; Graham, Barney (NIH/VRC) [E]; Schmaljohn, Connie (NIH/NIAID) [E]; Holbrook, Michael (NIH/NIAID) [C]; Hensley, Lisa (NIH/NIAID) [E]; Baric, Ralph; Munster, Vincent (NIH/NIAID) [E]; (b) (6) (b) (6) Vasan, Vasan (H&B, Geelong AAHL); (b) (6) (b) (6)

Kayvon Modjarrad

Cc: HENAO RESTREPO, Ana Maria; GSELL, Pierre; COSTA, Alejandro Javier; RIVEROS

BALTA, Alina Ximena

Subject: RE: WHO Consultation regarding the Wuhan coronavirus

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Professor & Director
Programme in Emerging Infectious Disease
Duke-NUS Medical School,
8 College Road, Singapore 169857
Tel: (b) (6)

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From: Wang Linfa Sent: Fri, 24 Jan 2020 06:32:54 +0000 William Dowling; Carolyn Clark; Florence, Clint (NIH/NIAID) [E]; Wolfraim, Larry (NIH/NIAID) [E]; Raul Gomez Roman; Carroll, Miles; Graham, Barney (NIH/VRC) [E]; Schmaljohn, Connie (NIH/NIAID) [E]; Holbrook, Michael (NIH/NIAID) [C]; Hensley, Lisa (NIH/NIAID) [E]; Baric, Ralph; Munster, Vincent (NIH/NIAID) [E]; (b)(6)(b) (6) Vasan, Vasan (b) (6) (b) (6) (H&B, Geelong AAHL); (b) (6) (b) (6) (b) (6) (b) (6) (b) (6) (b) (6) Damon, Inger K. (CDC/DDID/NCEZID/DHCPP); (b) (6) Kayvon Modjarrad Cc: HENAO RESTREPO, Ana Maria; GSELL, Pierre; COSTA, Alejandro Javier; RIVEROS BALTA, Alina Ximena Subject: RE: WHO Consultation regarding the Wuhan coronavirus Thanks Bill. Yes I will attend. LF Linfa (Lin-Fa) WANG, PhD FTSE **Professor & Director Programme in Emerging Infectious Disease** Duke-NUS Medical School, 8 College Road, Singapore 169857 Tel: (b)(6)From: William Dowling < (b) (6) Sent: Friday, 24 January 2020 5:40 AM To: Carolyn Clark < (b) (6) Florence, Clint (NIH/NIAID) [E] < (b)(6)(b) (6) Raul Gomez Roman < (b)(6)(b) (6) (b) (6) Schmaljohn, Connie (NIH/NIAID) [E] < (b)(6)(b) (6) (b)(6)(b)(6)(b) (6) (b)(6)(b) (6) Vasan, Vasan (H&B, Geelong AAHL) (b) (6) Wang Linfa < (b) (6) (b) (6) (b)(6)(b) (6) (b)(6)(b)(6)(b)(6)(b)(6)(b) (6) Damon, Inger K. (CDC/OID/NCEZID) < (b) (6)

(b) (6) Kayvon Modjarrad <

Subject: WHO Consultation regarding the Wuhan coronavirus

(b) (6) RIVEROS BALTA, Alina Ximena <

(b) (6)

(b) (6)

(b) (6) COSTA,

(b) (6) GSELL, Pierre <

- External Email -

Alejandro Javier <

Cc: HENAO RESTREPO, Ana Maria <

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#### William Dowling, PhD

Non-Clinical Vaccine Development Leader





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of the material in this e-mail is strictly prohibited.				

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From: Munster, Vincent (NIH/NIAID) [E] on behalf of Munster, Vincent (NIH/NIAID) [E]

**Sent:** Thu, 23 Jan 2020 09:11:36 -0700

To: (b) (6); Plowright, Raina
Subject: Re: Time sensitive request - one last question

Hi (b) (6)

Facility fully funded by HHS (health and human services).

Small (very) parts of research (so not facility) is funded by DoD, CEPI

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

On 1/21/20, 2:41 PM, (b) (6) wrote:

Vincent/Raina,

Thank you for the quick turn around. One more question:

- 4. Source(s) of financing of the reported activity, including indication if the activity is wholly or partly financed by the Ministry of Defense
- List all sources of funding, including operation and maintenance (O&M) funding, using the following categories:
  - o If federally funded, list the Department; do not list subordinate agencies.
  - o Note whether facility is "wholly" or "partially" funded by DoD.
  - -Non-USG funding sources are listed as "Universities," "Private sector companies" or "Non-profit associations."

Thanks.

(b) (6)

Support to Biological Technologies Office, DARPA

Science and Technology Associates, Inc.

(b) (6)

Lead Scientist

----Original Message----

From: Plowright, Raina < (b) (6)

Sent: Tuesday, January 21, 2020 4:24 PM

To: (b) (6)
Cc: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Subject: Re: Time sensitive request

Hi Monica,

Here is the information, provided by Vincent Munster. He is cc'd in case you have follow up questions.

raina

(b)(6)

(b) (6) > wrote:

Yes. Please call them or send their phone number. I need the information asap.

Thank you (b) (6)

(b)(6)

Lead Scientist

Support to Biological Technologies Office, DARPA

Science and Technology Associates, Inc.

(b) (6)

----Original Message-----

From: Plowright, Raina (b) (6)

Sent: Tuesday, January 21, 2020 3:51 PM

To: (b) (6)

Subject: Re: Time sensitive request

Importance: High

I have forwarded to RML to answer questions below. Obviously, we are doing BSL4 work at RML.

On Jan 21, 2020, at 1:30 PM, (b) (c)

(b) (6) wrote:

#### Hi PREEPT Performers,

Those of you who are working with BSL4 containment facilities, please send the following information ASAP:

1. Name(s) of facility (the name of the subcontractor performing the work) 2. Responsible public or private organization or company (List the departments and agencies that operates the facility. If a third-party contractor runs the facility, note the contracting company as well) 3. Location and postal address (A physical address is required; PO boxes can be listed in addition to, but not instead of, the physical address) 4. N/A 5. Number of maximum containment units within the research center and/or laboratory, with an indication of their respective size (m2). If the facility contains more than one BSL-4 laboratory, list each lab (and corresponding area) separately. Area is reported in square meters, not square feet. Use a conversion tool (e.g.,

hxxxp://xxx.metric-conversions.org/area/square-feet-to-square-meters.h tm) to report laboratory area in m2.

Scope and general description of activities, including type(s) of micro-organisms and/or toxins as appropriate.

- -Provide a brief description of research conducted at the facility.
- . Include URL for one weblink where the reader can go for more

information.

. Do not list specific microorganisms and toxins (MoT) held at the

facility.

Instead, include generalized references to MoT used in laboratory studies.

Please send negative responses as well.

Thank you.
(b) (6)

(b) (6)

Lead Scientist

Support to Biological Technologies Office, DARPA Science and

Technology Associates, Inc.

(b) (6)

From: Plowright, Raina

**Sent:** Wed, 22 Jan 2020 15:02:24 +0000 **To:** Munster, Vincent (NIH/NIAID) [E]

Cc: (b) (6) Kwe Claude, Yinda (NIH/NIAID) [F]; Bushmaker, Trenton

(NIH/NIAID) [E]; Mandy Todd; Tamika Lunn; Hamish McCallum; Alison Peel

Subject: Re: Next Hendra batch of testing

Agree we can't wait. Just send them and take the loss, time is more valuable than lost dollars right now. Not having results is costing us more than lost money on shipping (eg Multiple PhDs affected, no prelim results to use to get next grants, not meeting deadlines to get to Phase II DARPA).

Sent from my iPhone

On Jan 22, 2020, at 7:47 AM, Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote:

Hi Ali,

Yes the delay of the shipment is unfortunate. From our end we will do whatever is possible to screen the samples. However, given the current situation with the novel coronavirus outbreak in China (and US), it will be hard to predict what impact this will have on our ability to screen these samples. Nothing to worry about just a word of caution as Trent will be busy with that outbreak so the speed of processing would be slower than usual (although Kwe would still be able to do this).

I would suggest, if speed is of issue here to send the samples ASAP and not wait until the WC stuff is sorted out.

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

Subject: Next Hendra batch of testing

Hi Vincent, Kwe and Trent,

Tamika is in the last year of her PhD now, and unfortunately, the shipment that got rejected at the border included samples that she needs for her analyses. We're still trying to reorganise shipment of samples to you guys, but as we work towards that, I wanted to check in with you what your workload was in the coming months? I know you've got a lot of different commitments that you're juggling, and I wonder if there are any particular time windows that would be better than others for processing Australian samples?

Thanks Ali From: Plowright, Raina

**Sent:** Tue, 21 Jan 2020 21:24:16 +0000

To: (b)

Cc: Munster, Vincent (NIH/NIAID) [E]

Subject: Re: Time sensitive request

Attachments: DARPA.docx

(b) (6)

Here is the information, provided by Vincent Munster. He is cc'd in case you have follow up questions.

raina

On Jan 21, 2020, at 1:57 PM,

(b) (6)

wrote:

Yes. Please call them or send their phone number. I need the information

asap. Thank you

(b)(6)

(b) (6)

Lead Scientist

Support to Biological Technologies Office, DARPA

Science and Technology Associates, Inc.

(b) (6)

----Original Message----

From: Plowright, Raina < (b) (6)

Sent: Tuesday, January 21, 2020 3:51 PM

10:

Subject: Re: Time sensitive request Importance: High

I have forwarded to RML to answer questions below. Obviously, we are doing

BSL4 work at RML.

On Jan 21, 2020, at 1:30 PM,

(b) (6)

(b) (6)

(b) (6) wrote:

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1. Name(s) of facility (the name of the subcontractor performing the work) 2. Responsible public or private organization or company (List the departments and agencies that operates the facility. If a third-party contractor runs the facility, note the contracting company as well) 3. Location and postal address (A physical address is

required; PO boxes can be listed in addition to, but not instead of, the physical address) 4. N/A 5. Number of maximum containment units within the research center and/or laboratory, with an indication of their respective size (m2). If the facility contains more than one BSL-4 laboratory, list each lab (and corresponding area) separately.

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Instead, include generalized references to MoT used in laboratory studies.

Please send negative responses as well.	
Thank you.	
(b) (6)	

(b) (6)

Lead Scientist

Support to Biological Technologies Office, DARPA Science and Technology Associates, Inc.

(b) (6)

1. Name(s) of facility

#### Rocky Mountain Laboratories (RML)

https://www.niaid.nih.gov/about/rocky-mountain-laboratories

2. Responsible public or private organization or company

#### NIH/NIAID

3. Location and postal address (A physical address is required; PO boxes can be listed in addition to, but not instead of, the physical address)

#### 903S 4th street, Hamilton, 59840, MT

5. Number of maximum containment units within the research center and/or laboratory, with an indication of their respective size (m2)

The Laboratory of Virology (LV) is located in the Integrated Research Facility (IRF) on the campus of Rocky Mountain Laboratories (RML) in Hamilton, Montana. RML houses several Laboratories of the NIAID Division of Intramural Research (DIR). All LV laboratory space is located in the IRF.

LV has presently been assigned 6140 sq.-ft. of BSL2 laboratory space. These labs are equipped with all necessary items that are needed to perform classic virology, basic immunology and advanced molecular biology/virology. Larger equipment includes: freezers, refrigerators, C02-incubators, class II biosafety cabinets, PCR thermocyclers, LightCycler, SmartCycler, ultracentrifuge, high speed centrifuge, microcentrifuges, FACS, electrophoreses equipment for protein and nucleic acid work, power supplies, spectrophotometer, ELISA reader, plate washer, light microscopes, fluorescence microscopes, and a confocal microscope.

The IRF houses "state-of-the-art" BSL-4 laboratory and animal space which is maintained by the Director of NIAID DIR as Director's Reserve. The IRF houses approximately 3500 square feet (SF) (325 m²) of BSL-4/BSL-3 lab space (flexible space). The BSL-4 lab is equipped with all necessary items needed to perform classic virology, basic immunology and molecular biology. The equipment includes: freezers, refrigerators, C02-incubators, class II biosafety cabinets, ultracentrifuge, high speed centrifuge, low speed centrifuges, microcentrifuges, ELISA reader, plate washer, microscopes, fluorescence microscope and computers.

The Rocky Mountain Veterinary Branch (RMVB) at RML has BSL-2 animal space of approximately 12,255 sq.-ft., which can house species such as mice, rats, guinea pigs,

hamsters, bats, rabbits and nonhuman primates. The BSL-2 animal space is in a dedicated facility near the IRF. RMVB is led by Dr. D. Gardner, DVM, PhD, and is staffed by Board Certified clinical veterinarians, veterinary pathologists and well-trained animal care staff. RMVB provides the entire RML staff, including LV, with service on all levels of animal handling and care and procedures such as blood sampling, infections, necropsies, and euthanasia. Complete histopathology services are provided, including immunohistochemistry and in situ hybridization. All animal facilities at RML are fully accredited by AAALAC.

In addition, the IRF contains approximately 3000 sq.-ft. (280 m²) of animal space in high containment (ABSL-4/ABSL-3 – flexible space). This space is equipped for handling caged animals including bats, ferret, rodent and nonhuman primates (cynomolgus and rhesus macaques) species as well as smaller livestock animals such as pigs, goats and sheep. RMVB staff provides animal care and handling support. Procedures on animals are performed by fully trained personnel of LV or RMVB.

6. Scope and general description of activities, including type(s) of micro-organisms and/or toxins as appropriate.

The Laboratory of Virology (LV) conducts innovative scientific research on viral agents requiring high or maximum containment (biosafety level-2 to biosafety level-4). These agents include filoviruses, bunyaviruses, arenaviruses, and flaviviruses. Research studies focus on vector/reservoir transmission, viral ecology, pathogenesis, pathophysiology, and host immune response of these viral pathogens. A significant goal is to develop diagnostics, vaccines, and therapeutics against these agents.

LV scientists broadly study pathogens that cause viral hemorrhagic fevers, viral encephalitis, and certain respiratory diseases. This work employs investigations in cell culture; animal models, including nonhuman primates; reservoir species; and arthropod hosts in order to elucidate the viral pathogenesis, immune responses, molecular evolution, cellular and molecular biology, and vector-host interactions.

View all Division of Intramural Research laboratories

# **Major Areas of Research**

- Study pathogenesis and pathophysiology of high-containment viral pathogens using molecular technologies, including reverse genetics.
- Study immune responses to infection and vaccination of high-containment viral pathogens, and develop new vaccine candidates.
- Study vector/reservoir transmission of high-containment viral pathogens using appropriate animal models

- Use in vitro and in vivo systems to study the interactions between viral pathogens or viral components and host cells, and develop new antiviral strategies.
- Study the epidemiology and ecology of high-containment pathogens using newly developed rapid, sensitive, and specific diagnostic-test systems, including those that can be applied under field conditions.

https://www.niaid.nih.gov/research/lab-virology-new

 From:
 Munster, Vincent (NIH/NIAID) [E]

 Sent:
 Tue, 21 Jan 2020 13:59:15 -0700

To: Plowright, Raina; Bushmaker, Trenton (NIH/NIAID) [E]; Kwe Claude, Yinda

(NIH/NIAID) [F]

Cc: LaTrielle, Sara

Subject: Re: Time sensitive request

Attachments: DARPA.docx

#### Here it is

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: "Plowright, Raina" < (b) (6)

Date: Tuesday, January 21, 2020 at 1:50 PM

To: ' (b) (6) < (b) (6) Trenton Bushmaker

< (b) (6) "Kwe Claude, Yinda (NIH/NIAID) [F]"

(b) (6)

Cc: "LaTrielle, Sara" < (b) (6)

Subject: Fwd: Time sensitive request

### Hi Vincent,

Can someone from your team answer all these questions and reply to me? I'll forward to 60 (6) with you ccd. They say it is urgent.

Thanks, Raina

#### Begin forwarded message:

From: (b) (6)

Subject: Time sensitive request

Date: January 21, 2020 at 1:30:33 PM MST

```
To: Ariel Weinberger < (b) (6) "Carla SALEH" < (b) (6) Greg Gray

(b) (6) Jose Garcia < (b) (6) Luke Alphey

(b) (6) Patrick Blair (b) (6) Peter A Barry

(b) (6) "Plowright, Raina" < (b) (6) "Robert Huebner"

(b) (6)
```

Cc: (b) (6)

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Please send	negative	resnonses	as well
ricase sellu	HERALIVE	1 620011363	as well.

(b) (6)

Thank you.
(b) (6)

Lead Scientist
Support to Biological Technologies Office, DARPA
Science and Technology Associates, Inc.

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https://www.niaid.nih.gov/about/rocky-mountain-laboratories

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The IRF houses "state-of-the-art" BSL-4 laboratory and animal space which is maintained by the Director of NIAID DIR as Director's Reserve. The IRF houses approximately 3500 square feet (SF) (325 m²) of BSL-4/BSL-3 lab space (flexible space). The BSL-4 lab is equipped with all necessary items needed to perform classic virology, basic immunology and molecular biology. The equipment includes: freezers, refrigerators, C02-incubators, class II biosafety cabinets, ultracentrifuge, high speed centrifuge, low speed centrifuges, microcentrifuges, ELISA reader, plate washer, microscopes, fluorescence microscope and computers.

The Rocky Mountain Veterinary Branch (RMVB) at RML has BSL-2 animal space of approximately 12,255 sq.-ft., which can house species such as mice, rats, guinea pigs,

hamsters, bats, rabbits and nonhuman primates. The BSL-2 animal space is in a dedicated facility near the IRF. RMVB is led by Dr. D. Gardner, DVM, PhD, and is staffed by Board Certified clinical veterinarians, veterinary pathologists and well-trained animal care staff. RMVB provides the entire RML staff, including LV, with service on all levels of animal handling and care and procedures such as blood sampling, infections, necropsies, and euthanasia. Complete histopathology services are provided, including immunohistochemistry and in situ hybridization. All animal facilities at RML are fully accredited by AAALAC.

In addition, the IRF contains approximately 3000 sq.-ft. (280 m²) of animal space in high containment (ABSL-4/ABSL-3 – flexible space). This space is equipped for handling caged animals including bats, ferret, rodent and nonhuman primates (cynomolgus and rhesus macaques) species as well as smaller livestock animals such as pigs, goats and sheep. RMVB staff provides animal care and handling support. Procedures on animals are performed by fully trained personnel of LV or RMVB.

6. Scope and general description of activities, including type(s) of micro-organisms and/or toxins as appropriate.

The Laboratory of Virology (LV) conducts innovative scientific research on viral agents requiring high or maximum containment (biosafety level-2 to biosafety level-4). These agents include filoviruses, bunyaviruses, arenaviruses, and flaviviruses. Research studies focus on vector/reservoir transmission, viral ecology, pathogenesis, pathophysiology, and host immune response of these viral pathogens. A significant goal is to develop diagnostics, vaccines, and therapeutics against these agents.

LV scientists broadly study pathogens that cause viral hemorrhagic fevers, viral encephalitis, and certain respiratory diseases. This work employs investigations in cell culture; animal models, including nonhuman primates; reservoir species; and arthropod hosts in order to elucidate the viral pathogenesis, immune responses, molecular evolution, cellular and molecular biology, and vector-host interactions.

View all Division of Intramural Research laboratories

# **Major Areas of Research**

- Study pathogenesis and pathophysiology of high-containment viral pathogens using molecular technologies, including reverse genetics.
- Study immune responses to infection and vaccination of high-containment viral pathogens, and develop new vaccine candidates.
- Study vector/reservoir transmission of high-containment viral pathogens using appropriate animal models

- Use in vitro and in vivo systems to study the interactions between viral pathogens or viral components and host cells, and develop new antiviral strategies.
- Study the epidemiology and ecology of high-containment pathogens using newly developed rapid, sensitive, and specific diagnostic-test systems, including those that can be applied under field conditions.

https://www.niaid.nih.gov/research/lab-virology-new

From: Munster, Vincent (NIH/NIAID) [E]
Sent: Tue, 21 Jan 2020 11:31:59 -0700

To: Baric, Toni C; Baric, Ralph; van Doremalen, Neeltje (NIH/NIAID) [E]; Alexandra

Schaefer

Subject: Re: Human ACE2 mice

Sounds good! 3 pm ET/1 pm MT it is,

Any preferred number?

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: "Baric, Toni C" < (b) (6)

Date: Tuesday, January 21, 2020 at 11:21 AM

**To:** ' (b) (6) < (b) (6) "Baric, Ralph"

< (b) (6) Neeltje van Doremalen < (b) (6) Alexandra

Schaefer < (b) (6)

Subject: RE: Human ACE2 mice

Hi Vincent,

Unfortunately that time slot was recently filled. Can you make today after 3pm ET/1 pm MT?

Or 4PM ET/2 PM MT on Wednesday?

Toni

From: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Sent: Tuesday, January 21, 2020 1:04 PM

To: Baric, Toni C < (b) (6) Baric, Ralph S < (b) (6) van

Doremalen, Neeltje (NIH/NIAID) [E] < (b) (6) Schaefer, Alexandra

(b) (6)

Subject: Re: Human ACE2 mice

Hi Toni,

I east coast times (we are two hours behind in MT), I can do 2-3 on Wednesday (12-1 Mountain Time),

Let me know if this still works,

Cheers,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

(b) (6) From: "Baric, Toni C" Date: Tuesday, January 21, 2020 at 6:50 AM (b) (6) (b) (6) " To: "Baric, Ralph" < (b) (6) Neeltje van Doremalen (b)(6)(b) (6) Alexandra Schaefer < Subject: RE: Human ACE2 mice Dear Vincent, Please see Ralph's availability below: Wednesday 2-3 Thursday 11-4:30 Friday after 1:30. Let me know if these times work for you. Toni From: Baric, Ralph S < Sent: Monday, January 20, 2020 4:18 PM (b) (6) van Doremalen, Neeltje (NIH/NIAID) To: Munster, Vincent (NIH/NIAID) [E] < (b) (6) Schaefer, Alexandra < (b) (6) [E] < Cc: Baric, Toni C (b)(6)Subject: RE: Human ACE2 mice I've cc'd toni so that she can set up a call to chat. Hope you are all well. Ralph From: Munster, Vincent (NIH/NIAID) [E] < (b)(6)Sent: Monday, January 20, 2020 12:40 PM To: van Doremalen, Neeltje (NIH/NIAID) [E] (b) (6) Baric, Ralph S (b) (6) Schaefer, Alexandra < (b)(6)Subject: Re: Human ACE2 mice Hi guys, just to emphasize that this all a collaborative effort,

In short, we would like a mouse model to test vaccine efficacy

But, this looks a lot like pH1N1, so if we can show a strong UNC/NIAID effort it would be (very) good. Hope you guys are making progress with the rg work, no clear info on the availability of strain sharing (NIH nor WHO).

Cheers,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: Neeltje van Doremalen < (b) (6)

Date: Monday, January 20, 2020 at 10:11 AM

To: "Baric, Ralph" < (b) (6) Alexandra Schaefer < (b) (6)

Cc: " (b) (6) < (b) (6)

Subject: RE: Human ACE2 mice

Hi Ralph and Alex,

Thank you for the emails regarding the ACE2 mice. We do not want to duplicate work either, thus a phone call would be highly appreciated to ensure we aren't chasing the same research goals. When would you be available? I am currently in the UK until Sunday but can be flexible with timing.

Neeltje

From: "Baric, Ralph S" < (b) (6)

Date: Monday, January 13, 2020 at 3:48 PM

To: " (b) (6) < (b) (6)

Cc: "Baric, Ralph" < (b) (6)

Subject: RE: Human ACE2 mice

Sounds good to me to, we should do a short call. Ralph

From: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Sent: Monday, January 13, 2020 5:43 PM
To: Baric, Ralph S < (b) (6)

Subject: Re: Human ACE2 mice

Sounds good, let me know what your thinking,

Would be good to expand our collaboration even more (got these continuous calls with NIAID intramural and extramural so I make sure you name gets dropped often).

#### Cheers,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

From: "Baric, Ralph S" < (b) (6)

Date: Monday, January 13, 2020 at 3:41 PM

To: " (b) (6) < (b) (6)

Subject: RE: Human ACE2 mice

Hi Vincent, We do. we have put up a number of breeders last week to amplify our colony. They are available in a few weeks-although I don't want to cross lines so we should talk. Ralph

From: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Sent: Monday, January 13, 2020 5:37 PM

To: Baric, Ralph S < (b) (6) Schaefer, Alexandra < (b) (6)

Cc: van Doremalen, Neeltje (NIH/NIAID) [E] < (b) (6)

Subject: Human ACE2 mice

Hi guys,

We're expecting that the Wuhan virus will bind human ACE2, do you have a good transgenic mouse model we could potebtially use? We are primarily thinking vaccines for now.

Cheers,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH From: Munster, Vincent (NIH/NIAID) [E]

Sent: Sun, 19 Jan 2020 07:54:01 -0700

To: Wang Linfa; Broder, Chris (USU-DoD)

Cc: De wit, Emmie (NIH/NIAID) [E]

Subject: Re: SINGAPORE: Wuhan virus: Suspected cases in Singapore go up to 5, MOH

warns of more to come

#### Hi Linfa,

Absolutely right and have been talking with Ralph from the beginning (but would like to have wt isolates as well, sometimes the rg created ones are slightly less pathogenic). We are planning to do some bat studies here as well, as soon as we get our hands on the virus, I think it would be great if we collaborate with you on this if you're interested,

#### Cheers,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: Wang Linfa <		(b) (6)	
Date: Sunday, January	19, 2020 at 6:48 A	M	
To: '	(b) (6) <		(b) (6) "Broder, Chris (USU-DoD)"
<	(b) (6)		
Cc: Emmie De wit <	(b)	(6)	

**Subject:** RE: SINGAPORE: Wuhan virus: Suspected cases in Singapore go up to 5, MOH warns of more to come

Dear Vincent,

Just got back in SG from Wuhan. Your description of "gaining momentum" is spot on!

But all the cases in SG are "suspected" and I am NOT involved in any of these as Duke-NUS is an academic institute and not on the front line in the context of outbreak responses. But if the hospital makes an isolation, we can certain request for research in to diagnosis, etc. So will keep in touch.

My bet is the Ralf Baric will be the first one to get a live virus (by rescue) in USA and, if I were you, I would line up with Ralf for the all the expts you want to do and focus on the ones that he is not/unable to do!

As it is SARS-like, I am sure he will be able to do that in weeks, if not days!

Cheers,

Linfa (Lin-Fa) WANG, PhD FTSE
Professor & Director
Programme in Emerging Infectious Disease
Duke-NUS Medical School,
8 College Road, Singapore 169857
Tel: (b) (6)

From: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Sent: Friday, 17 January 2020 11:10 PM

To: Wang Linfa < (b) (6)

(b) (6)

Cc: De wit, Emmie (NIH/NIAID) [E] < (b) (6)

Subject: FW: SINGAPORE: Wuhan virus: Suspected cases in Singapore go up to 5, MOH warns of more to

come

Importance: High

- External Email -

Hi Linfa,

The Wuhan coronavirus seems to be gaining momentum with quite significant spread outside of China (including Singapore). We have been gearing-up and are very interested in any potential of obtaining virus isolates, novel sequences etc to do our work. Our work is initially focused at animal model design and countermeasure development (vaccines with Jenner/CEPI) and antivirals (Emmie).

Let me know what your thoughts are,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: "Marston, Hilary (NIH/NIAID) [E]" (b) (6)

**Date:** Friday, January 17, 2020 at 7:53 AM **To:** NIAID Coronavirus Response SWAT 2020

(b) (6)

Subject: FW: SINGAPORE: Wuhan virus: Suspected cases in Singapore go up to 5, MOH warns of

more to come

From: Folkers, Greg (NIH/NIAID) [E] < (b) (6)

Sent: Friday, January 17, 2020 9:53 AM

Subject: SINGAPORE: Wuhan virus: Suspected cases in Singapore go up to 5, MOH warns of more to

come

Wuhan virus: Suspected cases in Singapore go up to 5, MOH warns of more to come By Asyraf Kamil
Published17 January, 2020
Updated 17 January, 2020

SINGAPORE — Two more people with pneumonia who have travelled to Wuhan, China were warded here and isolated as a precautionary measure, bringing the tally of such cases to five.

The Ministry of Health (MOH) cautioned on Friday (Jan 17) that Singapore is "likely to see more suspect cases that will need to be investigated".

Advertisement

In the latest reported cases, a 64-year-old man from China and a 61-year-old female Singapore resident were admitted to a hospital for further assessment and treatment after they arrived here from Wuhan.

They are in stable condition, MOH said, adding that the two did not visit the Huanan Seafood Wholesale Market, which is a large seafood and animal market that has been associated with the cluster of pneumonia cases in Wuhan.

Advertisement

In an update on the case involving the first Singaporean who was warded on Thursday for pneumonia, the MOH said that epidemiological investigations, clinical assessment and laboratory test results showed that the 69-year-old man's case is not linked to the pneumonia cluster in Wuhan.

The patient has also tested negative for coronavirus.

The virus behind the outbreak at Wuhan city in the Hubei province of China is said to be a new coronavirus, known as 2019-nCoV, which belongs to a family of coronaviruses that cause illness in people and that circulate among animals.

In rare instances, animal coronaviruses can evolve and infect people and then spread from human to human, as it was with the severe acute respiratory syndrome (Sars) outbreak and the Middle East respiratory syndrome (Mers).

The health authorities in Wuhan have diagnosed 41 people with the coronavirus.

Read also: MOH aware of severe pneumonia cases in Wuhan, China; doctors to look out for suspected cases

Most of the patients in Wuhan have reportedly had some link to the Huanan Seafood Wholesale Market, although some patients did not report visiting this market, suggesting that some limited person-to-person spread may be occurring, the World Health Organization said.

So far, there have been two confirmed cases in Thailand and one in Japan. In China, wwo people who were infected and had underlying medical conditions have died.

Countries in Asia are on alert as the Chinese New Year approaches, given that it is a peak period for people from China to travel.

In Singapore, temperature screening measures have been put up at Changi Airport for inbound flights arriving from Wuhan and suspected cases will be referred to hospitals for further assessment,

MOH said that it will continue to monitor the situation closely.

"As medical practitioners are on the lookout for cases with pneumonia who have recently returned from Wuhan, Singapore is likely to see more suspect cases that will need to be investigated for possible links to the Wuhan cluster," it said.

The ministry also urged the public to remain vigilant and to adopt good personal hygiene practices at all times.

It added that travellers to Wuhan should monitor their health closely and seek medical attention promptly if they feel unwell, and also inform their doctor of their travel history.

Read more at <a href="https://www.todayonline.com/singapore/wuhan-virus-suspected-cases-singapore-go-5-moh-warns-more-come">https://www.todayonline.com/singapore/wuhan-virus-suspected-cases-singapore-go-5-moh-warns-more-come</a>

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From: Munster, Vincent (NIH/NIAID) [E]
Sent: Fri, 17 Jan 2020 14:06:56 -0700

To: Plowright, Raina; Letko, Michael (NIH/NIAID) [F]

Cc: Kevin Olival; Steph Seifert

Subject: Re: For you records: NRM manuscript - submitted version

Sounds good, added us both for the DARPA PREEMPT,

Cheers,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: "Plowright, Raina" < (b) (6)

**Date:** Friday, January 17, 2020 at 2:06 PM **To:** Michael Letko < (b) (6)

Subject: Re: For you records: NRM manuscript - submitted version

thanks for the ms copy. I don't think figures were attached? Looking forward to seeing this one in print! When it comes back from review, I'll need to add funding info. Forgot to do that on this version. Raina

On Jan 16, 2020, at 5:16 PM, Letko, Michael (NIH/NIAID) [F] < (b) (6) wrote:

Dear all,

Attached are the submitted manuscript and figures.

Cheers, -michael

--

Michael Letko, Ph.D
Postdoctoral IRTA
Dr. Vincent Munster Laboratory
Virus Ecology Unit, Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

## 903S 4th Street Hamilton MT 59840 (b) (6)

Begin forwarded message:

From: "Letko, Michael (NIH/NIAID) [F]" < (b) (6)

Date: January 16, 2020 at 3:55:54 PM MST

To: "Munster, Vincent (NIH/NIAID) [E]" < (b) (6)

Subject: Re: NRM manuscript - with latest SnS, RP, KJO, ML changes

Attached is an updated version of the manuscript draft.

Below us an updated version of our response.

1. I've discussed your article with Andrea and we both had expected a slightly broader scope; in particular, many of our readers won't be familiar with the diversity of viruses found in bats and what makes these animals unique host. I think this information needs to be spelled out for readers to appreciate the discussion of emergence.

- a. We feel the scope has now been broadened by including the editors' suggesting additions.
- 2. 2. My specific suggestion would be to add two new main sections: a first one right after the introduction that discusses viruses found in bats. You mention some that have spilled over to humans in the introduction. Can you expand on that? Are there other viruses with the potential to infect humans? Do bats have more diverse viruses than other animals? How well do we understand the diversity of bat viruses? To complement this section, you could add a table on bat viruses with subsections, e.g. on viruses directly emerged from bats, indirectly emerged, with proposed links to bats (e.g., I seem to remember some discussion of ZIKV in bats) etc.
  - a. We have now added text discussing viral diversity in bats
- 3. After this section on diversity, I would suggest to have a section on virus infection bats, which would include the section you already have on innate immunity and add more details (is there more to say about the IFN pathways in bats?). In addition, is there anything to say about adaptive immunity? Also, you could mention recent literature describing the role of metabolism and flight in relation to immunity and viral infection. Finally, it would be good to then link immunity and metabolism to viral persistence and shedding. You could have a schematic figure for this section that highlights some of the unique features of bat immunity (e.g. something like the figures in this review: https://www.mdpi.com/1999-4915/11/2/192).
  - a. We have re-structured the section on the molecular biology of zoonotic viruses for clarity.

- b. We have also added a new section on adaptive immunity in bats.
- c. We have also added a new section on metabolism and flight in bats and how that may relate to immunity. How these two concepts intersect is still very much speculative in the field, and there is not much data-supported literature actually supporting the theory.
- d. We have also included a section on viral persistence and proposed mechanisms.
- 4. I realise that this means quite a bit of new text and I'm fine with extending the word limit to ~5500. You could also streamline the spillover/barrier sections a little, e.g. by shortening or removing the knowledge gap and limitations sections (some of the things like need for better models, systems and reagents are mentioned repeatedly; instead of having all these sections on limitations you could mention this once in the bat model box or in the conclusions).
  - a. We have streamlined the barriers section by significantly parsing the knowledge gaps section.
- 5. Finally, to reflect this broader scope, I'd suggest changing the title to 'Bat-borne virus diversity, spillover and emergence'.
  - a. We agree with the editors and have made the title change.

--

Michael Letko, Ph.D
Postdoctoral IRTA
Dr. Vincent Munster Laboratory
Virus Ecology Unit, Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH
903S 4th Street
Hamilton MT 59840
(b) (6)

From: "Letko, Michael (NIH/NIAID) [F]" < (b) (6)

Date: Wednesday, January 15, 2020 at 3:56 PM

To: "Munster, Vincent (NIH/NIAID) [E]" < (b) (6)

Subject: Re: NRM manuscript - with latest SnS, RP, KJO, ML changes

Another response from us to add:

3d. We have also included a section on viral persistence and proposed mechanisms.

--

Michael Letko, Ph.D
Postdoctoral IRTA
Dr. Vincent Munster Laboratory
Virus Ecology Unit, Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH
903S 4th Street
Hamilton MT 59840
(b) (6)

On Jan 15, 2020, at 3:53 PM, Letko, Michael (NIH/NIAID) [F] <

Hi Vincent,

Attached is the updated NRM manuscript and figures.

Below is the initial feedback from the editors with our responses underneath each comment – feel free to edit these. I tried not be a jerk with comment 3c.

(b) (6) wrote:

Let me know if you need anything else, -michael

- 1. I've discussed your article with Andrea and we both had expected a slightly broader
  - scope; in particular, many of our readers won't be familiar with the diversity of viruses found in bats and what makes these animals unique host. I think this information needs to be spelled out for readers to appreciate the discussion of emergence.
    - a. We feel the scope has now been broadened by including the editors' suggesting additions.
  - 2. 2. My specific suggestion would be to add two new main sections: a first one right after the introduction that discusses viruses found in bats. You mention some that have spilled over to humans in the introduction. Can you expand on that? Are there other viruses with the potential to infect humans? Do bats have more diverse viruses than other animals? How well do we understand the diversity of bat viruses? To complement this section, you could add a table on bat viruses with subsections, e.g. on viruses directly emerged from bats, indirectly emerged, with proposed links to bats (e.g., I seem to remember some discussion of ZIKV in bats) etc.

## a. We have now added text discussing viral diversity in bats

- 3. 3. After this section on diversity, I would suggest to have a section on virus infection bats, which would include the section you already have on innate immunity and add more details (is there more to say about the IFN pathways in bats?). In addition, is there anything to say about adaptive immunity? Also, you could mention recent literature describing the role of metabolism and flight in relation to immunity and viral infection. Finally, it would be good to then link immunity and metabolism to viral persistence and shedding. You could have a schematic figure for this section that highlights some of the unique features of bat immunity (e.g. something like the figures in this review: https://www.mdpi.com/1999-4915/11/2/192).
  - a. We have re-structured the section on the molecular biology of zoonotic viruses for clarity.
  - b. We have also added a new section on adaptive immunity in bats.
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- 4. I realise that this means quite a bit of new text and I'm fine with extending the word limit to ~5500. You could also streamline the spillover/barrier sections a little, e.g. by shortening or removing the knowledge gap and limitations sections (some of the things like need for better models, systems and reagents are mentioned repeatedly; instead of having all these sections on limitations you could mention this once in the bat model box or in the conclusions).
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- 5. Finally, to reflect this broader scope, I'd suggest changing the title to 'Bat-borne virus diversity, spillover and emergence'.
  - a. We agree with the editors and have made the title change.

\_\_\_\_\_

\_\_

Michael Letko, Ph.D
Postdoctoral IRTA
Dr. Vincent Munster Laboratory
Virus Ecology Unit, Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH
903S 4th Street
Hamilton MT 59840

<NRM DRAFT 1\_15\_20\_(all authors)\_ML.docx>
<NRM FIGURES 1\_15\_20.docx>
<NRM DRAFT 1\_16\_20 (for submission).docx>

From: Letko, Michael (NIH/NIAID) [F] Sent: Fri, 17 Jan 2020 00:16:11 +0000

To: Raina Plowright; Kevin Olival; Steph Seifert

Cc: Munster, Vincent (NIH/NIAID) [E]

Subject: For you records: NRM manuscript - submitted version Attachments: NRM DRAFT 1\_16\_20 (for submission).docx, ATT00001.htm

Dear all,

Attached are the submitted manuscript and figures.

Cheers, -michael

Michael Letko, Ph.D Postdoctoral IRTA Dr. Vincent Munster Laboratory Virus Ecology Unit, Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH 903S 4th Street Hamilton MT 59840

(b) (6)

## Begin forwarded message:

(b) (6) From: "Letko, Michael (NIH/NIAID) [F]" <

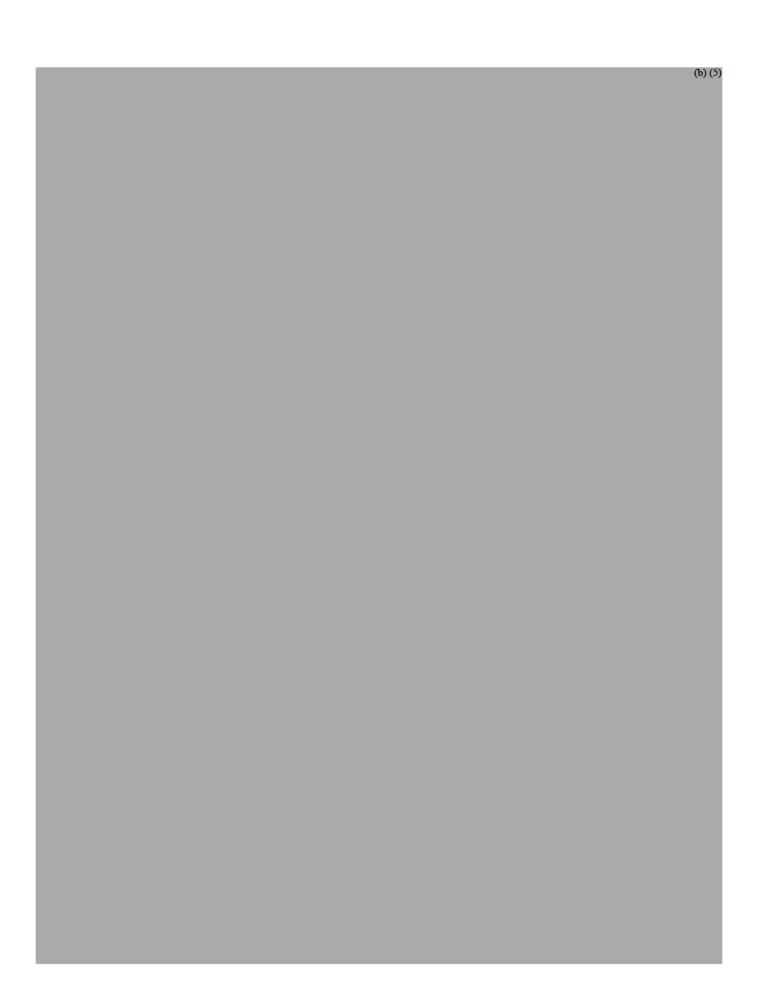
Date: January 16, 2020 at 3:55:54 PM MST

To: "Munster, Vincent (NIH/NIAID) [E]" < (b) (6)

Subject: Re: NRM manuscript - with latest SnS, RP, KJO, ML changes

Attached is an updated version of the manuscript draft.

Below us an updated version of our response.



--

Michael Letko, Ph.D
Postdoctoral IRTA
Dr. Vincent Munster Laboratory
Virus Ecology Unit, Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH
903S 4th Street
Hamilton MT 59840
(b) (6)

From: "Letko, Michael (NIH/NIAID) [F]" < (b) (6)

Date: Wednesday, January 15, 2020 at 3:56 PM

To: "Munster, Vincent (NIH/NIAID) [E]" < (b) (6)

Subject: Re: NRM manuscript - with latest SnS, RP, KJO, ML changes

Another response from us to add:

(b) (5)

\_\_

Michael Letko, Ph.D
Postdoctoral IRTA
Dr. Vincent Munster Laboratory
Virus Ecology Unit, Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH
903S 4th Street
Hamilton MT 59840

(b) (6)

On Jan 15, 2020, at 3:53 PM, Letko, Michael (NIH/NIAID) [F] < (b) (6) wrote:

## Hi Vincent,

Attached is the updated NRM manuscript and figures.

	 	(

Below is the initial feedback from the editors with our responses underneath each comment

- feel free to edit these. I tried not be a jerk with comment 3c.

(b) (5)

--

Michael Letko, Ph.D

Postdoctoral IRTA

Dr. Vincent Munster Laboratory

Virus Ecology Unit, Laboratory of Virology

Rocky Mountain Laboratories

NIAID/NIH

903S 4th Street

Hamilton MT 59840

(b) (5)

<NRM DRAFT 1\_15\_20\_(all authors)\_ML.docx>
<NRM FIGURES 1\_15\_20.docx>

15

40

41

 From:
 Munster, Vincent (NIH/NIAID) [E]

 Sent:
 Thu, 16 Jan 2020 16:46:50 -0700

To: Alison Peel; Halpin, Kim (AAHL, Geelong AAHL)

Cc: Plowright, Raina

Subject: Re: (b) (4) and face to face meeting

Hi guys,

If needed we can provide some assistance with the sequencing, we are working on a (b) (4)

but more than willing to give it a try,

Take care and we can very much relate to the fires here in Montana (we have quite big fire season here as well), so hope it will be under control soon,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: Alison Peel < (b) (6).

Date: Thursday, January 16, 2020 at 4:42 PM

To: "Halpin, Kim (AAHL, Geelong AAHL)" < (b) (6).

Cc: "Plowright, Raina" < (b) (6) " (b) (6).

Subject: Re: (b) (4) and face to face meeting.

Ok, thanks for the update Kim! Of most interest would be sequences from the duration of our study (from December 2016), so that we can compare these to (b) (4) Vincent-please pipe up if there's anything I've missed.

Thanks again, Ali

On Fri, 17 Jan 2020 at 9:34 am, Halpin, Kim (AAHL, Geelong AAHL) < (b) (6) wrote: Hi Ali

Happy New Year to you too. Fortunately I have not been affected by the fires – but the smoke has been a very haunting reminder of what has taken place on the eastern side of the state. It was bad for 3 days – then cleared after the rain – but it is expected to come back early next week.

Take your time - there is no rush. And good luck with the grants.

Regarding (b) (4)
And I will look into what we have done with the previous cases. I will have to get back to you about that.
Bye for now Kim
From: Alison Peel < (b) (6)  Sent: Friday, 17 January 2020 10:27 AM  To: Halpin, Kim (AAHL, Geelong AAHL) < (b) (6)  Cc: Plowright, Raina < (b) (6) Vincent Munster < (b) (6)  Subject: Re: (b) (4) and face to face meeting
Hi Kim,
Happy New Year. I hope you're not too affected by smoke where you are?
I know that I still need to get back to you about PhD students I'm currently focussed on meeting a grant deadline, but also had some great conversations with Ina Smith, so will get back to you on that in the next few weeks.
In the meantime, I was also hoping to follow up on our request about obtaining (b) (4)
Chat more soon, Cheers Ali
On Wed, 16 Oct 2019 at 13:03, Alison Peel < (b) (6) wrote: Hi Kim,
Thanks for your email. Glad to hear the symposium went well!
Great to hear that all the samples from (b) (4) are saved. I have cc'd Vincent Munster from Rocky Mountain Laboratory whom you may have already met, and Raina, whom you know! Vincent and his team are working on (b) (4)
We'd be happy to work on this in a collaborative way with AAHL and would be happy to facilitate a discussion on how to do work together on this.
Cheers
Ali
On Tue, 15 Oct 2019 at 20:36, Halpin, Kim (AAHL, Geelong AAHL) < 6) (6) wrote:

## Hi Alison

The symposium started this morning. So far so good!

	(b) (4)
What is the timeline on your project?	
Bye for now Kim	
From: Alison Peel < (b) (6)  Sent: Wednesday, 16 October 2019 8:35 AM  To: Halpin, Kim (AAHL, Geelong AAHL) < (b) (6)  Subject: Re: HeV sequencing and face to face meeting	
Hi Kim,	
I hope you're well and everything went well with the EAD symposium!	
See below, our research group are starting to	(b) (4)
Thanks Alison  ALISON PEEL BSc(Vet) BVSc MSc PhD	
DECRA Research Fellow, Griffith Wildlife Disease Ecology Group  Environmental Futures Research Institute, Sir Samuel Griffith Centre (N78) 2,23	
Griffith University, Nathan Campus, 170 Kessels Rd, Nathan, QLD, 4111, Australia	
Office days: Monday - Thursday	
E: (b) (6)	
W: <b>(b) (6)</b>	
M: (b) (6)	
@ali_bat	
www.mccallum-disease-ecology.com/alison-peel https://experts.griffith.edu.au/academic/a.peel	
If you have received an email from me outside of normal working hours, I'm sending it at a time that suits me. I am not expecting you	to read or reply to it
until normal working hours.	

On Wed, 25 Sep 2019 at 17:27, Paul Freeman < 60 wrote:

I don't have any information on sequences. I think AAHL does that work. The person I would contact there would be Kim Halpin

Kim Halpin BVSc, MVSc, MPH, MANZCVS, PhD Pathology and Pathogenesis Group Leader Australian Animal Health Laboratory CSIRO

E	(b) (6)
T	(b) (6) M (b) (6)
5	ortarlington Road, East Geelong, VIC 3219
w	w.csiro.au   www.csiro.au/AAHL
ht	://www.linkedin.com/pub/kim-halpin/13/5b3/4a4

Peter Kirkland would also know I guess. Do you have his contact details.

Paul Freeman, Senior Veterinary Offic Biosecurity and Food Safety NSW Primary Industries	cer		
Animal Health Building   1243 Bruxne	r Hwy   Wollongba	r NSW 2477	
T: (b) (6)   F: (b) (6) (b) (6)	) (6)   M:	ь) (6)	
W: www.dpi.nsw.gov.au			
From: Alison Peel <	b) (6)		
Sent: Thursday, 26 September 2019 7:5	S8 AM		
To: Paul Freeman <	(b) (6)		
Subject: (b) (4) and face to fa	ce meeting		
Hi Paul,			
Our project team at Rocky Mountain La	abs in Montana ai	e starting	(b) (4)
They have asked me whet	her sequences ar	e available from recent HeV spillov	ers, but I'm
unsure whether		(b) (4) I wanted to check whether	you're aware
of this and whether it's ok for me to try	and seek out the	se sequences?	
Also, it would be nice to come down an	nd say hi face to fa	ace and give an update on our proj	ect to you,
Phil, David and whoever else is appropri	riate. If that is of i	nterest to you, would Thursday 7t	h
November work? I'm travelling a bit in	October.		
Thanks			
Ali			

ALISON PEEL BSc(Vet) BVSc MSc PhD

DECRA Research Fellow, Griffith Wildlife Disease Ecology Group

Environmental Futures Research Institute, Sir Samuel Griffith Centre (N78) 2.23

Griffith University, Nathan Campus, 170 Kessels Rd, Nathan, QLD, 4111, Australia

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E:	(b) (6)	(b) (6)
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@ali_bat		
www.mcca	allum-disease-ecology	.com/alison-pee
https://exp	erts.griffith.edu.au/a	cademic/a.peel

If you have received an email from me outside of normal working hours, I'm sending it at a time that suits me. I am not expecting you to read or reply to it until normal working hours.

This message is intended for the addressee named and may contain confidential information. If you are not the intended recipient, please delete it and notify the sender. Views expressed in this message are those of the individual sender, and are not necessarily the views of their organisation.

From: Munster, Vincent (NIH/NIAID) [E]
Sent: Thu, 16 Jan 2020 15:56:22 -0700

To: Jamie Lloyd-Smith; Hector Aguilar-Carreno; Amandine Gamble; Plowright,

Raina; LaTrielle, Sara

Subject: Great job!

Good job on the talk guys!

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH From: Munster, Vincent (NIH/NIAID) [E]
Sent: Thu, 16 Jan 2020 15:19:37 -0700
To: Alison Peel; Plowright, Raina
Cc: Kwe Claude, Yinda (NIH/NIAID) [F]

Subject: Hendra

Hi team,

Were we ever successful in getting the sequence of the last Hendra spillover from the horse?

I know we talked about this, but have no idea on the status,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH From: Munster, Vincent (NIH/NIAID) [E]
Sent: Wed, 15 Jan 2020 11:49:36 -0700

To: Alexandra Schaefer

Cc: Baric, Ralph
Subject: Re: Sop for SARS

Hi Alex,

Thanks! I think if we ever go that route we have to make our "positive strand" room a select agent room. We'll wait for that in case there is need,

Cheers an hope all is well, at least exiting times with the novel coronavirus

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: "Schaefer, Alexandra" < (b) (6)

Date: Wednesday, January 15, 2020 at 9:02 AM

To: ' (b) (6) < (b) (6)

Cc: "Baric, Ralph" < (b) (6)

Subject: Re: Sop for SARS

HI Vincent,

This is pretty much the procedure we do it here here at UNC--except for the difference that we have a designated BSL2 lab for Select Agentsthis allows us to transfer SARS RNA (with Police Escort) to Select Agent BSL2, there we do RNA
extraction, cDNA synthesis, RNase treatment, and then you can run a PCR outside

Without the Select Agent BSL2 we would have to handle the RNA exactly the way RML Bisoafety wants you to handle it

I can go ahead and check with our Biosafety if I can send our SOP, if you want me to.

#### Alex

From: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Sent: Wednesday, January 15, 2020 7:29 AM

To: Schaefer, Alexandra < (b) (6)

Cc: Baric, Ralph S < (b) (6)

Subject: Sop for SARS

## Hi Alex,

Could you share your SOP for taking material out of BSL3 for SARS? Our biosafety wants us to extract RNA in 3 and then run cDNA and then take it out of containment. This seems like a very elaborate and stupid process, so I'm trying to fight this.

## Cheers,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH From: Munster, Vincent (NIH/NIAID) [E]
Sent: Wed, 15 Jan 2020 11:47:23 -0700

To: Laing, Eric; Letko, Michael (NIH/NIAID) [F]; van Doremalen, Neeltje (NIH/NIAID)

[E]

Cc: Kevin Olival,; Broder, Chris (USU-DoD); Seifert, Stephanie (NIH/NIAID) [E];

Avanzato, Victoria (NIH/NIAID) [F]

Subject: Re: Coronavirus serology

For the antisera we'll have three or four routes, peptide based (rabbits S and N), Vaccine (S) and infection (upon arrival of infectious clone or WT) potentially mice, ferrets and NHPs. I expect some degree of cross reactivity between wuhan, SARS and WIV would be interesting to see.

Michael is synthesizing a codon-optimized spike, so you could compare yours against his to double check. Neeltje, can you check for the Rousettus sera which were WIV-1 positive? I believe bat 6 and 7 were both positive for S and N (but not neutralizing), so would be good to share some with Eric as a control. Neeltje might also be able to share some NHP MERS S positive sera if your interested.

#### Cheers,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

Prom: Eric Laing < (b) (6)

Date: Wednesday, January 15, 2020 at 8:43 AM

To: ' (b) (6) < (b) (6)

Cc: "Kevin Olival," < (b) (6) "Broder, Chris (USU-DoD)"

< (b) (6) "Seifert, Stephanie (NIH/NIAID) [E]"

< (b) (6) Victoria Avanzato < (b) (6)

Subject: Re: Coronavirus serology

Hi Vincent,

Good timing. I was just decompressing the fasta seq to pull the spike region and design it for expression in our 293 system.

The number one goal for an RA in our lab in this first quarter is to complete our CoV-multiplex. We were able to get a head start on the CoV S expression thru a 1-yr DTRA supported project in Bangkok with Supaporn (Chu).

Here's what we have right now.

HKU1	S <sub>e</sub>	GCN	troubleshooting
------	----------------	-----	-----------------

SARS-CoV	Se	GCN	in production
	S <sub>1</sub>	GCN	in production
La.	S <sub>1</sub>		in production
Bat SARS-like coronavirus WIV16/R.sinicus/CHN/2013	Se	GCN	completed
Bat SARS-like coronavirus Rs4231/R.sinicus/CHN/2013	Se	GCN	completed
MERS-CoV/H. sapiens/2012	Se	GCN	in production
	S <sub>1</sub>	GCN	in production
	S <sub>1</sub>	AME.	in production
Bat MERS-like-CoV/Uganda	Se	GCN	in production
	S <sub>1</sub>	Suppliers 	in production

# <sup>1</sup>S<sub>e</sub>, S ectodomain

Are you doing infections or antigen inoculations to generate the control sera? We have an open PO with SVL to make antigen-reactive rabbit sera but won't chase a redundant effort to build controls. We have the pooled MERS+/- camel sera from you and I have been reaching out to a colleague at WRAIR to get some human subject samples that received the vaccine to test specificity to MERS and off-target reactivity to heterologous CoVs.

Chris might have some insight into DoD and current collaborative work with Chinese institutions.

- Eric

Eric D. Laing, Ph.D.
Research Assistant Professor
Department of Microbiology and Immunology
Uniformed Services University
4301 Jones Bridge Road
Bethesda, MD 20814
cell: (b) (6)

office: (b) (6) lab: (b) (6)

On Wed, Jan 15, 2020 at 10:02 AM Munster, Vincent (NIH/NIAID) [E] < 6) (6) wrote:
Hi guys,

I know we discussed previously Luminex serology for coronaviruses (like MER-CoV). I think with the current Wuhan situation we should add the novel coronavirus to the list as well. We have ordered the synthesis of spike and N constructs and will do some protein expression. We could share constructs (and proteins) to set-up a bat coronavirus luminex assay asap.

In our lab, we are also generating control sera (rabbit) and will likely have mouse sera (S) soon as well (and in a later stage NHP and bat sera). MERS sera is available and SARS sera can be obtained from BEI resources.

There will be a great demand for ecological investigations of wet markets in China, and it would be great if we could leverage the platform even further, and maybe see if we have a DARPA or other program officer interested in providing some seed funds?

Cheers,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH From: Munster, Vincent (NIH/NIAID) [E]
Sent: Tue, 14 Jan 2020 13:47:14 -0700
To: Plowright, Raina; LaTrielle, Sara

Cc: Hector Aguilar-Carreno; Amandine Gamble; Peter Hudson; Jamie Lloyd-Smith;

David William Buchholz

Subject: Re: Updated slides

Sounds good!

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

Subject: Re: Updated slides

Hi All,

Thanks so much for all your work to put a lovely presentation together.

I spent 2 hrs and 10 minutes (!!!) yesterday presenting our project to Ro so he can present us to leadership as a 'hot topic' -- I talked a lot about how the G-P work fits in (at a very broad level)... therefore, I do not need to do an introduction and I think we are best to have Jamie start at slide 4. I may be calling in on my cell phone, so thats another reason for you guys to lead.

A few observations — Ro didn't know that 'paramyxovirus' refers to the family and that 'henipaviruses' are a genus within that family. But he knows now!! This is just an indication of his level of knowledge in this area and reminder to explain concepts at very high level.

He asked if all paramyxovirus are respiratory viruses — Vincent, would be great if you can touch on this — I talked about the route of infection through nasal/respiratory mucosa to lungs or olfactory nerves then brain and he got that and thought it was interesting. We talked about syncytia and fusion and I think he is primed to hear more details on this.

Really looking forward to the presentation.

Raina

On Jan 14, 2020, at 12:36 PM, LaTrielle, Sara < (b) (6) wrote:

Thanks to all who contributed to putting this slide-deck together- just wow.

I will make a few additions at the end of the slides for a few more basic slides that DARPA like to see- keeping these especially brief as the G-P slides will take the full hour.

Look forward to listening to your presentation.

Best, Sara

From: Hector Aguilar-Carreno <	(b) (6)	
Sent: Tuesday, January 14, 2020 11:	40 AM	
To: Amandine Gamble <	(b) (6) Plowright, Raina	
(b) (6)	(b) (6) <	(b) (6) Peter Hudson
< (b) (6) LaTrielle, Sara <	(b) (6)	
Cc: Jamie Lloyd-Smith <	(b) (6) David William Buchholz <	(b) (6)
Subject: Re: Fw: Undated slides		

Dear all,

Here are the slides that our G-P team has put together. Please let us know if you see any issues with them. Otherwise, we are ok for these slides to be sent to DARPA for our presentation this Thursday. The plan is that Jamie will present slides 7-25, and that I will present slides 26-40. Raina, would you prefer to present slides 1-6 as a way of Introducing the team, or would your rather only present slides 1-3, and Jamie starts at slide 4, or would you want Jamie or I to present the first 6 slides? I am flexible to any of these options.

I made one more little change in the colors for slide 36 in this version.

Best,

Hector

Hector Aguilar-Carreno
Associate Professor
Microbiology and Immunology
College of Veterinary Medicine
Cornell University

Office: (b)(6)From: Hector Aguilar-Carreno < (b)(6)Sent: Tuesday, January 14, 2020 1:37 PM To: Amandine Gamble < (b) (6) Plowright, Raina (b) (6) < (b) (6) (b) (6) Peter Hudson (b) (6) (b)(6)Cc: Jamie Lloyd-Smith < (b) (6) David William Buchholz < Subject: Re: Fw: Updated slides Dear all, Here are the slides that our G-P team has put together. Please let us know if you see any issues with them. Otherwise, we are ok for these slides to be sent to DARPA for our presentation this Thursday. The plan is that Jamie will present slides 7-25, and that I will present slides 26-40. Raina, would you prefer to present slides 1-6 as a way of Introducing the team, or would your rather only present slides 1-3, and Jamie starts at slide 4, or would you want Jamie or I to present the first 6 slides? I am flexible to any of these options. All the best to all. Hector Hector Aguilar-Carreno Associate Professor Microbiology and Immunology College of Veterinary Medicine Cornell University Office: (b)(6)(b) (6) From: Hector Aguilar-Carreno < Sent: Tuesday, January 14, 2020 1:18 PM To: Amandine Gamble < (b) (6) David William Buchholz < (b) (6) Cc: Jamie Lloyd-Smith < Subject: Re: Fw: Updated slides Great. I will send the slides now. Hector Hector Aguilar-Carreno Associate Professor Microbiology and Immunology

College of Veterinary Medicine

Cornell University

Office:

Sent: Tuesday, January 14, 2020 1:17 PM (b)(6)To: Hector Aguilar-Carreno < Cc: Jamie Lloyd-Smith < (b) (6) David William Buchholz < (b) (6) Subject: Re: Fw: Updated slides I think it is all good (and Jamie missed my last e-mail, hence why he mentioned formatting issues). Thanks Hector for the finalization! Amandine Le mar. 14 janv. 2020 à 10:00, Hector Aguilar-Carreno < (b) (6) a écrit: Tomorrow at 4:30 works for me. Any other typos/formatting errors anyone sees? Hector Hector Aguilar-Carreno Associate Professor Microbiology and Immunology College of Veterinary Medicine Cornell University Office: (b)(6)(b)(6)From: Jamie Lloyd-Smith Sent: Tuesday, January 14, 2020 12:58 PM (b) (6) To: Hector Aguilar-Carreno < Cc: Amandine Gamble < (b) (6) David William Buchholz (b) (6) Subject: Re: Fw: Updated slides Hi, The slides look great to me. Once final typos/formatting errors are fixed, they can be sent from my point of view. As for tomorrow, I could do a call at 1:30/4:30 if that works. Or earlier (1:15ish?) from my car. Jamie On Tue, Jan 14, 2020 at 9:07 AM Hector Aguilar-Carreno < Amandine, David pointed out some formatting errors in Slide 28. Are those something you could easily fix? Thank you, Hector

(b)(6)

From: Amandine Gamble <

Hector Aguilar-Carreno
Associate Professor
Microbiology and Immunology
College of Veterinary Medicine
Cornell University

Office: (b) (6)

From: Amandine Gamble < (b) (6)

Sent: Tuesday, January 14, 2020 11:17 AM

To: Hector Aguilar-Carreno < (b) (6)

Cc: Jamie Lloyd-Smith < (b) (6) David William Buchholz < (b) (6)

Subject: Re: Fw: Updated slides

One tiny comment (not important, can be ignored): you are written as "Hector Aguilar-Carreno" on slide 29, but "Hector Aguilar" on all the other slides. Otherwise, all good for me!

# Amandine

Le mar. 14 janv. 2020 à 08:11, Hector Aguilar-Carreno < (b) (6) a écrit : Jamie and Amandine,

Could you please make sure that this final version (with slide 26 deleted) has all your desired edits/changes? As soon as you give me the ok, I will send it to Raina/Sara.

David, could you please also take a look at the slides to see if you catch anything that is incorrect or mislabeled?

If anyone makes any changes, please let me know which slide you changed, so I can stitch the final changes together.

Thank you all,

Hector

Hector Aguilar-Carreno
Associate Professor
Microbiology and Immunology
College of Veterinary Medicine
Cornell University

Office: (b) (6)

From: Amandine Gamble < (b) (6)

Sent: Tuesday, January 14, 2020 10:26 AM

To: Hector Aguilar-Carreno < (b) (6)

Subject: Re: Updated slides

Hi Hector,

Sorry if some of the slide content got lost in the switch to the DARPA template, thanks for the correction! It looks all good to me, except that slide 26 re-appeared (not sure why, but every thing else seems up to date). I will be available tomorrow around 4-5 pm (EST) to explain the slide 29 and 33 (now 28 and 32). I will try to send you some written explanations before.

Great for the non-PK13 cell lines!

## Amandine

Le mar. 14 janv. 2020 à 06:29, Hector Aguilar-Carreno < (b) (6) a écrit: Here are some answers (I hope):

I am ok with deletion of prior slide 26 (Amandine did it already), and with me presenting new slides 26 to the end. Note to blame anyone, just to clarify, please note that when my slides were moved to a white background, somehow that highlights and colors disappeared, were moved around, or changed completely so that they did not make sense anymore. I just went back and edited those slides so that they make sense again. If you guys are ok with the attached slides, I can send them to Raina and Sara (just want to make sure that no new changes are made, and if they are, I approve them).

Jamie, I like the new wording of the summary slide. Love the map (new slide 36). Also, yes, the plan is to perform BSL2 experiments on the cell lines shown in slides 19-35, from different host species (in addition to the PK13 lines). These will be very basic experiments, such as binding, fusion and likely pseudotyped entry, provided that time and money allows.

Could we have a short meeting to make sure I can explain slides 29 and 33 (in the attached set of slides)? Alternatively, just send me some verbiage, to make sure I don't screw it up. I have time today 3-5 pm (EST) or tomorrow 1-5 pm (EST) if you want to quickly touch base.

Thank you all,

Hector

Office:

Hector Aguilar-Carreno Associate Professor Microbiology and Immunology College of Veterinary Medicine Cornell University (b)(6)

From: Amandine Gamble < (b) (6)

**Sent:** Tuesday, January 14, 2020 2:14 AM

To: Jamie Lloyd-Smith < (b) (6)

Cc: Hector Aguilar-Carreno < (b) (6) David William Buchholz < (b) (6)

Subject: Re: Updated slides

Hi Jamie,

Thanks for the reminder! It looks all good to me. I have deleted slide 26 and corrected a few remaining typos.

See you tomorrow!

# Amandine

Le lun. 13 janv. 2020 à 23:07, Jamie Lloyd-Smith < (b) (6) a écrit : Hi everyone,

Well we blew our 'extension' and now our slides are due tomorrow (Tues) afternoon. I've just had a look through the latest version and made another set of edits. Here's what I did:

- edited the Summary slide at the end (please check to make sure you agree!)
- fleshed out slide 34 on syncytia
- tweaked the intro series slightly (just the graphics)
- fixed little typos throughout

There is one loose end I have not dealt with — slide 26, which looks like it was intended to be a summary of the G-to-P mapping effort? I don't have time to add the example questions now, and I'm thinking we could **just delete it**? My revised summary slide might meet this need. But we need to decide, and either add content or delete before we send the slides!

# A few more questions for Hector:

- are you happy with the slide order as shown? I'm imagining that I do slides 7-25, then you take over at slide 27 to the end, but are you comfortable doing slides 29 and 33-34? If yes, great. If not, should we switch back and forth, or re-order?
- Important: did you see Amandine's question in her 'follow-up to visit' email about the plan to do BSL2 experiments on the cell lines from different host species (in addition to the PK13 lines)? Our understanding from the Montana meeting was that we would use the same cell lines at BSL2 and BSL4, so the experiments would form a coherent dataset to link traits across scales with the models. This is shown on slides 19 and 35, and is (to my mind) a key feature of our project. I just wanted to confirm that this was still the plan, since we're going to emphasize it in this talk. As Amandine said, it doesn't need to be the full set of F:G ratio expts etc, but measurements of the basic traits shown in our proposal figure would be hugely valuable.

OK, that's all from me. FYI I'm teaching from ~10:45-3:00 PST tomorrow, with a brief break around 12:30, so my ability to correspond about this will be limited after mid-morning.

cheers, Jamie

On Wed, Jan 8, 2020 at 7:12 AM Amandine Gamble < (b) (6) wrote: Hi,

Thank you Hector! I guess we have a few more days now...

# Tiny changes:

- New slides formatted
- BLS2 achievement slide moved at the beginning of the "specific questions" section
- Screening number slide made into a map + pictures to make clear they are bat samples the team collected in the field (I took them from one of Cara's old reports)

# Suggestion:

- I think current slide 32 (NiV/CeV chimera) would fit better just after the BLS2 achievement slide as a general illustration of the type of functional characterization BSL2 works allows before going into the more specific and quantitative questions, but I let Hector do whatever fits best for him.

I am available anytime for the DARPA call. Hector, let us know if you think we need to organize a Skype before, otherwise I think we should be good by e-mail.

Have a nice day everyone!

# Amandine

Le mer. 8 janv. 2020 à 06:02, Hector Aguilar-Carreno < (b) (6) a écrit : Here are the most recent updates. I think we could make improvements if the meeting this Friday is cancelled.

# Hector

Hector Aguilar-Carreno
Associate Professor
Microbiology and Immunology
College of Veterinary Medicine
Cornell University
Office:
(b) (6)

\_\_

James O. Lloyd-Smith

Professor
Department of Ecology & Evolutionary Biology
Department of Biomathematics
University of California, Los Angeles
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Los Angeles, CA 90095-7239

Phone: (b) (6)

https://www.eeb.ucla.edu/Faculty/lloydsmith/ Office: 4135 Terasaki Life Sciences Building Lab: 4000 Terasaki Life Sciences Building

James O. Lloyd-Smith

Professor Department of Ecology & Evolutionary Biology Department of Biomathematics University of California, Los Angeles 610 Charles E Young Dr South Box 723905 Los Angeles, CA 90095-7239

Phone: (b) (6)

https://www.eeb.ucla.edu/Faculty/lloydsmith/

Office: 4135 Terasaki Life Sciences Building Lab: 4000 Terasaki Life Sciences Building

From: Schountz, Tony

**Sent:** Tue, 14 Jan 2020 15:02:48 +0000

To: Cisar, Alphie (NIH/OD/ORS) [E]; Ayers, Jessica; Kendall, Lon

Cc: LaCasse, Rachel (NIH/NIAID) [E]; Lovelace, Charla; Munster, Vincent (NIH/NIAID)

[E]

Subject: Re: Bats to ship FROM CSU

All, in my communications with Dr. Munster last week, I believe the actual number of bats to ship will be 34. I have cc'd him for confirmation.

Thanks,

Tony

\_\_\_\_\_

Tony Schountz, PhD Associate Professor Arthropod-borne and Infectious Disease Laboratory

Department of Microbiology, Immunology and Pathology

College of Veterinary Medicine Colorado State University

3185 Rampart Road

Fort Collins, CO 80523-1692

(b) (6)

(b) (6)

From: Cisar, Alphie (NIH/OD/ORS) [E] < (b) (6)

Sent: Tuesday, January 14, 2020 8:00 AM

To: Ayers, Jessica < (b) (6) Kendall, Lon < (b) (6) Cc: LaCasse, Rachel (NIH/NIAID) [E] < (b) (6) Lovelace, Charla

< (b) (6) Schountz, Tony < (b) (6)

Subject: RE: Bats to ship FROM CSU

I'll work on the details, yes familiar as I've been working on arranging for the bats from Zoo Miami to you all. Will use same style crate as we are using for that transport.

I'll be in touch.

Alf

Alphie Cisar, LATG 🔊

NHP & Large Animal Procurement Specialist and Resource Manager

DVR, ORS

NIH Animal Center

Ph: (b) (6) Fax 301-480-0644

From: Ayers,Jessica <	(b) (6)		
Sent: Tuesday, January	14, 2020 9:56 AM		
To: Kendall,Lon <	(b) (6) Cisar, A	Alphie (NIH/OD/ORS) [E] <	(b) (6)
Cc: LaCasse, Rachel (NI	H/NIAID) [E] <	(b) (6) Lovelace, Charla	
<	(b) (6) Schountz, Tony <	(b) (6)	
Subject: RE: Bats to shi	p FROM CSU		

Yes, we were hoping you knew all the details of shipping bats-since we haven't done it before!

- -We can do a health certificate for them, shouldn't be anything else on our end, you may want to check with Montana state vet.
- -Yes, shipper will need to bring whatever crates you want to put bats in-we can provide fruit in cages for fluid content. What I have seen before is small plastic cat/dog carriers lined with mesh of some sort for the bats to cling to-but not sure if the carrier or you guys have something else in mind. I know Tony uses wire mesh bird cages here for small studies, so something like that inside of a sturdier solid box might also work.
- -How many bats are being shipped-this will help with timing-but I wouldn't think more than 30 minutes or so if it's not a huge number.
- -Weekdays between 8 and 2pm MST for packing bats up would be best. The shipper would have their preferred days-I assume they don't want to get too close to a weekend-although you aren't a huge drive away.
- \*\*Tony-do you want your staff to catch the bats and pack them, or do you want us to do it? If you guys are doing it-you may want to weigh in on good times for you.
- -Lead times would be a few days as long as shipper is bringing the crates-if that isn't happening and we have to figure out shipping containers, we might need some more time.

Let me know if you need anything else! Jessica

# Jessica Ayers, DVM, DACLAM

Associate Director, Laboratory Animal Resources (b) (6) C: 0:

From: Kendall,Lon < (b)(6)Sent: Tuesday, January 14, 2020 7:47 AM

(b)(6)

To: Cisar, Alphie (NIH/OD/ORS) [E] < Cc: LaCasse, Rachel (NIH/NIAID) [E] < (b) (6) Ayers, Jessica

(b) (6) Lovelace, Charla < (b)(6)

Subject: RE: Bats to ship FROM CSU

Forgot to copy Jessica and Charla.

### Lon

Lon V. Kendall, DVM, PhD, DACLAM
Director, Laboratory Animal Resources and
Attending Veterinarian, Colorado State University
2007 Painter Center
Colorado State University
Fort Collins, CO 80523

Voice: (b) (6) Cell: (b) (6) Fax: 970-491-2496

(b) (6)

From: Kendall, Lon

Sent: Tuesday, January 14, 2020 7:47 AM

To: Cisar, Alphie (NIH/OD/ORS) [E] < (b) (6)
Cc: LaCasse, Rachel (NIH/NIAID) [E] < (b) (6)

Subject: RE: Bats to ship FROM CSU

Alf,

Tony gave us the heads up so we know about it.

I'm going to have Jessica and Charla answer these questions.

I don't think we need a permit to proceed. I don't know what RML needs from MT though.

Lon

Lon V. Kendall, DVM, PhD, DACLAM
Director, Laboratory Animal Resources and
Attending Veterinarian, Colorado State University
2007 Painter Center
Colorado State University
Fort Collins, CO 80523
Voice: (b) (6)

Cell: (b) (6) Fax: 970-491-2496

(b) (6)

From: Cisar, Alphie (NIH/OD/ORS) [E] < (b) (6)

Sent: Tuesday, January 14, 2020 5:15 AM

To: Kendall,Lon < (b) (6)

Cc: LaCasse, Rachel (NIH/NIAID) [E] < (b) (6)

Subject: Bats to ship FROM CSU

Good morning Sir, RML reached out and is requesting I work on setting up transport of 26 bats from your facility to RML. What is needed on the Colorado side of things to ship the bats, do we need to have a export permit and /or would we need to wait on the Collection permit to proceed?

# Couple of other questions:

I'm assuming the transporter would need to bring transport crates with them, please confirm? How long would it take to pack the bats after the transporter arrived with crates? What would be your preferred shipping time line, day of the week and time? What would be your preferred lead time for a potential shipment?

Thanks, please advise. Alf

Alphie Cisar, LATG NHP & Large Animal Procurement Specialist and Resource Manager DVR, ORS

NIH Animal Center

Ph: (b) (6)

Fax 301-480-0644

From: Munster, Vincent (NIH/NIAID) [E]
Sent: Mon, 13 Jan 2020 16:54:02 -0700

To: Baric, Ralph

Subject: Re: Human ACE2 mice

Sounds good, somewhere between 2 and 3 would work best for me, pretty busy on this end too

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

From: "Baric, Ralph S" < (b) (6)

Date: Monday, January 13, 2020 at 4:51 PM

To: ' (b) (6) < (b) (6)

Subject: RE: Human ACE2 mice

Tomorrow afternoon would be better. Busy Evening. Hope things are well. Ralph

From: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Sent: Monday, January 13, 2020 5:51 PM
To: Baric, Ralph S < (b) (6)

Subject: Re: Human ACE2 mice

Pretty open now, or could do tomorrow (and any of the other days) as well

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

From: "Baric, Ralph S" < (b) (6)

Date: Monday, January 13, 2020 at 3:48 PM

To: " (b) (6) < (b) (6)

Cc: "Baric, Ralph" < (b) (6)

Subject: RE: Human ACE2 mice

Sounds good to me to, we should do a short call. Ralph

From: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Sent: Monday, January 13, 2020 5:43 PM

To: Baric, Ralph S < (b) (6)

Subject: Re: Human ACE2 mice

Sounds good, let me know what your thinking,

Would be good to expand our collaboration even more (got these continuous calls with NIAID intramural and extramural so I make sure you name gets dropped often).

Cheers,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: "Baric, Ralph S" < (b) (6)

Date: Monday, January 13, 2020 at 3:41 PM

To: " (b) (6) < (b) (6)

Subject: RE: Human ACE2 mice

Hi Vincent, We do. we have put up a number of breeders last week to amplify our colony. They are available in a few weeks-although I don't want to cross lines so we should talk. Ralph

From: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Sent: Monday, January 13, 2020 5:37 PM

To: Baric, Ralph S < (b) (6) Schaefer, Alexandra < (b) (6)

Cc: van Doremalen, Neeltje (NIH/NIAID) [E] < (b) (6)

Subject: Human ACE2 mice

Hi guys,

We're expecting that the Wuhan virus will bind human ACE2, do you have a good transgenic mouse model we could potebtially use? We are primarily thinking vaccines for now.

Cheers,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: Munster, Vincent (NIH/NIAID) [E]
Sent: Mon, 13 Jan 2020 13:18:11 -0700

To: Schountz, Tony

Subject: Re: Action needed: check your proof 10.1093/infdis/jiz648

Attachments: TrinBatProofs[1].pdf

Here they are!

Good luck

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: Tony Schountz < (b) (6)

Date: Monday, January 13, 2020 at 1:13 PM

To: ' (b) (6) < (b) (6)

Subject: FW: Action needed: check your proof 10.1093/infdis/jiz648

Vincent, is it possible for you to email this proof to me? I rec'd official study section assignment for the grant you, Eric and I submitted last fall and I can now submit any "in press" materials. This will show that the three of us are already collaborating and could help with the score a bit.

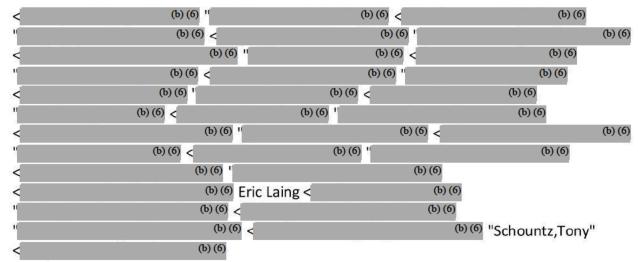
Thanks,

Tony

Tony Schountz, PhD
Associate Professor
Arthropod-borne and Infectious Disease Laboratory
Department of Microbiology, Immunology and Pathology
College of Veterinary Medicine
Colorado State University
3185 Rampart Road
Fort Collins, CO 80523-1692
(b) (6)

From: ' (b) (6) < (b) (6)

Date: Sunday, January 12, 2020 at 11:02 PM



Subject: Action needed: check your proof 10.1093/infdis/jiz648

Dear Dr. Vincent Munster,

You must check your proof now to avoid delaying publication.

# What you need to do now:

- 1. Access your proof <a href="https://pubkit.newgen.co/auth\_token\_login/af89fcf9-b35f-40b5-a782-420952f1a4a4">https://pubkit.newgen.co/auth\_token\_login/af89fcf9-b35f-40b5-a782-420952f1a4a4</a>
- 2. Respond on the proof to any copyeditor queries.
- 3. Approve your proof for publication or submit minor formatting corrections within one working day.

Please note that this is causing a delay to the publication of your manuscript. Please contact us if you need any help.

Best wishes,

The Journal of Infectious Diseases production team

Oxford University Press

(b) (6)

# Action: respond to our copy-editing questions (b) (5)

(b) (5)

# Action: check your manuscript information

(b) (5)

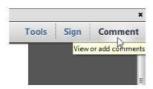
# How to add your responses

These instructions show you how to add your responses to your proof using Adobe Acrobat Professional version 7 onwards, or Adobe Reader DC. To check what version you are using, go to 'Help', then 'About'. The latest version of Adobe Reader is available for free from <a href="https://get.adobe.com/uk/reader/">https://get.adobe.com/uk/reader/</a>.

# Displaying the toolbars

### Adobe Reader DC

In Adobe Reader DC, the Comment toolbar can be found by clicking 'Comment' in the menu on the top-right-hand side of the page (shown below).

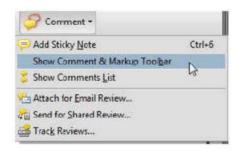


The toolbar shown below will then display along the right-hand-side of the page.



# Acrobat Professional 7, 8 and 9

In Adobe Professional, the Comment toolbar can be found by clicking 'Comment(s)' in the top toolbar, and then clicking 'Show Comment & Markup Toolbar' (shown below).



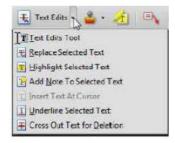
The toolbar shown below will then be displayed along the top of the page.



# Using text edits and comments in Acrobat

This is the easiest method to both make changes, and for your changes to be transferred and checked.

- 1. Click 'Text Edits'
- Select the text to be annotated or place your cursor at the insertion point and start typing.
- 3. Click the 'Text Edits' drop down arrow and select the required action.
- You can also right click on selected text for a range of commenting options, or to add sticky notes.



# Using commenting tools in Adobe Reader

All commenting tools are displayed in the toolbar. You cannot use text edits, however you can still use highlighter, sticky notes, and a variety of insert/replace text options.



# Pop-up notes

In both Reader and Acrobat, when you insert or edit text, a pop-up box will appear.

# Saving comments

In order to save your comments and notes, you need to save the file ('File', 'Save') before closing the document.

NB: Do not make any edits directly into the text, use commenting tools only

# SUPPLEMENT ARTICLE



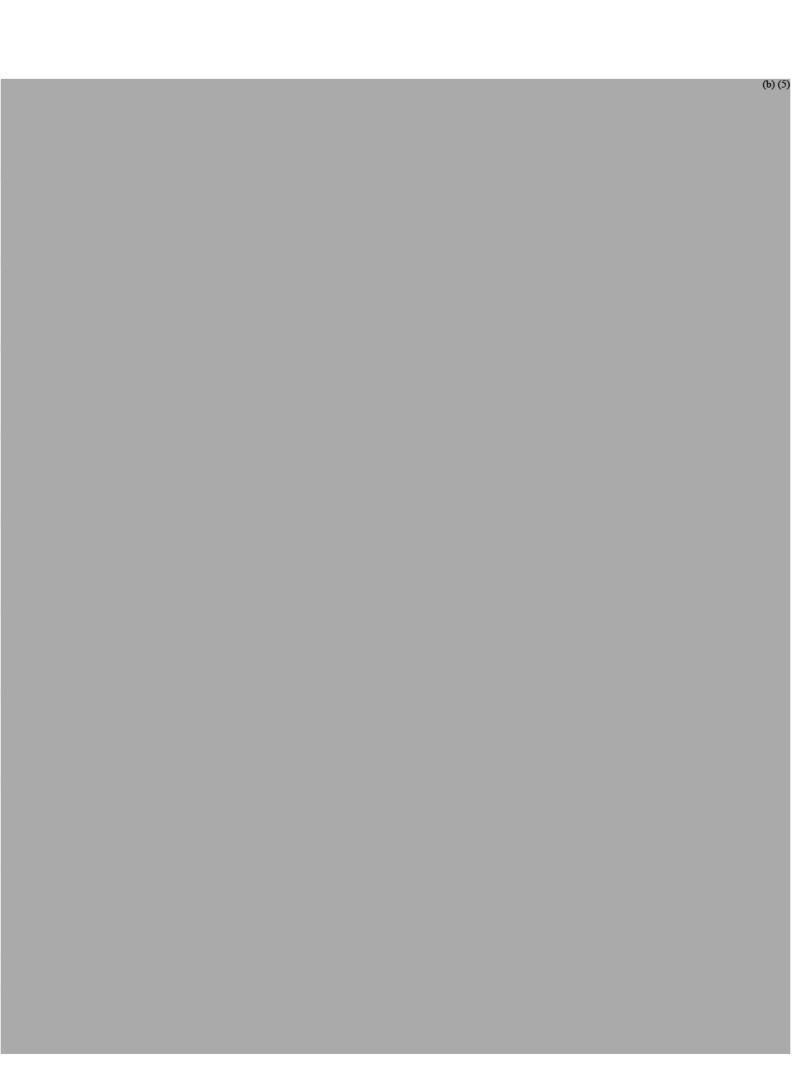


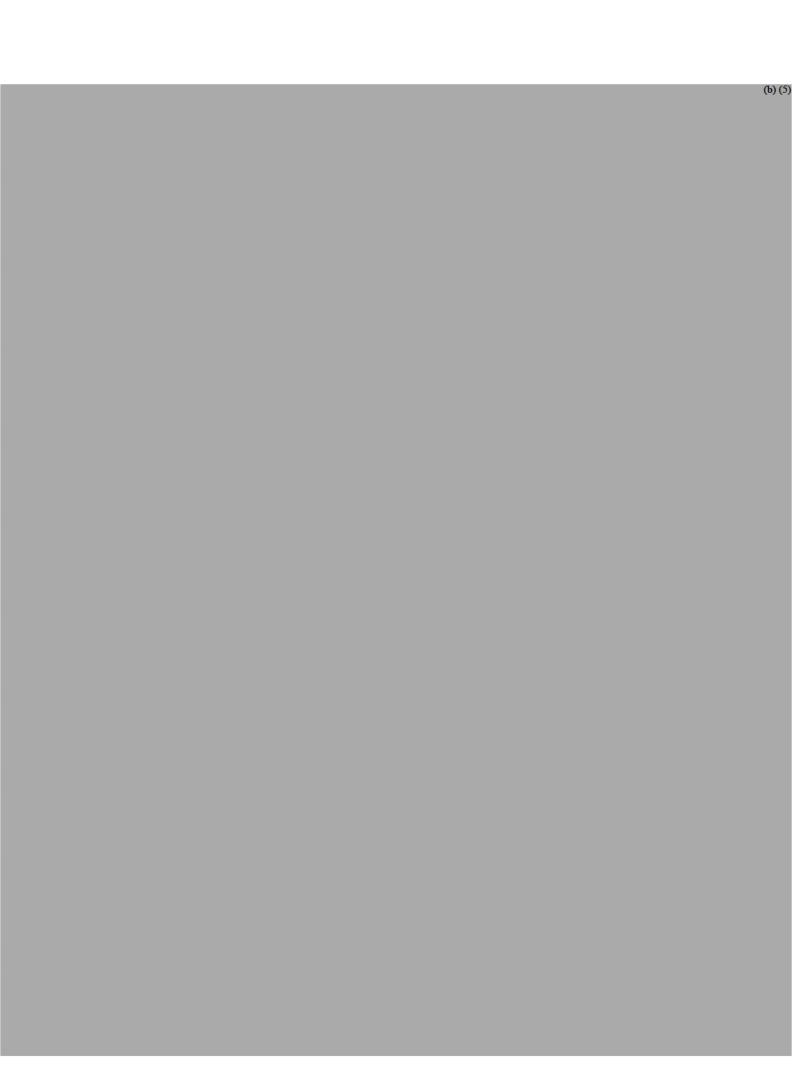


(b) (5)















From: Munster, Vincent (NIH/NIAID) [E]
Sent: Mon, 13 Jan 2020 12:55:45 -0700

To: van Doremalen, Neeltje (NIH/NIAID) [E]; Letko, Michael (NIH/NIAID) [F]

Subject: Re: Strain comparison

You could actually highlight the clusters with colors (blocks) rather than the individual viruses, I think the majority of the sequences are human and very few are camel, so highlighting actual camel isolates should be relatively easy.

I think Steph is looking a bit at this and will be able to at least a little wording on the analyses side. Given that she is a co-author it shouldn't be too much to ask from her to make a pretty and informative tree. Regardless, would be good if we have a draft we could send to the co-authors soon

Cheers,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: Neeltj	e van Doremalen <	(b) (6)
Date: Friday,	January 10, 2020 at 8:16 AM	
To: '	(b) (6) <	(b) (6) Michael Letko
<	(b) (6)	
Subject: RE:	Strain comparison	

Highlighting the human and camel isolates is going to be quite a messy tree, since they are not clustering together at all. This has been demonstrated in several papers to which we refer as well.

Regarding larger hospital outbreaks, this would be more interesting I think. However, we need to know how to get this information and what we would class as a larger outbreak. I am not aware of any lists of larger MERS-CoV outbreaks, so I imagine this will take a lot of checking into every isolate. Maybe Steph has a better understanding of how easy this would be.

Neeltje

From: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Sent: Friday, January 10, 2020 7:21 AM

To: van Doremalen, Neeltje (NIH/NIAID) [E] < (b) (6)

Letko, Michael (NIH/NIAID) [F] < (b) (6)

Subject: Re: Strain comparison

So the only thing I still think is to make a better tree (so I disagree), as these papers will be read by a wider audience it would not be bad to put a bit more effort in it.

For one, highlight human and camel isolates and some of the major hospital outbreaks in the tree. I think it I not just about showing diversity, I think we are also showing origin and relationship to larger (hospital) outbreaks. Don't forget you need to sell papers like this, I'm saying we need to run a different tree I think you should make it more informative based on the data you have. Also you don't do anything with the data. I don't see any good description of the data, if you just wanted to show diversity a identity matrix would be more informative.

Other than that I think we are almost there

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

From: Neeltje van Do	remalen		(b) (6)	
Date: Thursday, Janua	ary 9, 2020 at 4:44 PM			
To: Michael Letko <	(b) (	5) "		(b) (6)
<	(b) (6)			
Subject: Strain compa	arison			

Hi,

I made a few small changes and responded to some of the comments. I will get a better description of morphometrical analysis tomorrow morning from Greg.

I will also run a VESPA analysis comparing camel and human strains – to see if there are any obvious differences there.

We still need to sort out affiliations.

Neeltje

From:	Munster, Vincent (NIH/NIAID) [E]			
Sent:				
To:	Raina Plowright; Letko, Michael (NIH/NIAID) [F]			
Subject:	Re: ProMED Digest, Vol 91, Issue 27			
Yep, working on this sir	ice Friday,			
Exciting and busy times				
Cheers,				
Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH				
From: Raina Plowrigh Date: Saturday, Janua	ery 11, 2020 at 7:33 PM			
To: '	(b) (6) < (b) (6) Michael Letko			
	(b) (6)			
Subject: Fwd: ProME	D Digest, Vol 91, Issue 27			
I'm sure you saw this well ahead of me — coronavirus sequence now online. forwarding just in case :-)				
Begin forwarded messa	ge:			
From: (b) (6) Subject: ProMED Digest, Vol 91, Issue 27 Date: January 11, 2020 at 2:09:53 PM MST To: (b) (6)				
Reply-To:	(b) (6)			
Today's Topics:				
	agnosed pneumonia - China (HU) (10): genome			
available, Hong Kong	AND			
2. PRO/AH/EDR> Hantavirus - Americas (01): Argentina (BA) (b) (6)				
3. PRO/AH/EDR> Tremorgenic toxin - Canada: (NS) dogs, susp. ( (b) (6)				

\_\_\_\_\_\_

Message: 1

Date: Sat, 11 Jan 2020 17:25:54 +0000

From: (b) (6

Subject: PRO/AH/EDR> Undiagnosed pneumonia - China (HU) (10): genome

available, Hong Kong surveill.

To: (b) (6) (b) (6)

Message-ID:

(b) (6)

Content-Type: text/plain; charset=UTF-8

UNDIAGNOSED PNEUMONIA - CHINA (HUBEI) (10): GENOME AVAILABLE, HONG KONG SURVEILLANCE

\*

A ProMED-mail post

<a href="http://www.promedmail.org">http://www.promedmail.org</a>
ProMED-mail is a program of the
International Society for Infectious Diseases
<a href="http://www.isid.org">http://www.isid.org</a>

[1]

Date: Sat 11 Jan 2020

Source: Hong Kong CHP (Centre for Health Protection) letter to

physicians [edited]

<a href="https://www.chp.gov.hk/files/pdf/letters">https://www.chp.gov.hk/files/pdf/letters</a> to doctors 20200111.pdf>

[11 Jan 2020]

Dear Doctor,

Updates on the Cases of Infection with Novel Coronavirus in Wuhan

Further to our letter dated [9 Jan 2020], we would like to update you with the latest situation of the reported cluster of pneumonia cases in Wuhan, Hubei Province.

After the preliminary determination that the pathogen of "viral pneumonia with unknown cause" is a novel coronavirus, the expert groups have immediately revised and improved the protocols on diagnosis, treatment and surveillance of viral pneumonia with unknown cause. The Wuhan Municipal Health Commission has arranged the samples of existing patients to be tested for nucleic acid of the novel coronavirus, and the Expert Groups have made overall assessments on the patients hospitalised for observation and treatment, taking into

consideration information on clinical picture, epidemiological information and laboratory testing results, etc.

As of yesterday ([10 Jan 2020]), 41 patients have been diagnosed to have infection of the novel coronavirus. The earliest and most recent cases had onset of illness on [8 Dec 2019] and [2 Jan 2020], respectively. Symptoms include fever, malaise, dry cough and shortness of breath. The vital signs were stable in most of the cases. Among them, 2 patients have been discharged, 7 patients are in serious condition and 1 died, while the remaining patients are in stable condition. The fatal case affected a 61-year-old man with abdominal tumour and chronic liver disease who was admitted to a hospital due to respiratory failure and severe pneumonia. The diagnoses included severe pneumonia, acute respiratory distress syndrome, septicaemic shock and multi-organ failure.

According to information from the National Health Commission, epidemiological investigations revealed that the patients are mainly business operators at a market called "Hua Nan Seafood Wholesale Market" in Wuhan, which has been closed since [1 Jan 2020]. A total of 739 close contacts have been identified and 419 of them are healthcare workers. All have been put under medical surveillance, and no related cases have been detected so far. There have been no new cases since [3 Jan 2020]. For the time being, the Mainland's investigation has neither identified any infection of healthcare workers nor definite evidence of human-to-human transmission.

Regarding the laboratory tests, relevant experts have released a coronavirus genome from a case of the Wuhan outbreak. The sequence can be downloaded from the following website: <a href="http://virological.org/t/initial-genome-release-of-novel-coronavirus/319">http://virological.org/t/initial-genome-release-of-novel-coronavirus/319</a>. The Public Health Laboratory Services Branch of the Centre for Health Protection is conducting molecular testing for a number of coronaviruses, and the current test is able to detect the novel coronavirus based on sequence comparison but not yet evaluated due to unavailability of the novel coronavirus.

We will closely monitor the situation and update you further when more information becomes available. You may visit the designated webpage (<a href="https://www.chp.gov.hk/en/features/102465.html">https://www.chp.gov.hk/en/features/102465.html</a>) for updated information on the reported cases fulfilling the reporting criteria for Severe Respiratory Disease associated with a Novel Infectious Agent and the relevant health advice. Please draw the attention of the healthcare professionals and supporting staff in your institution/working with you to the above. Thank you for your continuous support in combating communicable diseases.

Yours faithfully,

(Dr. SK Chuang) for Controller, Centre for Health Protection Department of Health

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Communicated by:

ProMED-mail



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[2]

Date: Sat 11 Jan 2020

Source: Taiwan News [edited]

<a href="https://www.taiwannews.com.tw/en/news/3854953">https://www.taiwannews.com.tw/en/news/3854953></a>

Taiwan is expected to develop a screening test in a week's time for the new type of coronavirus that has killed one and sickened dozens in the Chinese city of Wuhan, according to Taiwanese health authorities on Saturday ([11 Jan 2020]).

The coronavirus, believed to have originated at a local seafood market in Wuhan, has afflicted 41 as of Friday ([10 Jan 2020]). On Wednesday ([9 Jan 2020]), it took the life of a 61-year-old man who had developed severe pneumonia, according to the Wuhan Municipal Health Commission.

The man, who was found to have frequented the Huanan Seafood Market for business, also suffered from chronic liver disease as well as abdominal tumors. Those who have come down with the virus have shown such symptoms as fever, cough, difficulty breathing, and fatigue, said the Commission.

Taiwan's Centers for Disease Control (CDC) said it is working on analyzing the virus' genome sequence, which has been provided by Chinese health authorities. Preliminary mapping indicated the coronavirus bears an 87.6% likeness to a virus carried by bats, while it is 79% similar to SARS and 52% similar to MERS. The transmission methods have yet to be identified.

The CDC believes a fast screening test can be developed in a week and will be able to detect the coronavirus in 4 hours, reported UDN. The health authorities also rebuffed rumors that Taiwan has reported its 1st confirmed case of the illness, warning that those spreading disinformation could be subject to a fine of up to TWD 3 million (USD 100 082) in accordance with the Communicable Disease Control Act.

[Byline: Huang Tzu-ti]

--

Communicated by:

Mary Marshall

(b) (6)

\*\*\*\*\*

[3]

Date: Sat 11 Jan 2020, HKT 19:30

Source: Hong Kong Government [edited]

<a href="https://www.info.gov.hk/gia/general/202001/11/P2020011100694.htm?fontSize=1">https://www.info.gov.hk/gia/general/202001/11/P2020011100694.htm?fontSize=1</a>

# HKSARG representatives to go to Wuhan

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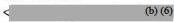
In response to media enquiries, a spokesman for the Food and Health Bureau gives the following reply today ([11 Jan 2020]):

With the arrangement of the National Health Commission, the Under Secretary for Food and Health, Dr. Chui Tak-yi, together with representatives from the Department of Health and Hospital Authority, will depart for Wuhan, Hubei Province on [Mon 13 Jan 2020] to learn about the situation of the cluster of pneumonia cases in Wuhan, prevention and control measures and clinical management. They will return to Hong Kong on [Tues 14 Jan 2020].

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Communicated by:

ProMED-mail



[With the public release of the genome and the opening up for professional visits from outside of Wuhan, it is hoped there will be speed in further defining the coronavirus, as well as confirmation from an outside reference laboratory. We await further feedback from Hong Kong, Taiwan, Singapore, South Korea and other countries who have been identifying arriving passengers from Wuhan for febrile respiratory illness as to whether this virus has travelled outside of the Seafood Market, and outside of Wuhan City.

The information on the reported fatality is one of an individual with multiple co-morbidities, including abdominal tumors (not further defined), severe pneumonia, ARDS (acute respiratory distress syndrome), septicemic shock and multi-organ failure.

A map showing locations of major cities in China can be found at <a href="https://www.chinadiscovery.com/china-maps/city-maps.html">https://www.chinadiscovery.com/china-maps/city-maps.html</a>. - Mod.MPP

HealthMap/ProMED-mail map: Hubei, China: <a href="http://healthmap.org/promed/p/5294">http://healthmap.org/promed/p/5294</a>] See Also: Undiagnosed pneumonia - China (HU) (09): novel coronavirus, more info, fatality http://promedmail.org/post/20200110.6883253 Undiagnosed pneumonia - China (HU) (08): novel coronavirus, WHO http://promedmail.org/post/20200110.6881082 Undiagnosed pneumonia - China (HU) (07): official confirmation of novel coronavirus http://promedmail.org/post/20200108.6878869 Undiagnosed pneumonia - China (06): (HU) Hong Kong surveillance, USA CDC alert http://promedmail.org/post/20200108.6876648 Undiagnosed pneumonia - China (05): (HU) novel coronavirus identified http://promedmail.org/post/20200108.6877694 Undiagnosed pneumonia - China (04): (HU) Hong Kong surveillance http://promedmail.org/post/20200106.6874277 Undiagnosed pneumonia - China (03): (HU) updates, SARS, MERS ruled out, WHO, RFI http://promedmail.org/post/20200105.6872267 Undiagnosed pneumonia - China (02): (HU) updates, other country responses, RFI http://promedmail.org/post/20200103.6869668 Undiagnosed pneumonia - China (01): (HU) wildlife sales, market closed, RFI http://promedmail.org/post/20200102.6866757 2019 ----Undiagnosed pneumonia - China: (HU) RFI http://promedmail.org/post/20191230.6864153] .....mpp/rd/ml Message: 2 Date: Sat, 11 Jan 2020 18:17:37 +0000 (b) (6) From: Subject: PRO/AH/EDR> Hantavirus - Americas (01): Argentina (BA) (b)(6)(b) (6) (b) (6) Message-ID: (b) (6)

Content-Type: text/plain; charset=UTF-8

HANTAVIRUS - AMERICAS (01): ARGENTINA (BUENOS AIRES)

A ProMED-mail post <a href="http://www.promedmail.org">http://www.promedmail.org</a> ProMED-mail is a program of the International Society for Infectious Diseases

# <a href="http://www.isid.org">http://www.isid.org</a>

Date: Thu 9 Jan 2020

Source: Telefe Noticias [in Spanish, trans. Mod.TY, edited]

<a href="https://telefenoticias.com.ar/actualidad/internaron-a-una-embarazada-con-hantavirus-investigan-">https://telefenoticias.com.ar/actualidad/internaron-a-una-embarazada-con-hantavirus-investigan-

como-se-produjo-el-contagio/>

A pregnant woman from an area in Buenos Aires [province] was admitted to hospital with [a] hantavirus [infection], so the local health authorities are investigating how she was infected in order to predict if there are possibilities of more cases.

The patient is (currently) 28 weeks pregnant and was taken into the health system this past [5 Jan 2020] for a physical illness that later was recognized by the physicians attending her as [a] hantavirus [infection]; currently she is hospitalized in the interzonal hospital San Martin in La Plata.

The municipal Secretary of Health, Diego Schiaffino, stated that the woman "never met the serious condition criterion" and indicated that her progress was favorable, so that she will be released in the coming hours.

"We are dedicated to tracking down and evaluating [the situation] in order to see how and where she was infected. We wish to see if she was infected in the area, what is the situation where she lives, if she has traveled elsewhere, if she has worked in the countryside," the local official remarked.

To avoid panic in the population, Schiaffino stated that "the virus that generally circulates in the region is less aggressive and is not transmitted by the respiratory route, such as happened in Epuyen last year [2019]," a reference to an epidemiologically [investigated] outbreak that affected the Chbut [province] town and took the lives of 9 people.

In any case, he asked [the residents] to fight the longtail mouse, the vector [reservoir] of the disease [virus] that transmits the virus in its urine and feces.

This past Wednesday [8 Jan 2020], a football [soccer] player from the Etcheverry Neighboring Union was released from the same hospital after spending 10 days hospitalized also for [a] hantavirus [infection] that he contracted working as a gardener.

--

Communicated by:



[The hantavirus responsible for these 2 cases is not mentioned. Cases of hantavirus infection with hantavirus pulmonary syndrome have been reported from various parts of Argentina in recent years. As noted in ProMED-mail archive no. http://promedmail.org/post/20110430.1348, several endemic hantaviruses have been associated with human infection in Argentina: Andes virus (western Argentina; in the long-tailed pygmy rice rat host, \_Oligoryzomys longicaudatus\_); related Andes-like viruses Hu39694 (in central Argentina; rodent host unknown); Marciel virus (in the dark bolo mouse, \_Bolomys obscurus\_); Lechiguana and Central Plata (in central Argentina; in the yellow pygmy rice rat \_O. flavescens\_); Oran (in northwestern Argentina; in \_O. longicaudatus\_); Anajatuba and Juquitiba (in Oligoryzomys forensi ) and Bermejo (western Argentina; in O. chaoensis ). There is always the possibility of infection with Seoul hantavirus, widely distributed in the world in brown rats ( Rattus norvegicus ). Without laboratory confirmation, it is not possible to say with certainty which hantavirus was involved in these cases. - Mod.TY

HealthMap/ProMED-mail map:

Buenos Aires, Argentina: <a href="http://healthmap.org/promed/p/53505">http://healthmap.org/promed/p/53505</a>]

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[See Also:
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2019

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Hantavirus - Americas (31): Argentina (JY) comment http://promedmail.org/post/20190730.6594939 2018

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Hantavirus - Americas (52): Argentina (Buenos Aires) http://promedmail.org/post/20180908.6016182

Hantavirus - Americas (36): Argentina (BA) suspected

http://promedmail.org/post/20180524.5817474

Hantavirus - Americas (35): Argentina (SA), USA (Texas) susp.

http://promedmail.org/post/20180522.5812466

Hantavirus - Americas (25): Argentina (BA)

http://promedmail.org/post/20180322.5702232

Hantavirus - Americas (13): Argentina (BA)

http://promedmail.org/post/20180228.5655058

Hantavirus - Americas (12): Chile (AR, AI) Argentina (BA) Panama (LS)

http://promedmail.org/post/20180218.5634982

Hantavirus - Americas (01): Argentina (BA) Chile (BB)

http://promedmail.org/			
	sb/ml/ty/rd/m	1	
Message: 3			
Date: Sat, 11 Jan 2020 2	1:09:45 +0000		
From:	(b) (6)		
Subject: PRO/AH/EDR>	Fremorgenic toxin - C	Canada: (NS) dogs, susp.	
To:	(b) (6)	(b) (6)	

(b) (6)

Message-ID:

(b) (6)

Content-Type: text/plain; charset=UTF-8

TREMORGENIC TOXIN - CANADA: (NS) DOGS, SUSPECTED

A ProMED-mail post <a href="http://www.promedmail.org">http://www.promedmail.org</a> ProMED-mail is a program of the International Society for Infectious Diseases <a href="http://www.isid.org">http://www.isid.org</a>

Date: Wed 8 Jan 2019

Source: The Chronicle Herald [edited]

< the chronic leheral d. ca/news/provincial/three-dogs-experience-sudden-illness-after-walking-at-amherst-golf-club-395666/>

An Amherst veterinarian is urging pet owners to always be aware of their animal's surroundings. This after 3 dogs in 5 days came down with a sudden illness having brought about seizures.

"The 1st case involved a dog walking with its owner at the golf club and on the way home in the car began to seize. It was put in a drug-induced coma and just got well enough to go home," Carolyn Hollis said. "It was a long process and it was a close call."

Just as the 1st dog was recovering, someone came in with 2 more dogs experiencing seizures, one was in full seizure and the other was simply tremoring. The veterinarian said staff were able to evacuate the bowels of the dog experiencing tremors.

Upon investigation by one of the owners, it was determined there was something at the golf course making the dogs sick. "One of the owners retraced her steps and found an open plastic lunch container with

rotten food in it that someone had disposed there," Hollis said. "It was in the woods away from one of the tees. It was just left there."

The veterinary hospital hasn't determined for sure if the food container is the cause. Hollis said many would not understand the danger presented to animals by leaving open containers of food lying around. In this case, the food was rotten, and the dogs were attracted to it. When they ingested it, they took in some pretty powerful neurotoxins that easily could have killed them.

"Rotting food and things like the mold that comes with it can be extremely toxic to animals," she said. "Composting food is very dangerous."

She estimates it was 30 minutes from the time the dogs ingested the food until they began experiencing seizures. The veterinarian said the dogs were saved by the owners' quick thinking in getting the animals to the veterinary hospital.

In no way is she blaming the golf course since it is private property, and any spraying it would've done would've been completed several months ago, but she is urging those who use the course and public areas around the community to be aware of what they do with items of food after they're finished.

The golf course is sometimes popular with people walking their dogs, at least until deep snow prevents it. With a lack of snow so far this winter, the club has been used by dog owners since their pets can run free and get some exercise.

"There are lots of garbage receptacles at the golf course just as there are around town; please use them," she said. "Owners also need to be aware of where their dogs are at all times and what they may be getting into or eating."

The best advice, she said, is to keep their dog on a leash unless they are absolutely aware of the surroundings.

[Byline: Darrell Cole]
-Communicated by:
Karyn Bischoff
< (b) (6)

[While several fungal metabolites may cause this intoxication, current research supports penitrem A as the primary mycotoxin involved. The fungi most commonly associated with penitrem A, \_Penicillium\_ species,

grow on meat, cereals, nuts, cheese, eggs, fruits, processed/refrigerated food, refuse, and compost (<a href="https://todaysveterinarypractice.com/practical-toxicologytremorgenic-mycotoxin-intoxication-dogs/">https://todaysveterinarypractice.com/practical-toxicologytremorgenic-mycotoxin-intoxication-dogs/</a>).

Roquefortine and penitrem A are tremorgenic mycotoxins associated with decaying organic matter, moldy walnut hulls, and spoiled dairy products. These toxicoses are associated with muscle tremors, salivation, vomiting, and clonic-tonic convulsions. Differential features are the lack of miosis (or lack of constriction of the pupil of the eye) and the general absence of respiratory signs.

A mycotoxin, penitrem A is produced by several \_Penicillium\_spp., \_Aspergillus\_, and \_Claviceps\_. Ingestion results in severe generalized tremors, opsoclonus [uncontrolled eye movement], and seizures in dogs. Numerous sources associated with the production of mycotoxin include mold contamination of cream cheese, macaroni and cheese, walnuts, bread, rice, and compost. Tremors occur approximately 2 to 3 hours following the ingestion. The severity of the tremors may be related to the amount of mycotoxin ingested. Vomiting often precedes tremors.

Clinical signs typically begin to appear within 30 minutes of toxin ingestion but can be delayed for several hours (rare). Early signs of restlessness, panting, and excessive salivation often progress to include mild to moderate whole-body muscle tremors. In high-dose exposures, the tremors may become severe, and seizure activity is not uncommon. Poisoned patients often display hyperresponsiveness to external stimuli (e.g., touch and noise). Untreated muscle tremors lead to hyperthermia, exhaustion, and dehydration, along with possible metabolic acidosis (mild) and rhabdomyolysis (rare).

In asymptomatic animals, decontamination procedures should include induction of emesis followed by oral administration of activated charcoal and an osmotic cathartic. Symptomatic patients should be sedated or anesthetized, and gastric lavage performed to remove the ingested material. This procedure should be followed by instillation of activated charcoal and a cathartic. Diazepam can be used to control agitation, muscle tremors, or seizure activity. Methocarbamol (either intramuscularly or intravenously) or barbiturates have been used successfully to control tremors and seizures when the patient does not respond to diazepam. A venous port should be established to provide intravenous fluids for the first 24 hours.

The majority of poisoned patients recovers uneventfully following aggressive therapy within 24 to 48 hours; however, with excessive exposures, clinical signs can be prolonged for up to 4 to 5 days (<a href="https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/penitrem-a">https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/penitrem-a</a>).

Be aware of where you are and what your pet is consuming. Dead and spoiled items can contain toxins and bacteria capable of sickening or even killing your pet. These animals were fortunate, as the owners sought rapid treatment for their pets. - Mod.TG

HealthMap/ProMED-mail map: Nova Scotia Province, Canada: <a href="http://healthmap.org/promed/p/271">http://healthmap.org/promed/p/271</a> ]
[See Also: 2000
2000
Mycotoxins: a review http://promedmail.org/post/20001130.2089]tg/rd/ml
List-Unsubscribe: https://join.isid.org/promed/
End of ProMED Digest, Vol 91, Issue 27

From: Munster, Vincent (NIH/NIAID) [E]
Sent: Sun, 12 Jan 2020 12:30:53 -0700

To: Kevin Olival

Cc: Letko, Michael (NIH/NIAID) [F]; Seifert, Stephanie (NIH/NIAID) [E]; Plowright,

Raina

**Subject:** Re: Initial editorial feedback for manuscript NRMICRO-18-165V1

Hi Kevin,

Just write your part and we'll put it in the right order. Any cool wording on the Wuhan coronavirus would be cool. Now id the time to have this finalized as there will be a lot of demand for the review.

Good work on the tree, but noticed you caught some flak,

Cheers,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: "Kevin Olival," < (b) (6)

Date: Saturday, January 11, 2020 at 10:24 PM

To: ' (b) (6) < (b) (6)

Cc: Michael Letko < (b) (6) "Seifert, Stephanie (NIH/NIAID) [E]"

< (b) (6) "Plowright, Raina" < (b) (6)

Subject: Re: Initial editorial feedback for manuscript NRMICRO-18-165V1

Sorry V and all... this is on my plate to write up a couple new intro paragraphs. Will do my best to get to it tomorrow night. If there's a new draft you want me to work with, please send it along.

Kevin

On Jan 10, 2020, at 9:35 AM, Munster, Vincent (NIH/NIAID) [E] < 6) (6) wrote:

Hi Kevin,

Any update on this? Might be good to update some of the data with the current Wuhan outbreak / coronavirus diversity?

Would be good time to get this finished as there will be a lot of need for information now, so the faster we can finalize the better,

Cheers,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH 
 From:
 Munster, Vincent (NIH/NIAID) [E]

 Sent:
 Fri, 10 Jan 2020 20:57:45 -0700

To: Baric, Ralph

Subject: Re: Rg novel coronavirus

Perfect! Right between your favorite viruses :-)

On Jan 10, 2020, at 18:22, (b) (6) wrote:

http://virological.org/t/initial-genome-release-of-novel-coronavirus/319

On Jan 8, 2020, at 10:28, Baric, Ralph S < (b) (6) wrote:

Hi Vincent, Absolutely! Can NIH help get hold of the full length or spike sequence? I imagine the outside world is going to have to wait awhile before the genome length sequence or the S sequence becomes available. Ralph

From: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Sent: Wednesday, January 8, 2020 10:16 AM

To: Baric, Ralph S < (b) (6)

Cc: van Doremalen, Neeltje (NIH/NIAID) [E] < (b) (6) De wit, Emmie (NIH/NIAID) [E] < (b) (6) Schaefer, Alexandra < (b) (6) Letko,

Michael (NIH/NIAID) [F] < (b) (6) Feldmann, Heinrich (NIH/NIAID) [E]

(b) (6)

Subject: Rg novel coronavirus

Hi Ralph,

Would you be willing to share (collaborate on) any rg viruses of the novel coronavirus when you would have resqued it? We would be primarily interested in the development of NHP models.

Let me know what you think and see what we need to get in place for the transfer as soon as a virus becomes available,

Cheers,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: Baric, Ralph S

Sent: Sat, 11 Jan 2020 03:09:08 +0000

To: Munster, Vincent (NIH/NIAID) [E]

Subject: RE: Rg novel coronavirus

### Already on it.

From: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Sent: Friday, January 10, 2020 8:23 PM
To: Baric, Ralph S < (b) (6)

Subject: Re: Rg novel coronavirus

http://virological.org/t/initial-genome-release-of-novel-coronavirus/319

On Jan 8, 2020, at 10:28, Baric, Ralph S < (b) (6) wrote:

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Michael (NIH/NIAID) [F] < (b) (6) Feldmann, Heinrich (NIH/NIAID) [E]

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Let me know what you think and see what we need to get in place for the transfer as soon as a virus becomes available,

Cheers,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH From: Munster, Vincent (NIH/NIAID) [E]
Sent: Fri, 10 Jan 2020 15:25:05 -0700

To: Baric, Ralph

Cc: van Doremalen, Neeltje (NIH/NIAID) [E]; De wit, Emmie (NIH/NIAID) [E];

Feldmann, Heinrich (NIH/NIAID) [E]

Subject: Re: Rg novel coronavirus

No news yet on sequences, do we need to put an SLA already in place?

Let's hope we at least have access to a sequence soon! The Science interview with the Chinese heas researcher was not very informative,

https://www.sciencemag.org/news/2020/01/mystery-virus-found-wuhan-resembles-bat-viruses-not-sars-chinese-scientist-says

cheers,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

```
From: "Baric, Ralph S" < (b) (6)

Date: Wednesday, January 8, 2020 at 10:28 AM

To: ' (b) (6) < (b) (6)

Cc: Neeltje van Doremalen < (b) (6) Emmie De wit

< (b) (6) Alexandra Schaefer < (b) (6) Michael Letko

< (b) (6) Heinrich Feldmann < (b) (6)

Subject: RE: Rg novel coronavirus
```

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```
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Sent: Wednesday, January 8, 2020 10:16 AM

To: Baric, Ralph S < (b) (6)

Cc: van Doremalen, Neeltje (NIH/NIAID) [E] < (b) (6) De wit, Emmie (NIH/NIAID) [E] < (b) (6) Schaefer, Alexandra < (b) (6) Letko, Michael (NIH/NIAID) [F] < (b) (6) Feldmann, Heinrich (NIH/NIAID) [E] < (b) (6)

Subject: Rg novel coronavirus
```

Hi Ralph,

Would you be willing to share (collaborate on) any rg viruses of the novel coronavirus when you would have resqued it? We would be primarily interested in the development of NHP models.

Let me know what you think and see what we need to get in place for the transfer as soon as a virus becomes available,

Cheers,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH From: Schountz, Tony

Sent: Fri, 10 Jan 2020 16:31:47 +0000

To: Janine Seetahal; Christine Carrington
Cc: Munster, Vincent (NIH/NIAID) [E]

Subject: Re: Bat flu data

I'm not sure NIH would be interested in funding such a project, so NSF would be the likely source to target. However, if we expanded it to include henipas, filos, rabies et al., perhaps DTRA would be interested. I wonder if we should contact someone at NAMRU6? Vinnie, do you know anyone there?

Tony Schountz, PhD
Associate Professor
Arthropod-borne and Infectious Disease Laboratory
Department of Microbiology, Immunology and Pathology
College of Veterinary Medicine
Colorado State University
3185 Rampart Road
Fort Collins, CO 80523-1692
(b) (6)

From: Janine Seetahal < (b) (6)

Date: Friday, January 10, 2020 at 9:14 AM

To: Christine Carrington < (b) (6)

Cc: "Schountz, Tony" < (b) (6) "Munster, Vincent (NIH/NIAID) [E]"

(b) (6)

Subject: Re: Bat flu data

Hi all,

Happy New Year!

I'm very intrigued by these results. I agree there is much to be done and I'm happy to help further this along and promote more bat work within the Caribbean region.

As Prof C indicated I'm nearly done with the thesis and finishing up the MS on Desmodus pop genetics and I'm almost complete with the revisions on the serology one which should be out soon (fingers crossed).

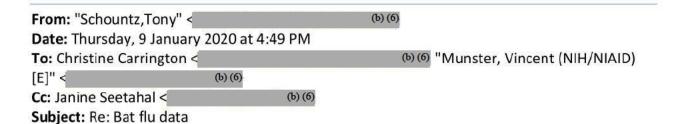
After this PhD is complete | just cannot imagine not working on bats anymore. I still have my volunteer work coordinating the regional rabies group but I think I need a career shift as my interests have evolved. I'm open to any ideas and advice on potential options.

Take care and talk soon Janine

On Fri, Jan 10, 2020 at 11:25 AM Christine Carrington < (b) (6) wrote: Interesting. A lot to explore. Janine is in the final throes of submitting her thesis and also completing a manuscript on the population genetics of *D. rotundus* in Trinidad versus mainland which looks at patterns of mainland-island geneflow based on microsatellite and cyt b sequence data. Really nice work (if I may say so myself). She is very eager to leave her Ministry job and continue in the bat research world so if there is scope for developing a grant proposal for this influenza work (or for another bat related project) she (we) would be very, very interested!

Let's talk soon.

C



Yes, and the list of positives is congruent with the published literature. No one has yet isolated either of these viruses (H17N10, H18N11) and it's unknown if there are more out there. The genetic differences between these two viruses is greater than all H1-H16 influenza A viruses, which suggests there may be more out there. They're very peculiar in that they appear to use MHC class II (DR beta) as an entry receptor. The function of the neuraminidase has yet to be determined, but it does not cleave sialic acid residues like conventional influenza A viruses.

No luck finding tissues in the -80 freezer, unfortunately.

Tony Schountz, PhD
Associate Professor
Arthropod-borne and Infectious Disease Laboratory
Department of Microbiology, Immunology and Pathology
College of Veterinary Medicine
Colorado State University
3185 Rampart Road
Fort Collins, CO 80523-1692
(b) (6)

```
From: Christine Carrington < (b) (6)

Date: Wednesday, January 8, 2020 at 10:56 AM

To: "Munster, Vincent (NIH/NIAID) [E]" < (b) (6)

Cc: Janine Seetahal < (b) (6)
```

Subject: Re: Bat flu data

Dear Vincent and Tony

Just got back into office after a lovely vacation. Had a quick look at the data. A lot of positives. It would be nice to follow up so we can certainly discuss.

C

From: "Munster, Vincent (NIH/NIAID) [E]" < (b) (6)

Date: Wednesday, 8 January 2020 at 1:00 PM

To: "Schountz, Tony" < (b) (6)

Cc: Janine Seetahal < (b) (6) Christine Carrington

(b) (6)

Subject: Re: Bat flu data

Ill check whether three is anything left, given we used it for a lot of studies. I'll get back to you soon.

On Jan 8, 2020, at 09:55, Schountz, Tony < (b) (6) wrote:

Yes, we'll do endpoint titers. We only have 1:100 aliquots of each serum sample – I think you have the original sera?

This semester is a good time for me to travel because I do not teach.

Τ.

Tony Schountz, PhD
Associate Professor
Arthropod-borne and Infectious Disease Laboratory
Department of Microbiology, Immunology and Pathology
College of Veterinary Medicine
Colorado State University
3185 Rampart Road
Fort Collins, CO 80523-1692
(b) (6)

From: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Sent: Wednesday, January 8, 2020 8:28 AM

To: Schountz, Tony < (b) (6) Janine Seetahal < (b) (6) Christine

Carrington < (b) (6)

Subject: Re: Bat flu data

Hi Tony,

Are you going to do titration of the positives (or some of the positives?) and are you going to do VN assays with the virus

Cool data, btw should we revisit our plans with Trinidad soon? It would be nice to set-up some longitudinal surveillance there?

What do you thing Janine and Christine?

Vincent Munster, PhD

Chief, Virus Ecology Section

Laboratory of Virology

**Rocky Mountain Laboratories** 

NIAID/NIH

From: Tony Schountz (b) (6)

Date: Tuesday, January 7, 2020 at 4:42 PM

To: " (b) (6) < (b) (6) Janine Seetahal < (b) (6) Christine Carrington < (b) (6)

Subject: Bat flu data

Hi all,

We are now formally testing the bat sera for antibodies to H18 influenza virus nucleoprotein and I've attached the initial ELISA screening for your review. I've also attached a table from Tong et al. 2013 PLOS Pathogens paper that has their seroprevalence data. We'll work on the ELISA titers and western blot confirmation in the next couple of weeks and then I'll get a draft manuscript to you for review. I don't recall if we have the intestine or rectal swabs here at CSU, or if we shipped them to RML. I have a freezer in another building that may have the samples in them and I'll check on that tomorrow morning. I'll let you know what I find.

\_

Tony Schountz, PhD
Associate Professor
Arthropod-borne and Infectious Disease Laboratory
Department of Microbiology, Immunology and Pathology
College of Veterinary Medicine
Colorado State University
3185 Rampart Road
Fort Collins, CO 80523-1692

(b) (6)

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--

Janine Seetahal, DVM, MPH

Mobile: (b) (6) Email: (b) (6)

Veterinary Officer

Veterinary Diagnostic Laboratory, Ministry of Agriculture, Land and Fisheries Building 49, Eric Williams Medical Sciences Complex (EWMSC)

Champs Fleurs

Trinidad, West Indies

Tel: (b) (6) Fax: (868) 645 4593 
 From:
 Munster, Vincent (NIH/NIAID) [E]

 Sent:
 Thu, 9 Jan 2020 10:29:35 -0700

To: Cara Brook

Cc: Plowright, Raina; Kwe Claude, Yinda (NIH/NIAID) [F]

Subject: Re: Henna sequences

Hi Cara,

That sounds great and more than happy to work with the Pasteur guys. In terms of money, it would probably depend how much funding is needed and what that funding would provide, but as always open for discussion.

I think for u, having he sequence is actually the most important. We are currently developing a custom vircapseq method for henipa's and bat paramyxo's so any sequence info the biohub team could be provide would be very welcome (as this method depends on known sequences).

For our work with the genotype-to-phenotype we would be particularly interested in sequences of G (attachement glycoprotein) and F (fusion). That would actually give us most of the information we need to play around with (shy of working with the actual pathogen).

Also think about where the IP with this particular virus is at, with the Madagascar team and you, with biohub or with Pasteur. We the could potentially draft SLAs and MTAs to formalize our collaboration and your team would then alwayd be part of the downstream work.

Lastly: for any prospective fellows from Madagascar this would be a great opportunity:

https://www.fic.nih.gov/Funding/Pages/african-postdoctoral-training-initiative.aspx

I'm putting in one proposal for NSG approaches of EIDs I Africa (Minion, bioinformatics etc)

Cheers,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: Cara Brook < (b) (6)

Date: Wednesday, January 8, 2020 at 11:47 PM

To: ' (b) (6) < (b) (6) Cc: "Plowright, Raina" < (b) (6)

Subject: Re: Henna sequences

Hi Vincent,

Happy New Year. Or Tratra ny taona, amin'ny Malagasy. Apologies for delays--I am teaching modeling in Madagascar this week.

Samples are probably a 'no' in the short term. We only have RNA in country right now. If your team is interested in advising us to try to isolate in Mada, then that would be ideal I think. Pasteur is pretty excited to be involved in this, and they do have a BSL-3. I think that process is several months to 1-2 years down the road before completion. Would DARPA be amenable to providing some money for this effort after the sequence is described, do you think?

Sequences we should be able to do. Biohub's computational team has kickstarted the sequence reconstruction process (trying to piece together the whole genome), and I was going to catch up with them when I get back in a couple weeks. I think we could have that info to you by sometime in Feb. Can you provide a bit more about what details exactly would be useful? For Hector too?

Thanks, Cara

On Mon, Jan 6, 2020 at 9:02 PM Munster, Vincent (NIH/NIAID) [E] < 6) (6) wrote: Hi Cara,

Is there any change we can get access to the sequences and samples? It would be fun to do some pseufortype analyses, crystal structure and potentially virus isolation.

Great job!!!

And happy New Year,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

 From:
 Munster, Vincent (NIH/NIAID) [E]

 Sent:
 Wed, 8 Jan 2020 13:24:51 -0700

To: Plowright, Raina

Cc: LaTrielle, Sara; Jamie Lloyd-Smith; Amandine Gamble; Hector Aguilar-Carreno;

Peter Hudson

Subject: Re: Friday call - need to move

## perfect

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: "Plowright, Raina" < (b) (6)

Date: Wednesday, January 8, 2020 at 1:23 PM

To: ' (b) (6) < (b) (6)

Cc: "LaTrielle, Sara" < (b) (6) Jamie Lloyd-Smith < (b) (6)

(b) (6)

Amandine Gamble < (b) (6) Hector Aguilar-Carreno

< (b) (6) Peter Hudson <

Subject: Re: Friday call - need to move

The calls are 1 hr.

Sent from my iPhone

On Jan 8, 2020, at 11:54 AM, Munster, Vincent (NIH/NIAID) [E] < 6) (6) wrote:

It will work if it is 4 EST, than I still have one hour available,

Does this work?

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

From: "LaTrielle, Sara" < (b) (6)

Date: Wednesday, January 8, 2020 at 9:52 AM

To: Jamie Lloyd-Smith < (b) (6) "Plowright, Raina"

< (b) (6)

Cc: Amandine Gamble <	(b) (6)	Hector Aguilar-Carre	no
(b) (6) Peter Hudson	n < (b) (6)		(b) (6)
(b) (6)			
Subject: Re: Friday call - need to mov	ve		
Sounds like Thurs 4pm EST is best. V	lincont: work for you	12	
Journal like Thurs 4pm LST is best. V	incent. Work for you	<b>4</b> :	
	42.40		
From: Jamie Lloyd-Smith <	(b) (6)		
Sent: Wednesday, January 8, 2020 8:39 To: Plowright, Raina <	(b) (6)		
Cc: Amandine Gamble <		or Aguilar-Carreno <	(b) (6)
LaTrielle, Sara <	(b) (6) Peter Hudson <		ent Munster
(b) (6)	_		
Subject: Re: Friday call - need to move			
Ok great. Update is that I could do the e		sday — forgot that Katy	y's teaching won't
have started yet. So any of the Thursday	times are good.		
Jamie			
, same			
On Wed, Jan 8, 2020 at 7:30 AM Plowrig	ght, Raina <	(b) (6) V	vrote:
Yes deadline now 48hrs b4 call.			
Cont from my iDhana			
Sent from my iPhone			
On Jan 8, 2020, at 8:15 AM, Jamie Lloyd	-Smith <	(b) (6) wrote:	
If these are EST than I could do Thurs at	· A or moubo (unhannil	u as I'm spanding the d	law with my visiting
If those are EST then I could do Thurs at parents) Fri at 3:30. Does this mean the			
parents, in at 3.30. Does this mean the	. deddille to subillit sil	des has similed too, i p	resurre:
Jamie			
	and the same of the same		
On Wed, Jan 8, 2020 at 6:19 AM Plowrig		(b) (6) <sub>V</sub>	
As I suspected — they want to reschedu	ile do any of these ti	mes work? These are a	II EST I assume.

Raina

Begin forwarded message:

From: (b) (6)
Subject: Friday call - need to move
<b>Date</b> : January 8, 2020 at 7:10:51 AM MST
To: "Plowright, Raina" (b) (6)
TO BOOK STORM
Hi Raina,
Can we move this Friday call to Thursday Jan 16 at 11 am/12pm/4pm? Otherwise Friday Jan 17 at 3:30 pm?
Thank you.
(b) (6)
Monica Zamisch, Ph.D.
Lead Scientist
Support to Biological Technologies Office, DARPA
Science and Technology Associates, Inc.
(b) (6)
James O. Lloyd-Smith
Professor
Department of Ecology & Evolutionary Biology
Department of Biomathematics  University of Colifornia Los Angeles
University of California, Los Angeles 610 Charles E Young Dr South
Box 723905
Los Angeles, CA 90095-7239
Phone: (b) (6)
https://www.eeb.ucla.edu/Faculty/lloydsmith/
Office: 4135 Terasaki Life Sciences Building
Lab: 4000 Terasaki Life Sciences Building
(inc.
James O. Lloyd-Smith
A STATE OF THE STA

Department of Ecology & Evolutionary Biology

Department of Biomathematics University of California, Los Angeles 610 Charles E Young Dr South Box 723905 Los Angeles, CA 90095-7239

Phone: (b) (6)

# /www.eeb.ucla.edu/Faculty/lloydsmith/

Office: 4135 Terasaki Life Sciences Building Lab: 4000 Terasaki Life Sciences Building 
 From:
 Munster, Vincent (NIH/NIAID) [E]

 Sent:
 Wed, 8 Jan 2020 12:17:43 -0700

To: Baric, Ralph

Cc: van Doremalen, Neeltje (NIH/NIAID) [E]; De wit, Emmie (NIH/NIAID) [E];

Alexandra Schaefer; Letko, Michael (NIH/NIAID) [F]; Feldmann, Heinrich (NIH/NIAID) [E]

Subject: Re: Rg novel coronavirus

Sounds good, we'll let you know as soon we hear anything via NIAID channels (hopefully soon). Hopefully full-length sequences, but we could always do a SARS-chimera if needed.

Let's keep in touch,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: "Bario	, Ralph S" <	(b) (6)			
Date: Wedn	esday, January	8, 2020 at 10:28 AM			
To: '		(b) (6) <	(b) (6)		
Cc: Neeltje v	an Doremalen	<	(b) (6) Emmi	ie De w	<i>r</i> it
<	(b) (6)	Alexandra Schaefer <		(b) (6)	Michael Letko
<	(b) (6)	Heinrich Feldmann <		(b) (6)	

Subject: RE: Rg novel coronavirus

Hi Vincent, Absolutely! Can NIH help get hold of the full length or spike sequence? I imagine the outside world is going to have to wait awhile before the genome length sequence or the S sequence becomes available. Ralph

```
From: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Sent: Wednesday, January 8, 2020 10:16 AM

To: Baric, Ralph S < (b) (6)

Cc: van Doremalen, Neeltje (NIH/NIAID) [E] < (b) (6) De wit, Emmie (NIH/NIAID) [E] < (b) (6) Schaefer, Alexandra < (b) (6) Letko, Michael (NIH/NIAID) [F] < (b) (6) Feldmann, Heinrich (NIH/NIAID) [E] < (b) (6)

Subject: Rg novel coronavirus
```

Hi Ralph,

Would you be willing to share (collaborate on) any rg viruses of the novel coronavirus when you would have resqued it? We would be primarily interested in the development of NHP models.

Let me know what you think and see what we need to get in place for the transfer as soon as a virus becomes available,

Cheers,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH From: Schountz, Tony

**Sent:** Tue, 7 Jan 2020 23:41:55 +0000

To: Munster, Vincent (NIH/NIAID) [E]; Janine Seetahal; Christine Carrington

Subject: Bat flu data

Attachments: Trinidad influenza.xlsx, Tong Table S12 2013 PLOS Path.DOCX

Hi all,

We are now formally testing the bat sera for antibodies to H18 influenza virus nucleoprotein and I've attached the initial ELISA screening for your review. I've also attached a table from Tong et al. 2013 PLOS Pathogens paper that has their seroprevalence data. We'll work on the ELISA titers and western blot confirmation in the next couple of weeks and then I'll get a draft manuscript to you for review. I don't recall if we have the intestine or rectal swabs here at CSU, or if we shipped them to RML. I have a freezer in another building that may have the samples in them and I'll check on that tomorrow morning. I'll let you know what I find.

Tony Schountz, PhD
Associate Professor
Arthropod-borne and Infectious Disease Laboratory
Department of Microbiology, Immunology and Pathology
College of Veterinary Medicine
Colorado State University
3185 Rampart Road
Fort Collins, CO 80523-1692
(b) (6)

(b) (6)

This document was exported from Numbers. Each table was converted to an Excel worksheet. All other objects on each Numbers sheet were placed on separate worksheets. Please be aware that formula calculations may differ in Excel.

Numbers Sheet Name	Numbers Table Name	Excel Worksheet Name
Sheet1 - Table 1		
	Table 1	Sheet1 - Table 1
Sheet 2		
	Table 1	Sheet 2

Animal IDSite	Species	Sex (M/F/I)	Age (A/J/N)	LISA (1:100 ELISA TT	WB
1 Mt. Hope	A. planirostris trinitatis	F	A	+	
2 Mt. Hope	A. planirostris trinitatis	U	J	+	
3 Mt. Hope	A. planirostris trinitatis	F	A	+	
4 Mt. Hope	A. planirostris trinitatis	U	J	+	
5 Mt. Hope	A. planirostris trinitatis	F	A	+	
6 Mt. Hope	A. planirostris trinitatis	F	A	+:	
7 Mt. Hope	A. planirostris trinitatis	U	J	+	
8 Mt. Hope	A. planirostris trinitatis	F	A	±0	
9 Mt. Hope	A. planirostris trinitatis	F	A	+	
10 Mt. Hope	A. planirostris trinitatis	F	A	+	
11 Mt. Hope	A. planirostris trinitatis	F	A	+	
12 Mt. Hope	A. planirostris trinitatis	M	J		
13 Mt. Hope	A. planirostris trinitatis	M	J	+	
14 Mt. Hope	A. planirostris trinitatis	F	A		
15 Mt. Hope	A. planirostris trinitatis	M	J		
16 Mt. Hope	A. planirostris trinitatis	M	J	+	
17 Mt. Hope	A. planirostris trinitatis	M	A	+	
18 Mt. Hope	A. planirostris trinitatis	F	A	+	
19 Mt. Hope	A. planirostris trinitatis	M	Ĵ	+	
20 Mt. Hope	A. planirostris trinitatis	F	A	+	
21 Mt. Hope	A. planirostris trinitatis	M	J	_	
22 Mt. Hope	A. planirostris trinitatis	M	J		
23 Mt. Hope	A. planirostris trinitatis	F	J	-2	
24 Mt. Hope	A. planirostris trinitatis	F	A	_	
25 Mt. Hope	A. planirostris trinitatis	F	J	+	
26 Mt. Hope	A. planirostris trinitatis	M	J	+	
27 Mt. Hope	A. planirostris trinitatis	M	J		
28 Lopinot	A. planirostris trinitatis	F	A	+	
29 Lopinot	A. planirostris trinitatis	M	J	4	
30 Lopinot	A. literatus	F	A	+	
31 Lopinot	A. literatus	M	J	+	
32 Lopinot	A. literatus	M	J	+	
33 Lopinot	A. literatus	F	J	-	
34 Lopinot	A. literatus	F	A		
35 Lopinot	A. literatus	F	A		
36 Lopinot	A. literatus	F	J	4:	
37 Lopinot	A. literatus	F	A		
38 Lopinot	A. literatus	M	J	+	
39 Lopinot	A. literatus	F	J	4	
40 Lopinot	A. literatus  A. literatus	F	A	+	
41 Lopinot	A. literatus	M	A	+	
42 Lopinot	Glossophaga soricina	F	A	+	
43 Lopinot	Glossophaga soricina	F	A	+	
44 Lopinot	A. planirostris trinitatis	M		+	
45 Lopinot	A. literatus	M M	A A		
		M		_	
46 Lopinot	A. literatus Sarcopteryx bilineata	-	A		
47 Lopinot		M	A	-	
48 Lopinot	Glossophaga soricina	F	A	-	
49 Lopinot	Sturnira 1ilium	M	A	+	
50 Lopinot 51 Lopinot	Sturnira lilium Sturnira lilium	F	A A	+	

52	Lopinot	Sarcopteryx bilineata	M	J		
		A. literatus	M	A	+	
54	Lopinot	A. planirostris trinit.	M	A		
55	Santa Cruz	A. literatus	M	A	= 1	
		A. literatus	M	A	<del></del>	
		Sarcopteryx bilineata	M	A	-0	
58	Santa Cruz	Sarcopteryx bilineata	F	A		
59	Santa Cruz	A. literatus	M	A		
60	Santa Cruz	A. literatus	M	A	+	
	A STATE OF THE PARTY OF THE PAR	A. literatus	M	A	-0	
		A. literatus	M	A	+	
		A. planirostris trinitatis	M	A	+	
64	Santa Cruz	A. literatus	M	A	_	
		A. literatus	M	A	+	
66	Santa Cruz	A. planirostris trinitatis	M	A		
67	Santa Cruz	Sarcopteryx bilineata	F	A	-6	
68	Santa Cruz	Sarcopteryx bilineata	F	A	=:	
		A. literatus	M	A	=3	
70	Santa Cruz	A. planirostris trinitatis	M	A	=== ]	
		A. literatus	M	A		
		A. planirostris trinitatis	M	A	+	
		Sarcopteryx bilineata	M	A		
74	Santa Cruz	A. literatus	M	A	= 1	
75	Santa Cruz	A. literatus	M	A	+	
		A. literatus	M	A	-0	
77	Maracas Va	C. perspicillata	M	A	+	
78	Maracas Va	C. perspicillata	F	A		
		A. planirostris trinitatis	F	A	+	
80	Maracas Va	A. literatus	M	A	+	
81	Maracas Va	A. literatus	M	A	+	
		C. perspicillata	M	A	===	
		A. literatus	F	A	<u></u> 8	
84	Maracas Va	C. perspicillata	F	A		
Control :	1	A. jamaicensis				
Control :	2	A. jamaicensis			-6	
Control:	3	A. jamaicensis			===	

Dilution	3	4	9	9	10	17	18	29	30	- 37	.38	41	- 44	49	50	53	. 56	59	61	63	64	69	60	72	73	75	77	78	79	83	84	673	678	679	680
100	0.251	0.268	0.384	0.412	0.487	0.287	0.377	6,396	6.378	0.691	0.604	0.802	0.661	0.344	0.521	0:412	0.1639	0.041	0.382	0.824	0.110	8.321	0.327	0.883	0.371	0.498	0.302	0.561	0.678	8, 201	0.866	L 377	1.024	1.369	0.060
260	0.466	6.107	0.217	0.217.	0.221	0.146	0.381	6, 139	0.190	0: 302	.0.330	0.472	0.114	0.168	: 0, 141	0: 189	0.323	0, 339	0.166	0.481	0.116	4: 139	0, 168	0, 696	0.187	0.261	0.147	0.288	0.341	0.001	0.427	0.782	0.498	0.743	0.061
400	0.014	0.064	0,098	0.103	0.131	0.088	0.068	0.061	6,668	0.164	0.211	0.304	0.155	0.641	0.075	6.091	0.157	0.155	0.091	0.382	0.081	6.077	0,077	0.237	0.092	0.101	0.066	6.119	0.171	0.014	0.204	0.396	0.259	0.386	0,019
800	0.168	-0,061	0.017	0,081	0.012	0.041	0.015	0,002	-9,000	0,081	0.096	0, 151	0.080	0.049	0.021	8,037	0,095	0, 097	0.0FL	0.327	.0.041	8,032	0,051	0, 126	0.011	0.068	0.119	11,060	0,093	0.029	0, 196	0.207	0, 159	0.241	-0.019
1690	0.461	-0:053	-0.051	0.036	0.001	0.022	0.925	9,709	0.021	0.014	0.014	0.091	0.011	0:023	0.003	0.7009	0.052	0.031	0.034	0.419	0.032	4:014	B. 024	0.031	0.023	0.019	0.024	0.102	0.00	-0.016	0.039	0.117	0.054	0.332	
3000	-0,429	-0,003	0.062	0.029	0.011	-0.011	0,009	0.001	0,011	0,019	0.035	0.054	0.029	0.011	0.011	6,013	0.061	0.034	0.029	0,851	0.014	0,019	0, 021	0.019	0.009	0.024	0.001:	0.021	-0,009	-0.052	0.019	0,011	0,063	0.091	
6600	0.041	0.014	0.014	0.011	0.012	-0.011	9.936	0,010	.0,001	0.015	0.021	0.029	0.943	-0.006	9,000	0.003	0.034	0.033	0.041	0.015	0.000	6,029	0.006	0.006	0.014	0.016	0.010	0.106	0.038	0,030	0.016	0.029	0.043	0.044	
12800	0.949	0.019	1020 /0	D. 0235	0.036	0.004	0.001	0,014	0.010	0.022	0.024	0.033	0.014	0.012	0.007	0.010	0.061	0.041	0.011	0.423	0.010	0.011	0,010	0.033	11, 005	0.070	0.007	0.017	0.021	0,014	0.034	0.010	0:010	0.043	
																																			0,063
Titer																																			
100	0.110	5, 207	0.323	0.351	0.42E	0.226	0.116	0.246	0.316	0.308	0.581	0.741	0.000	0.283	0.263	0.361	0.578	0.580	0.328	0.753	0.249	6.260	0.266	0.822	0,316	0:437	0.241	4.500	0.817	0.103	0.805	1.316	0.963	1.108	
200	-0.000	0.010	9, 156	0.196	0.103	0.085	0.110	0.078	0.131	0.201	0.291	0.016	0.263	0.000	0,060	0, 128	0.281	0.279	0.105	0.420	0.065	6.078	0.107	0.395	0.126	0, 200	0.066	0.528	6, 280	-0.001	0.300	0.721	0.417	0.682	
400	-6.618	-0.008	0.037	0.038	0, 076	0.027	0.007	-0.001	0.027	0, 183	0.150	0, 243	0.094	-6:621	0.014	8:033	0.000	0.097	0:035	0.201	0.000	4,016	0.010	0.176	0.031	0.676	0.005	8.069	0.110	-6.018	0.173	0,331	0.306	0.124	
800	0.006	-0.113	-0.015	0.030	-0,020	-0.023	-0.417	-0.000	-0.002	B. 020	0.025	0.099	0.419	-0.013	-9,038	-0.025	0.831	0.026	-0.011	0.966	0.018	-b. 030	-0.011	0.065	-0.018	0.097	-0.023	0.019	0.032	-0.037	0.015	0.146	0.098	0.180	
1600	-0.011	-0.116	-0.117	-0.036	-0.001	-0.040	-0.040	-0.063	-0,008	-0.018	-0.018	0,030	-0.421	-0.039	-0.019	-0,053	-0.010	-0.008	-0.028	-0.903	-0.030	-6,048	-0.033	-0.011	-0.011	-0.013	-0.018	-0, D30	-0:021	-0.078	0.027	0,056	-0.508	0.671	
3200	-0.091	-0.081	.0,001	-0.021	-0.01 €	-0.076	-0.048	-6: Dt1	-0.061	-0.913	-0.027	-0.008	-0.413	-0.061	-0.051	-0.009	-0.001	-0.026	-0.011	-0.411	-0.048	4.013	-0.041	-0.037	-0.051	-0.636	-0.661	-0.011	-0.071	-0.114	-0.011	-0.021	0.902	0.880	
6600	-0.021	-0.048	-0.008	-0, 018	-0.058	-0.093	-0.48h	-0.063	-9, 058	-0.017	-0.0.00	-0.013	-0.429	-0.068	-0.063	-0.010	0.008	-0.029	-0.021	-0.647	-0.053	-4.033	-0.056	-0.056	-0.048	-0.046	-0.043	-0.006	-0.024	-0.082	-0.049	-0.033	-0.920	-0.018	
12800	-0.013	-9,013	-0.03)	-0.034	-0.024	0.056	-0.011	-0, D(8	-0.095	-0.016	-0,038	-0.023	-0.048	-0.074	-9,000	-0, D08	-0,820	-0.021	-0.028	-0.029	-0.04%	-0.051	-0.003	-0.013	-0, 055	-0.043	-0.055	-0.045	-0,011	-0.039	-0,038	-0,031	-0.07%	-0.019	

Table S12. Seroprevalence of IgG in Guatemalan bats to H17 rHA by ELISA

Species sampled in 2009	ELISA +	Tested
Artibeus jamaicensis	9	12
Artibeus lituratus	2	7
Carolia perspicillata	1	3
Centurio senex	0	1
Desmodus rotundus	9	41
Glossophaga soricina	2	6
Micronicterius nicrotis	0	3
Phyllostomus discolor	2	2
Pteronotus davyi	0	5
Sturnira lilium	13	21
Sturnida ludovici	0	1
Vampyressa pusilla	0	2
Species sampled in 2010		
Artibeus jamaicensis	8	24
Artibeus lituratus	3	5
Artibeus phaeotis	1	1
Artibeus toltecus	0	1
Carollia perspicillata	2	8
Desmodus rotundus	5	26
Eptesicus fuscus	0	2
Glossophaga soricina	7	13
Macrophyllum macrophyllum	1	1
Molossus sinaloae	0	2
Myotis nigricans	0	2
Platyrrhinus helleri	0	10
Sturnira lilium	21	28
Uroderma bilobatum	0	1
Totals	86	228

From: Schountz, Tony

**Sent:** Fri, 3 Jan 2020 17:03:53 +0000

To: Munster, Vincent (NIH/NIAID) [E]; Kwe Claude, Yinda (NIH/NIAID) [F]

Cc: van Doremalen, Neeltje (NIH/NIAID) [E]

Subject: Re: Visit to RML in January

OK, I understand now. I thought it was about (b) (6) (my grad student).

Postponing is good - mid-February then? That will probably delay the early March DARPA reporting a bit but we should have some preliminary results by then. I'll push (b) (6) to get the PCRs done as soon as we get the samples to CSU.

Thanks,

Tony

Tony Schountz, PhD

Associate Professor

Arthropod-borne and Infectious Disease Laboratory

Department of Microbiology, Immunology and Pathology

College of Veterinary Medicine

Colorado State University

3185 Rampart Road

Fort Collins, CO 80523-1692

(b) (6)

(b) (6)

From: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Sent: Thursday, January 2, 2020 12:12 PM

To: Schountz, Tony < (b) (6) Kwe Claude, Yinda (NIH/NIAID) [F]

(b) (6)

Cc: van Doremalen, Neeltje (NIH/NIAID) [E] < (b) (6)

Subject: Re: Visit to RML in January

Hi Tony,

As discussed previously in the email, this will not be possible without proper planning ahead. We are currently completely booked with NHP experiments (so Neeltje will not be available) and I currently do not have any sufficiently trained personnel to spare (e.g. Trent or Bob). The problem is not so much the experiments, but all the things involved with doing experiments in BSL4, and mostly the correct handling of all the specimen and select agent record keeping. I myself, will be travelling to Ghana that week, otherwise I would have been able to help you.

Maybe we should push this back a bit until Kwe is fully trained and he can help you with this? Kwe, what is your current status with the BSL4 training? I think this work would be an excellent fit with Kwe's

interests so that would be a better poc for you. The only caveat is that he has not been completely signed of yet.

For the experiment I'm think we should do this in duplicate, we should also prepare all the labels on forehand so we can label the tubes here (and plan accordingly as there are restrictions who can make these tubes etc). Secondly, we need to transfer the virus to here, so that will take some time as well as the virus stock will need to be grown. How about we reschedule for a month – month and a half later and we'll prepare everything?

Cheers and happy new year!

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: Tony Schountz < (b) (6)

Date: Thursday, January 2, 2020 at 11:41 AM

To: ' (b) (6) < (b) (6) Cc: Neeltje van Doremalen < (b) (6)

Subject: Re: Visit to RML in January

Vincent,

I'm sorry, I somehow missed your email!

I won't bring Juliette with me and I'll chat with Kay while I'm there to see how we might get her there at a future date. If possible, I'd like to get there Sunday, Jan 19 and put the cells in the incubator. My badge was renewed the last time I was there so hopefully I can get in without having Neeltje as an escort. I'll then plate the cells in 12 well plates on Monday so they are ready to inoculate on Tuesday.

Based upon the CPE that Neeltje saw and with the data generated, I think only two days of sampling will be sufficient, although a 3<sup>rd</sup> day would be nice to have.

Here's what we'd do:

7 primary Aj cell cultures (from 7 different bats) Time: 0, 1, 24, 48 hrs CedV(wt), CedV(ic), NiV-B, HeV

That would be 112 samples if done in singles. If we added 72 hr that would be 140 samples.

For each we'd need cellular RNA (RLT) and supernatant RNA (AVL), so totals of 224 or 280 to process. We could do the qPCRs in duplicate (technical replicates) but I think the important thing is that we will have 7 biological replicates. Of course, your input is welcomed.

I will bring replacement RNEasy and Viral RNA kits to leave with you. I believe you still use the Qiagen kits? If you provide me the part numbers I will get them purchased and just bring them up with me. I'll also bring the plates and media so that everything is ready to go. We also need to get Eric's CedV to you. I'll contact Ricki about the refresher training since it's been >3 months since I've been there.

What do you think?

Thanks,

Τ.

Tony Schountz, PhD
Associate Professor
Arthropod-borne and Infectious Disease Laboratory
Department of Microbiology, Immunology and Pathology
College of Veterinary Medicine
Colorado State University
3185 Rampart Road
Fort Collins, CO 80523-1692

(b) (6)

From: "Munster, Vincent (NIH/NIAID) [E]" < (b) (6)

Date: Monday, November 25, 2019 at 2:19 PM

To: "Schountz,Tony" < (b) (6)

Cc: "van Doremalen, Neeltje (NIH/NIAID) [E]" < (b) (6)

Subject: Re: Visit to RML in January

Hey Tony,

Let me check whether we have enough bandwidth to accommodate this, as we have a couple of big studies coming up.

For your requirements, you need people who train you and be your buddy inside and take samples out? If you completely list your needs (e.g. x amount of entries, x amount of samples need to be taken out of 4 in X extraction buffer) would help me a bit better to make sure

Just make a complete calculation, XX cellines, XX time points, XX viruses = XX entries and XX samples to be taken out.

I'm not sure whether it would make sense to have a graduate student trained to do extractions (all AVL?), its typically quite a commitment to get people in (but not impossible). I'll check with Kay.

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology

# Rocky Mountain Laboratories NIAID/NIH

From: Tony Schountz < (b) (6)

Date: Monday, November 25, 2019 at 12:52 PM

To: ' (b) (6) < (b) (6)

Subject: Visit to RML in January

Hi Vinnie,

Just a reminder, I'm planning to come to RML in January to do another infection experiment with Cedar, Nipah and Hendra just like the one Neeltje helped me with last summer. I'd like to bring one of my PhD students (Juliette Dean) to finish the RNA extractions in the BSL-2. When we chatted at the October meeting at the B Bar Ranch you said there may be some training requirements for her. If you could let me know who to contact I'll get that rolling.

I've also started on a manuscript with serological data from the Trinidad bat samples and reactivity to the bat flu viruses. My tech has a bunch of western blots to do but I'm optimistic I will have a draft ready in the next 3 or 4 weeks to send you.

Thanks,

T.

Tony Schountz, PhD
Associate Professor
Arthropod-borne and Infectious Disease Laboratory
Department of Microbiology, Immunology and Pathology
College of Veterinary Medicine
Colorado State University
3185 Rampart Road
Fort Collins, CO 80523-1692

(b) (6)

 From:
 Munster, Vincent (NIH/NIAID) [E]

 Sent:
 Thu, 2 Jan 2020 13:10:11 -0700

To: Emily Gurley; Plowright, Raina; Alison Peel

Cc: Clif McKee; LaTrielle, Sara; Kwe Claude, Yinda (NIH/NIAID) [F]; Bushmaker,

Trenton (NIH/NIAID) [E]

Subject: Re: introducing Clif McKee - postdoc for PREEMPT Bangladesh

#### Welcome to the team!

Given the different results between Bangladesh and Oz, I think it would be good to have a methodological comparison between sampling techniques and strategies to make sure that the sampling between sites is largely standardized (so that any variation in prevalence is not caused by differences in methodologies).

I believe there will be a team travelling to Bangladesh soon? Maybe good to go over all the protocols and compare them with the ones used in Oz?

Within the Bangladesh samples we are finding some respiratory positives, so it might be good to put some more emphasis on this as well

Cheers,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: Emily Gurley <	(b) (6)		
Reply-To:		(b) (6)	
Date: Thursday, January	2, 2020 at 12:54 PM		
To: '	(b) (6) <	(b) (6)	
Cc: Clif McKee <	(b) (6) "LaTrielle	, Sara" < (b)	(6)
Subject: introducing Clif	McKee - postdoc for PREEMP	T Bangladesh	

# Dearest colleagues,

I'm writing to introduce you to Clif McKee, who is joining the PREEMPT Bangladesh team as a postdoctoral fellow. Clif recently completed a PhD in Ecology from Colorado State, where he worked with Colleen Webb and folks from CDC to study bartonella and bats (I'll leave the eloquent, full version for Clif when you meet him). We're thrilled to have him join us. He'll be based full-time in Baltimore, with travel to Bangladesh and Cambridge.

Please join me in welcoming Clif. Sara, thanks in advance for adding him to the distribution list and the Slack channels.

Wishing you all a wonderful 2020! Looking forward to all of the exciting collaborative work we have
planned.

Best, Emily From: Munster, Vincent (NIH/NIAID) [E]
Sent: Thu, 2 Jan 2020 11:28:35 -0700

To: Plowright, Raina; Kwe Claude, Yinda (NIH/NIAID) [F]

Cc: Emily Gurley; Ausraful Islam; Bushmaker, Trenton (NIH/NIAID) [E]

Subject: Re: NiV screening from last shipment

Thanks Kwe.

It would be good to track down the information on the 4 samples without information!

Encouraging results, more respiratory sampling?

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: "Plowright, Raina" < (b) (6)

Date: Thursday, January 2, 2020 at 10:43 AM

To: "Kwe Claude, Yinda (NIH/NIAID) [F]" < (b) (6)

Cc: Emily Gurley <egurley1@jhu.edu>, Ausraful Islam < (b) (6) Trenton

(b)(6)

Bushmaker < (b) (6) (7)

Subject: Re: NiV screening from last shipment

Such great news! Thank you Kwe.

Raina

On Jan 2, 2020, at 10:22 AM, Kwe Claude, Yinda (NIH/NIAID) [F] < (b) (6) wrote:

Hello all,

We have finished screening all the samples from the second BGD shipment (~2233 samples).

Overall we had a total of 15 positive for NiV (list of positive attached):

- 5 roost samples
- 2 Urine swab/Urine
- 4 throat swab
- · 4 without information

We will now put in some effort to screen the same samples for paramyxoviruses. This usually takes longer because it involves more processes

1. cDNA synthesis

- 2. Actual semi-nested PCRs
- 3. Gels
- 4. Sequencing

We'll keep you informed of all progress. Thanks Emily and Rajib for the hard work.

Kind regards

---

Kwe

<BGD\_Shipment2\_NiV-Positive.xlsx>

Sent: Thu, 26 Dec 2019 08:29:37 -0700 To: Thruston, Jeffrey (NIH/NIAID) [E]; (b) (6) Cc: Plowright, Raina Re: Griffith MTA Subject: Thank Jeff for the clarification, Cheers, Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology **Rocky Mountain Laboratories** NIAID/NIH (b) (6) From: "Thruston, Jeffrey (NIH/NIAID) [E]" < Date: Thursday, December 26, 2019 at 7:05 AM (b) (6) < (b) (6) To: ' Cc: "Plowright, Raina" < (b) (6) (b) (6) Subject: RE: Griffith MTA Hi Alison, (b) (4) Sincerely, Jeff Thruston From: Alison Peel < Sent: Thursday, December 19, 2019 1:37 AM To: Thruston, Jeffrey (NIH/NIAID) [E] < (b)(6)Cc: Plowright, Raina < (b) (6) Munster, Vincent (NIH/NIAID) [E] (b)(6)Subject: Re: Griffith MTA Hi Jeff,

Munster, Vincent (NIH/NIAID) [E]

From:

	(b) (4)
It seems like all other points below are addressed.	
Thanks! Alison	
On Thu, 19 Dec 2019 at 01:15, Thruston, Jeffrey (NIH/NIAID) [E] < 6) (6) wrote: Hi Alison,	
I will be around during the holidays, so drafting the amendments is doable. But, I want to make sure very dothis as efficiently as possible, so as to avoid voluminous amendments in the future.	
	(b) (4)



Once I hear from you, we can get to work drafting the template amendments.

Sincerely,

## Jeff Thruston

Jeffrey T. Thruston, J.D., M.S.
Technology Transfer and Patent Specialist
Immunology & Emerging Infections Branch
TTIPO/NIAID/NIH
5601 Fishers Lane, Suite 2G46, MSC 9804
Rockville, MD 20892-9804

(b) (6)

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From: Alison Peel < (b) (6)

Sent: Tuesday, December 17, 2019 1:30 AM

To: Thruston, Jeffrey (NIH/NIAID) [E] < (b) (6)

Cc: Plowright, Raina < (b) (6)

Subject: Re: Griffith MTA

Hi Jeff,

Thanks very much for your replies. I've added further responses in blue below. Our government departments and Griffith's legal department will be in a holiday shutdown mode between Christmas and New Year, with skeleton staff likely for a full 2-week period. I've indicated to the CVOs that we would pick this up in the New Year, and hopefully be able to present a draft amendment to the MTA then. Is it feasible from your end to make any progress on this during this week or between Christmas and New Year?

Many thanks, and all the best for the holiday period Alison

Let's take a step back to make sure everything is clear. We are

On Wed, 11 Dec 2019 at 06:15, Thruston, Jeffrey (NIH/NIAID) [E] < 6) (6) wrote: Hi Alison,

Thank you for the email. I have answered your questions in your email directly below. Let me know if you have any other questions.

Sincerely,

Jeff Thruston

From: Alison Peel < (b) (6)

Sent: Friday, December 6, 2019 3:17 PM

To: Plowright, Raina (b) (6)

Cc: Thruston, Jeffrey (NIH/NIAID) [E] < (b) (6)

Subject: Re: Griffith MTA

(b) (4)

Thanks very much Jeff.

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Thanks very much	
Ali	
On Sat 7 Day 2010 at 05:02 Playwight Pains	(b) (6) wrote:
On Sat, 7 Dec 2019 at 06:03, Plowright, Raina < This sounds like a good way forward.	(b) (4
	0.70
	(b) (4)
Thanks for your fast work on this. We appreciate that you ar	
Thanks for your fast work on this. We appreciate that you ar	
Thanks for your fast work on this. We appreciate that you ar Raina	
Raina	re giving this priority.
Raina On Dec 6, 2019, at 12:59 PM, Thruston, Jeffrey (NIH/NIAID)	re giving this priority.
	re giving this priority.  [E] < (b) (6) wrote:

that would be easier.

Sincerely,

### Jeff Thruston

Jeffrey T. Thruston, J.D., M.S.
Technology Transfer and Patent Specialist
Immunology & Emerging Infections Branch
TTIPO/NIAID/NIH
5601 Fishers Lane, Suite 2G46, MSC 9804
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(b) (6)

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From: Plowright, Raina < (b) (6)

Sent: Friday, December 6, 2019 2:55 PM

To: Thruston, Jeffrey (NIH/NIAID) [E] < (b) (6)

Cc: Munster, Vincent (NIH/NIAID) [E] < (b) (6) Alison Peel < (b) (6)

Subject: Re: Griffith MTA

Jeff, what is an SLA? the CVO concern is that we would alert AAHL and make an isolate available, if AAHL request it.

On Dec 6, 2019, at 12:50 PM, Thruston, Jeffrey (NIH/NIAID) [E] < (b) (6) wrote:

Hi Dr. Munster,

That would require (b) (4)

Sincerely,

# Jeff Thruston

Jeffrey T. Thruston, J.D., M.S.
Technology Transfer and Patent Specialist
Immunology & Emerging Infections Branch
TTIPO/NIAID/NIH
5601 Fishers Lane, Suite 2G46, MSC 9804
Rockville, MD 20892-9804

(b) (6)

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From: Munster, Vincent (NIH/NIAID Sent: Friday, December 6, 2019 12:		(b) (6)	
To: Thruston, Jeffrey (NIH/NIAID) [8		(b) (6)	
Cc: Alison Peel < Subject: Griffith MTA	(b) (6) Raina Plowright <		(b) (6)
Hi Jeff,			
Quick question, would it be possible	e to add the following la	nguage to the Griffith MTA	1?
			(b) (4)
			(b) (4)
		AAHL is the governm	ent BSL4 lab in
Australia.			
Let me know what you think,			
Cheers,			
Vincent			

Sent:	Wed, 18 Dec 2019 11:44:12 +0100							
To:	Plowright, Ra	ina						
Cc:	Alison Peel;		(b) (6)					
Subject:	Re:	(b) (4)						
you can probably ge	et a letter from amples which	CDC clearing would potentia	In the case that the samples this rather than a complete in ally contain pathogens),					
On Dec 18, 2019, at	04:57, Plowrig	ght, Raina <	(b) (6	wrote:				
•	day and I think i	f MSU gets our	vay). own CDC permit for low risk sa Istralia samples. We will start t					
From: "Munster, Vir Date: Monday, Deco To: Alison Peel < Cc: "Plowright, Rain	ember 16, 2019		(b) (6) <sup>11</sup>	(b) (6)				
Subject: Re:	(b) (4)							
Hi Ali,								
Good to get some clar depending on what yo		mater. So basio	cally we have two different sets	s of regulations				
(b) (6), 'Subject: Re:	(b) (4)	(b) (6) <	(b) (6)					
Hi Vincent,								
I'm just following up o	on this old email	l chain as I'm a I	ittle bit confused as to	(b) (4)				
and staff working with	n the samples. V	Ve are working	You have much more experient thing – both legally, and for the on our sample management played your input to clarify this.	e safety of students				
In the old chain below	, we discussed			(b) (4)				

Munster, Vincent (NIH/NIAID) [E]

From:

(b) (4) Is that still your	
interpretation?	
• correct	
Then, related to the email thread about the (b) (4)	E
	(b) (4 <sub>1</sub>
	(b) (4
What BSL level would you handle that serum at? I was discussing this with someone at Griffith last wee and they suggested that pathogen quantity needs to be taken into account, so that even for Hendra, that samples expected to have very low viral quantities could be potentially handled at in a hood to BSL 3 standards but in a BSL 2 lab.	
	(ъ) (4

I hope this makes sense, till (b) (6) but more than happy to discuss.

Thanks Ali	
From: "Munster, Vincent (NIH/NIAID) [E]" <	(b) (6)
Date: Tuesday, 1 October 2019 at 10:13 pm	
To: Alison Peel < (b) (6)	
Cc: "Plowright, Raina" <	(b) (6)
Subject: Re: (b) (4)	
Resent from: < (b) (6)	
Hi Alison,	
Your correct that	(b) (4)
	(b) (4)
Cheers,	
Vincent Munster, PhD	
Chief, Virus Ecology Section	
Laboratory of Virology	
Rocky Mountain Laboratories	
NIAID/NIH	
From: Alison Peel < (b) (6)	
Date: Sunday, September 29, 2019 at 10:46 PM	
To: ' (b) (6) <	(b) (6)
Cc: "Plowright, Raina" <	(b) (6) Trenton Bushmaker
< (b) (6) "Kwe Claude, Yinda	(NIH/NIAID) [F]"
< (b) (6)	
Subject: Re: (b) (4)	

Hi Vincent,

Another thing to discuss at (or before!) the October meetings is your experience with	(b) (4)
	Does that hold
true for shipment as well? I wonder if	(b) (4)
Cheers	
On Sun, 22 Sep 2019 at 01:25, Munster, Vincent (NIH/NIAID) [E] < Sounds good, typically universities will have long-term storage capacity so that might be	(b) (6) wrote: an option,
Hopefully we can continue this project in the future, then I think you should write in a defreezer for long-term storage where only very few people would have access too. This coas specific room etc. In addition, make sure that you have a specific inventory accounting sample (most problems start when there is no up-to-date inventory and people "loose" suse	ould be placed in g for each
But alternatively, given that you can't handle the specimen without proper containment samples at an appropriate facility might not be a bad idea. Here at RML,	, storing the (b) (4)
We can talk more about this in Bozeman / RML,	
Cheers,	
Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH	
From: Alison Peel < (b) (6)	
<b>Date:</b> Friday, September 20, 2019 at 4:48 PM <b>To:</b> " (b) (6) < (b) (6)	
Cc: "Plowright, Raina" (b) (6), Trenton Bushmaker	
(b) (6) "Kwe Claude, Yinda (NIH/NIAID) [F]"	
(b) (6) " (b) (6) < (b) (6)	
Subject: Re: (b) (4)	

Hi Vincent,

Thanks very much for following up on this. I asked Manuel to identify any duplicates/matched samples from the first round of results but will follow up again with these recent results and look into making it a defined step in our protocols when we receive results.

Our University Biosafety committee have been happy with (b) (4)
This would need to include how long they would need to be retained for beyond the life of the current project.
This is not something I have experience in planning. Ideally, we'd like to retain them within our possession until we have a clear plan rather than just pass them onto another Australian facility. I'd be happy to hear any thoughts anyone has on this. Perhaps it will be clearer once I start testing samples for a wider range of viruses.
Cheers
Ali
From: Munster, Vincent (NIH/NIAID) [E] < (b) (6)  Sent: 21 September 2019 01:58  To: Alison Peel < (b) (6)  Cc: Plowright, Raina < (b) (6) Bushmaker, Trenton (NIH/NIAID) [E]  < (b) (6) Kwe Claude, Yinda (NIH/NIAID) [F] < (b) (6)  Subject: (b) (4)  Hi Ali,
Given that this is not you guys's first rodeo, I think everything is stored and secured properly, but I just wanted to do my due diligence,
Cheers,
Vincent Munster, PhD

Chief, Virus Ecology Section

Laboratory of Virology

**Rocky Mountain Laboratories** 

NIAID/NIH

From: Plowright, Raina

**Sent:** Mon, 16 Dec 2019 02:58:56 +0000

To: Emily Gurley

Cc: Munster, Vincent (NIH/NIAID) [E]

Subject: Re: Congo

I love the epidemic curve — I'll keep that one for my disease ecology class!

On Dec 15, 2019, at 5:58 PM, Emily Gurley < (b) (6) wrote:

Cool photos! Lab capacity is so crucial - just imagine everything that's missed every day. Glad things are improving there. Safe travels.

On Sun, Dec 15, 2019 at 2:41 AM Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote:

Thought you guys might like this, epi curves in a peripheral hospital in Congo listing the amount of chikungunya cases this year (we helped them diagnose a massive outbreak).

Mainly diagnosed on clinical symptoms and absence of malaria. We have established lab capacity in the capital. Now doing hospital site visits

Btw tons of eidolon here

<IMG 6948.JPG>

<IMG 6953.JPG>

From: Munster, Vincent (NIH/NIAID) [E]
Sent: Fri, 13 Dec 2019 17:53:38 +0100

To: (b) (6) Bushmaker, Trenton (NIH/NIAID) [E]

Cc: Kwe Claude, Yinda (NIH/NIAID) [F]; Mandy Todd; Manuel Ruiz Aravena;

Plowright, Raina; Rynda-Apple, Agnieszka

Subject: Re: Shipping list Dec-2019

Sorry to hear, hopefully it will all be solved soon,

## Vincent

(b)(6)From: Alison Peel < (b) (6) < Reply-To: " (b) (6) Date: Thursday, December 12, 2019 at 9:26 PM To: Trenton Bushmaker < (b)(6)Cc: "Kwe Claude, Yinda (NIH/NIAID) [F]" < (b)(6) Mandy Todd (b) (6) Manuel Ruiz Aravena < (b)(6)(b) (6) < (b) (6) "Plowright, Raina" (b) (6) "Rynda-Apple, Agnieszka" < (b) (6)

Subject: Re: Shipping list Dec-2019

Thanks very much Trent, this is really helpful. I think Mandy will follow up with them today (she's been juggling this from the field this week).

We had looked into using SFS pharma previously and they are certainly a lot cheaper. If they are an approved courier for you guys, we'd certainly be interested in trying them. Let me know how you find them with your next shipment

Thanks again,

Ali

On Fri, 13 Dec 2019 at 2:09 am, Bushmaker, Trenton (NIH/NIAID) [E] (b) (6) wrote:

Ali,

I fully agree with assumption. For other shipments we send the brokerage team at World Courier the finial paper work beforehand. They approve the paper work and then, and only then the shipment is sent. I would send them an email to explaining we expect no additional charges for the samples to be reshipped to RML.

I have just looked back into my notes and we have only had one shipment sent back because of customs issues but it was via DHL, not World Courier.

On another note, I am working on a shipment of cells from Australia via SFS pharma. I will let you know how this goes, this might be an option. We can use it as a test shipment.

Sad situation		
-Trent		
From: Alison Peel < (b) (6)  Sent: Wednesday, December 11, 2019 9:40 PM  To: Plowright, Raina (b) (6)  Cc: Mandy Todd (b) (6); Bushr	maker, Trenton (NIH/NIAID)	(F)
(b) (6) Manuel Ruiz Aravena <		) (6) Munster,
	nda-Apple, Agnieszka	(1) (1) (1) (1) (1) (1) (1) (1) (1) (1)
(b) (6) Kwe Claude, Yinda (N	NIH/NIAID) [F] <	(b) (6)
Subject: Re: Shipping list Dec-2019		
Thanks Raina.  Mandy and Manuel are the most meticulous people I kn advice here.	ow, so it seems like we've b	een given poor
Trent - my assumption is that, as part of their service, W shipment and this is part of why they are so expensive. Shere. Is this your understanding, have you previously have	So, I feel like they have some	
Cheers		
Ali		
On Thu, 12 Dec 2019 at 14:26, Plowright, Raina < I'm so sorry to hear this, given how much work you and is. I hope the samples are in good condition. Can you tro Raina		o get it to where it
On Dec 11, 2019, at 9:16 PM, Mandy Todd <	(b) (6) wrote:	
Hi all,		
Unfortunately World Courier have just notified me that USFWS and will be returned to us. Please let me know	보이 하고 있었다. 그리고 하고 하면 바로 하면 하는데 있다면 가게 되어 그리고 있다고 아버지를 하는데 하는데 되었다.	and the state of t
Mandy		
From: Bushmaker, Trenton (NIH/NIAID) [E]	(b) (6)	
Sent: Thursday, December 12, 2019 2:58:15 AM	42.60	47.70
To: Mandy Todd (b) (6);  Manuel Ruiz Aravena < (b) (6)	(b) (6) <	(b) (6)
Cc: Munster, Vincent (NIH/NIAID) [E] <	(b) (6) Plowright, Raina	
(b) (6) Rynda-Apple, Agniesz		(b) (6) Kwe

Claude, Yinda (NIH/NIAID) [F] < (b) (6)

Subject: RE: Shipping list Dec-2019

Thank you Mandy. I will discuss this the brokerage team when they call. Keep me updated if you hear anything.

## -Trent

From: Mandy Todd <	(b)	(6)	
Sent: Wednesday, Decem	ber 11, 2019 9:50 AM		
To: Bushmaker, Trenton (I	NIH/NIAID) [E] <	(b) (6)	(b) (6) Manuel
Ruiz Aravena <	(b) (6)		
Cc: Munster, Vincent (NIH	/NIAID) [E] <	(b) (6) Plowright, Rain	a
<	(b) (6) Rynda-Apple, A	gnieszka <	(b) (6) Kwe
Claude, Yinda (NIH/NIAID)	[F] <	(b) (6)	
Subject: Re: Shinning list [	Dec-2019		

Thanks Trent. World Courier have responded and say that the "Cites was stamped by Australian quarantine prior to export" and that it is not possible to export without customs clearance, but we used three permits the WTA's email referred to only one of the permits so it's possible that one was missed.

Kind regards Mandy Todd

```
(b) (6)
From: Bushmaker, Trenton (NIH/NIAID) [E] <
Sent: Thursday, December 12, 2019 2:26:23 AM
To: Mandy Todd <
                                             (b)(6)
                                                                      (b) (6) a
                                                                                                (b)(6)
                                                   (b) (6)
Manuel Ruiz Aravena <
Cc: Munster, Vincent (NIH/NIAID) [E] <
                                                              (b) (6) Plowright, Raina
                             (b) (6) Rynda-Apple, Agnieszka <
                                                                                          (b) (6) Kwe
Claude, Yinda (NIH/NIAID) [F] <
                                                      (b)(6)
Subject: RE: Shipping list Dec-2019
```

Mandy,

I called World Courier to see if I can do anything on my end. The customs brokerage team should be calling me back very soon to discuss.

However, it is does not look good because of the "export documentation was not endorsed by an Australian Border Force official" what they said also. WC said the package might have to be sent back because of this.

If you have any updates or emails from Australian customs please forward.

### -Trent

Trenton Bushmaker
Biologist, Virus Ecology Unit
Rocky Mountain Laboratories
903 South 4th Street
Hamilton, MT 59840
Phone: (b) (6)

Email: (b) (6)

From: Mandy Todd < (b) (6)

Sent: Tuesday, December 10, 2019 10:39 PM

To: Bushmaker, Trenton (NIH/NIAID) [E] < (b) (6) (b) (6) Manuel Ruiz Aravena < (b) (6)

Cc: Munster, Vincent (NIH/NIAID) [E] < (b) (6) Plowright, Raina < (b) (6) Rynda-Apple, Agnieszka < (b) (6) Kwe Claude, Yinda (NIH/NIAID) [F] < (b) (6)

Subject: Re: Shipping list Dec-2019

. ...

Hi all,

I've just received an email from the Australian department that issues the CITES permits (the WTA), they advise they have received a request from the US Fish and Wildlife Service regarding two problems with the documentation. The first problem is that the specimen export records that accompany the copy of the permit had lines in them which were handwritten. The last couple of times the WTA has issued me permits the specimen export records have been incomplete/not on watermarked paper, etc. I had them re-issued but they still didn't have the lines in them so I wrote them myself, unaware that it was a requirement for them to be printed.

The second problem is that the export documentation was not endorsed by an Australian Border Force official, which leads me to believe that the samples didn't clear Australian customs. I have emailed World Courier seeking clarification on this.

The WTA representative has advised the USFWS that the samples are in fact authorised under the permits, however the final decision will be with the USFWS.

Kind regards,

Mandy Todd

## Senior Technical Officer

Environmental Futures Research Institute

N78\_2.11 Sir Samuel Griffith Building

Griffith University

Nathan, QLD 4111

Extension: (b) (6) Phone: (b) (6)

Mobile: (b)(6)

(b) (6) From: Bushmaker, Trenton (NIH/NIAID) [E] < Sent: Tuesday, 10 December 2019 3:07 AM (b) (6) < (b) (6) Manuel Ruiz Aravena To: (b) (6) Mandy Todd < Cc: Munster, Vincent (NIH/NIAID) [E] < (b) (6) Plowright, Raina (b) (6) Rynda-Apple, Agnieszka < (b) (6) Kwe Claude, Yinda (NIH/NIAID) [F] < Subject: RE: Shipping list Dec-2019

Update as 12/9/2019 at 10am Mountain Time:

Still not cleared USDA, I will call them this afternoon to push a little bit. WC said deliver still should be Tuesday morning. I will update everyone this afternoon.

-Trent

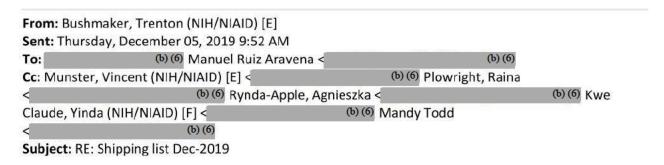
From: Bushmaker, Trenton (NIH/NIAID) [E] Sent: Friday, December 06, 2019 1:43 PM (b) (6) Manuel Ruiz Aravena < (b) (6) Mandy Todd To: (b) (6) (b) (6) Plowright, Raina Cc: Munster, Vincent (NIH/NIAID) [E] < (b) (6) Kwe (b) (6) Rynda-Apple, Agnieszka < (b) (6) Claude, Yinda (NIH/NIAID) [F] <

Subject: RE: Shipping list Dec-2019

Update as of 12/6/2019 at 1:30pm Mountain Time...

We are looking at delivery of the AUS samples early next week. They have not clear customs. I will monitor the situation over the weekend and update if something changes.

-Trent



Update as of 12/5/2019 at 10am Mountain time....

I have attached the email for World Courier this morning. I have giving them a call and the estimated customs clearance & delivery is this Saturday (7<sup>th</sup>). Everything is looking good!

Let me know if you have questions.

-Trent

```
From: Alison Peel <
Sent: Monday, December 02, 2019 5:06 PM
                                                                  (b)(6)
To: Bushmaker, Trenton (NIH/NIAID) [E] <
                                                      (b) (6) Munster, Vincent (NIH/NIAID) [E]
Cc: Manuel Ruiz Aravena <
                        (b) (6) Plowright, Raina <
                                                                            (b) (6) Rynda-Apple,
                                        (b) (6) Kwe Claude, Yinda (NIH/NIAID) [F]
Agnieszka <
                        (b) (6) Mandy Todd <
Subject: Re: Shipping list Dec-2019
```

Hi Trent,

Thanks for that. Yep - I agree that there a high level of mutual respect on both sides, and I think basically it just comes down to so many things going on and it being hard to keep track of everything -, especially across multiple email threads. No blame in any direction, and no need to apologise:) If we can get requests/instructions off emails and into written protocols, then I think it will be smoother sailing from then:)

Cheers

Ali

On Tue, 3 Dec 2019 at 10:00, Bushmaker, Trenton (NIH/NIAID) [E] < (b) (6) wrote:

Kwe and/or me should be around 16<sup>th</sup> if we required the meeting, just (b)(4)Vincent will be in Brazzaville, Congo during this time but might have some availability depending on internet access.

I just want to support Vincent's comments that nothing was directed specifically at your team. Hope you know we think your crew is awesome for getting these samples out in great condition.

My apologies to Manuel and you for any miscommunication that I may have caused. Will be better next shipment.

-Trent

From: Alison Peel < (b) (6)

Sent: Monday, December 02, 2019 4:21 PM

To: Manuel Ruiz Aravena < (b) (6)

Cc: Plowright, Raina < (b) (6) Munster, Vincent (NIH/NIAID) [E]

< (b) (6) Rynda-Apple, Agnieszka < (b) (6) Bushmaker,

Trenton (NIH/NIAID) [E] < (b) (6) Kwe Claude, Yinda (NIH/NIAID) [F]

< (b) (6) Mandy Todd < (b) (6)

Subject: Re: Shipping list Dec-2019

Hi all,

Perhaps we should aim to work through all this on a zoom call and modify the protocol on the spot? Would Monday 16th December (afternoon-US)/Tuesday 17th December (morning-Aus) work for everyone?

Cheers

Ali

On Tue, 3 Dec 2019 at 06:51, Alison Peel < 6) (6) wrote: Hi all,

To expand on Manuel's points, yes, the lists of sample numbers weren't finalised til just before the shipment, but I think all the different sample types were included in that original email, so I think that's the time that we need to be having the discussions about sample types.

Since Manuel will be leaving in a few weeks, it would be great to clarify a stepwise protocol for future shipments - including who at RML should be cc'd about shipments, how far in advance and with what level of detail (accounting for the fact that the actual numbers of samples may vary slightly in the week prior to shipment). We can also add a step into the protocol about confirming whether samples should be sent to RML or elsewhere (if permits allow).

Thanks everyone :)

Cheers

Ali

On Tue, 3 Dec 2019 at 06:12, Manuel Ruiz Aravena < 6) (6) wrote: Hi everyone,

My apologies Trent for the delay sending the final shipping list. I didn't want to send a list of samples that was changing in length and sample positions until last minute for different contingencies including the latest

(b) (4)

In addition, we had the final permits during the last week, therefore numbers could have changed until that moment

(b) (4)

If you are flexible with last minute changes we could share future lists as they are in progress, but this could involve, anyway, that the final list could be available just a few days before the shipment occurs or even as now, when the boxes are leaving Griffith.

So, to move forward, is there any specific timeframe in which receiving the list of samples would make things smoother in your end? (we would add this to our protocols for sample requests and shipment)

About the list format that could have been confusing with the preliminary lists, finally for this shipment I managed to put a few lines of R code to merge data and change formats from ours to the one you use at RML which would make things easier for future shipments.

I personally apologize for any inconveniences, I know how much effort sample management requires, and I hope this didn't make things too complicated in your end.

Please, let me know what needs to be fixed in the list and I would do it today.

Cheers,

M

PS: I'll check the bill # once I get to the office and send it to you.

```
From: Plowright, Raina < (b) (6)

Sent: Tuesday, 3 December 2019 5:35 AM

To: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Cc: Alison Peel < (b) (6) Rynda-Apple, Agnieszka < (b) (6)

Bushmaker, Trenton (NIH/NIAID) [E] < (b) (6) Kwe Claude, Yinda (NIH/NIAID) [F] < (b) (6) Mandy Todd < (b) (6) Manuel Ruiz Aravena < (b) (6)

Subject: Re: Shipping list Dec-2019
```

We would have to get a CDC import permit for slides. We can do this if you need but I don't have a staff member capable of this kind of thing, so I would have to do all of the paperwork. We can discuss by phone.

On Dec 2, 2019, at 12:32 PM, Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote:

Hi Raina,

We just figured out	(b) (4)
	so it would be good to have an idea what to do
with these?	

Thanks for all the help, especially Ali who has been very responsive. Just making sure thate everyone is aware, that there is a huge effort involved in both the front end (Oz) and back-end (RML), so it would be good that end users of samples are aware of this and that last-minute changes in shipping lists or "new" sample types can cause some confusion / sorting out,

Cheers,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: "Plowright, Raina" < (b) (6)

Date: Monday, December 2, 2019 at 12:25 PM

To: Alison Peel < (b) (6)

Cc: " (b) (6) < (b) (6) Trenton Bushmaker

< (b) (6) "Kwe Claude, Yinda (NIH/NIAID) [F]"

< (b) (6) Mandy Todd < (b) (6) Manuel Ruiz

Aravena < (b) (6)

Subject: Re: Shipping list Dec-2019

We have no import permit for (b) (4) (CDC suggested we go through RML) so slides would have to go through RML. Dan Becker was leading this part of the project but hasn't stayed involved since he left and there is no clear leader on the slides to ensure all protocols are adhered to. We really need a single 'sample tsar' to ensure all samples are cared for under the best protocols, but I think we have been understaffed in this respect and so it is messy, but everyone is stepping up and everyone is doing more than their best effort to pull it off (especially Manuel—thanks Manuel!). Thanks team for the enormous effort to get the samples away.

Raina

On Dec 2, 2019, at 12:15 PM, Alison Peel < (b) (6) wrote:

Thanks Vincent for the reminder and clarification on that. Similarly, it's quite a task on our end to get the shipments away, with requests (and last minute requests) from many people, changes to shipment lists

(b) (4) when results come in from Kwe, and many many layers of permits, agreements and approvals across multiple institutions. All good though, we can continue to refine the process.

I had it in my mind that MSU didn't have all the required import permits, but if they are obtained, then that would be much easier.

Raina- who is our best point of contact at MSU re import permits?

**Thanks** 

Ali

On Tue, 3 Dec 2019 at 5:07 am, Munster, Vincent (NIH/NIAID) [E] < 6) (6) wrote: Thanks Ali,

This info most have been "lost" then on this end. Thanks for replying so quickly, it is quite the task with multiple shipments coming on to make sure that everything runs smoothly. Just as a reminder that this is nothing directed specifically at your team, we'll have the same scrutiny with (b) (4)

Just want to make sure, that once they are at RML, they can only be released following RML established procedures. So anything which can be routed around RML to MSU is easier for us (as every inactivation will take-up significant time of the people here).

Cheers,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

From: Alison Peel < (b)(6)(b) (6) < Reply-To: " (b)(6)Date: Monday, December 2, 2019 at 11:59 AM (b) (6) < (b)(6)Cc: Trenton Bushmaker < (b) (6) "Kwe Claude, Yinda (NIH/NIAID) [F]" (b) (6) Mandy Todd < (b) (6) Manuel Ruiz (b) (6) "Plowright, Raina" < Aravena < (b)(6)Subject: Re: Shipping list Dec-2019

Hi all,

Still early here, so I or Manuel can respond more in full later on but I just wanted to say that we emailed details of the samples in this shipment on November 1st and had a discussion with Trent about the slides and the clots at that time. The slides were not sent on dry ice- just a regular box.

We should have sent the final list prior to shipment, but we did send this draft list well in advance and answered any questions posed by Trent. Let us know what else we can do for next time.

Cheers

On Tue, 3 Dec 2019 at 4:48 am, Munster, Vincent (NIH/NIAID) [E] < 6) (6) wrote: Hi Manuel,

You might want to consider sending the slides directly to MSU? That would make it a little bit easier from our end. If Raina can discuss this with their local IRB, if these are not considered infectious than there is no need for a CDC import permit. Also, these will not have to be shipped using a cold-chain. So they could be shipped using a regular package rather than a very expensive dry-ice shipment.

As Trent said, make sure these things are discussed well ahead of time, this would facilitate a better logistics from our end,

cheers

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: Trenton Bushmaker < (b) (6)

Date: Monday, December 2, 2019 at 11:26 AM

To: Manuel Ruiz Aravena < (b) (6) Mandy Todd

< (b) (6) " (b) (6) < (b) (6)

Cc: " (b) (6) "Kwe Claude, Yinda (NIH/NIAID)

[F]" < (b) (6) "Plowright, Raina" < (b) (6)

Subject: RE: Shipping list Dec-2019

## Hello,

Thank you for packing list, however Manuel I will talk with you individually because we need to have a few things to fixed on the packing list. I just want to reiterate that I need this packing list <u>before the samples are shipped</u>. This way we can discuss any discrepancies beforehand. This will delay the processing of samples and the results to you guys.

Most important for now.... will need the House Airway bill# and the Job# if you are still sending it via World Courier. I will need to track the package, we have had issues of them sending packages to different locations and via odd routes of travel.

Let me know if you have questions. Thank you again for sending the samples, can't wait to find something!

-Trent

Trenton Bushmaker
Biologist, Virus Ecology Unit
Rocky Mountain Laboratories
903 South 4th Street
Hamilton, MT 59840
Phone: (b) (6)
Email: (b) (6)

From: Manuel Ruiz Aravena < (b) (6)

Sent: Sunday, December 01, 2019 9:56 PM

To: Bushmaker, Trenton (NIH/NIAID) [E] < (b) (6)

Cc: (b) (6) Munster, Vincent (NIH/NIAID) [E] < (b) (6) Kwe Claude, Yinda (NIH/NIAID) [F] < (b) (6) Plowright, Raina < (b) (6)

Mandy Todd < (b) (6)

Subject: Shipping list Dec-2019

Hi Trent,

Samples are on their way to RML!

I attach the list of samples.

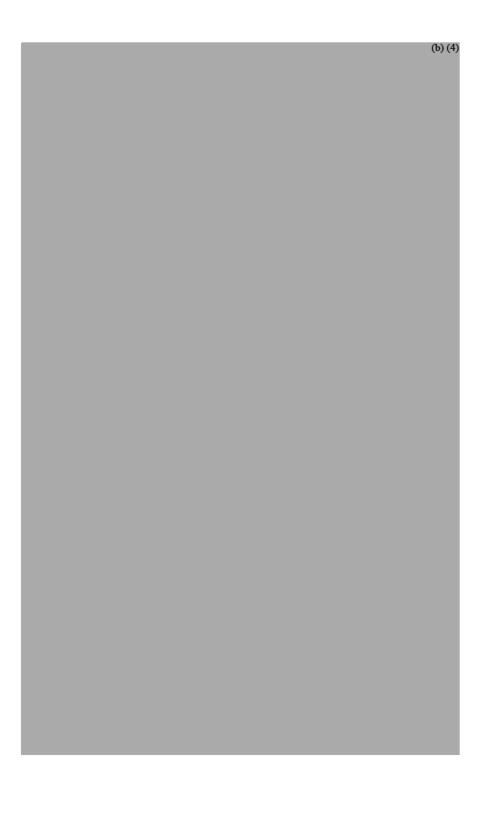
Samples are packed in a way that whole boxes can be transfer to MSU without moving samples among them.

(b) (4) for Vicky's experiments are in Box AUS\_155 (Locations F01 to F04)

Details of content and destinations are below.

Regards, Manuel





From: Munster, Vincent (NIH/NIAID) [E]
Sent: Fri, 13 Dec 2019 17:47:22 +0100

To: Lipkin, Ian W.; Hensley, Lisa (NIH/NIAID) [E]; Anthony, Simon J.; Mishra, Nischay;

Briese, Thomas; Rasmussen, Angela L.; McFadden, Diane C.; Magnus, Kelly

Subject: Re: Pandemic Collective

Great, let me know how we can contribute,

Cheers,

Vincent

On 12/13/19, 1:41 AM, "Lipkin, Ian W." (b) (6) wrote:

We have an opportunity to recompete GIDEoN with an increase in scope. At minimum we will need to add ICMR in India as well as sites in Africa. Others we should include ICAP, a modeling team eager to work in mobile phone/social media based surveillance, and engineers in POC diagnostics. Details to follow.

Ian

From: Letko, Michael (NIH/NIAID) [F]
Sent: Wed, 11 Dec 2019 22:31:24 +0000

To: Plowright, Raina

Cc: Munster, Vincent (NIH/NIAID) [E]; Kevin Olival,; Seifert, Stephanie (NIH/NIAID)

[E]

Subject: Re: Nat rev micr finalization

Sounds good to me!

-michael

--

Michael Letko, Ph.D
Postdoctoral IRTA
Dr. Vincent Munster Laboratory
Virus Ecology Unit, Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH
903S 4th Street
Hamilton MT 59840
(b) (6)

From: "Plowright, Raina" < (b) (6)

Date: Wednesday, December 11, 2019 at 3:12 PM

To: "Letko, Michael (NIH/NIAID) [F]" < (b) (6)

Cc: "Munster, Vincent (NIH/NIAID) [E]" < (b) (6) "Kevin Olival,"

< (b) (6) "Seifert, Stephanie (NIH/NIAID) [E]"

(b) (6)

Subject: Re: Nat rev micr finalization

Great. I can edit it and work on the logical flow when you send the next draft.

On Dec 11, 2019, at 3:09 PM, Letko, Michael (NIH/NIAID) [F] < (b) (6) wrote:

Hi Raina,

Thank you for getting back to us so quickly!

This looks perfect. I will let you know if I have any questions as I incorporate this new material into the revised manuscript.

Thank you, -michael

\_\_

Michael Letko, Ph.D
Postdoctoral IRTA
Dr. Vincent Munster Laboratory
Virus Ecology Unit, Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH
903S 4th Street
Hamilton MT 59840
(b) (6)

From: "Plowright, Rain	a"	(b) (6)	
Date: Wednesday, Dec	ember 11, 2019 at 11:28	AM	
To: "Munster, Vincent	(NIH/NIAID) [E]" <	(b) (6)	
Cc: "Kevin Olival," <	(b)	(6) "Seifert, Stephanie (N	IIH/NIAID) [E]"
<	(b) (6) "Letko, Michael (N	NIH/NIAID) [F]" <	(b) (6)

Subject: Re: Nat rev micr finalization

Hi Mike,

Raina

Here is a rough outline or really a set of notes on viral life-cycles in bats or persistence within bat populations. Can you let me know if this is the kind of info you are looking for? You could either try to incorporate something into the ms and then send back to me for editing (what I've sent is v rough and needs editing), or give me some feedback or more focus and I'll get you a second draft. Best,

On Dec 5, 2019, at 12:56 PM, Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote:

Just a quick reminder to see where we're at with the finalization of the review,

Hope all is going according to plan,

Cheers,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

From: Plowright, Raina

**Sent:** Wed, 11 Dec 2019 18:27:31 +0000 **To:** Munster, Vincent (NIH/NIAID) [E]

Cc: Kevin Olival,; Seifert, Stephanie (NIH/NIAID) [E]; Letko, Michael (NIH/NIAID) [F]

Subject: Re: Nat rev micr finalization

Attachments: Notes on persistence of pathogens in bat hosts and bat populations.docx

# Hi Mike,

Here is a rough outline or really a set of notes on viral life-cycles in bats or persistence within bat populations. Can you let me know if this is the kind of info you are looking for? You could either try to incorporate something into the ms and then send back to me for editing (what I've sent is v rough and needs editing), or give me some feedback or more focus and I'll get you a second draft.

Best, Raina

On Dec 5, 2019, at 12:56 PM, Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote:

Just a quick reminder to see where we're at with the finalization of the review,

Hope all is going according to plan,

Cheers,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

(b) (4), (b) (5), (b) (6)

From: Munster, Vincent (NIH/NIAID) [E]
Sent: Tue, 10 Dec 2019 11:55:23 +0800

To: LaTrielle, Sara

Cc: Raina Plowright; Laing, Eric; Broder, Chris (USU-DoD); Olivier Restif; Andrew

Cunningham; Louise Gibson; Alison Peel; Emily Gurley **Subject:** Re: PREEMPT serology screening

Hi guys,

I'll be in Congo, but Eric and Chris have a pretty good idea of the RML set-up.

I can try to make it, but depending a bit on the connection

Cheers,

Vincent

On Dec 10, 2019, at 00:08, LaTrielle, Sara < (b) (6) wrote:

All:

Please fill out the Doodle poll for this discussion. All dates are for next week. A Zoom link will be sent once a date/time has been established.

https://doodle.com/poll/3q633du96paee6wg

Best,

Sara LaTrielle Program Manager PREEMPT Project Montana State University (b) (6)

From: Raina Plowright < (b) (6)

Sent: Friday, December 6, 2019 1:07 PM
To: Laing, Eric < (b) (6)

Cc: Broder, Christopher < (b) (6) Olivier Restif < (b) (6) Andrew

Cunningham < (b) (6) Louise Gibson < (b) (6) Vincent Munster

< (b) (6) Alison Peel < (b) (6) Emily Gurley < (b) (6)

LaTrielle, Sara < (b) (6)

LaTrielle, Sara < (b) (6)

Subject: Re: PREEMPT serology screening

Hi Eric.

I look forward to talking with you. Sara, cc'd here, can start a doodle poll with the dates you mentioned so we can find a time that works for the majority of the group.

Best, Raina On Dec 6, 2019, at 11:41 AM, Laing, Eric < (b) (6) wrote:

Dear Raina.

Sounds good. My interest in HeV/NiV really started after I read some eco-immunology papers, but have had a challenging time condensing that nebulous. The first project I worked on with Chris was making a fragment antibody (Fab) specific to a bacterial-expressed P. alecto Ig mu heavy chain CD3-CD4 peptide (provided by Linfa and Michele Baker). The aim was to develop an anti-bat IgM thru phage panning to complement all the IgG serology (that was 10 years ago). We could never secure experimentally challenged sera in the time frame where we thought IgM would be circulating, so we were never able to test of the Fab was reactive with a positive control bat IgM. The field has progressed a lot since then with multiple genomes now available and labs such as Vincent's that do have experimental bat challenge models. I'm hopeful that in the next year we will be on track to make that anti-IgM and potentially a slew of viral cytokine/acute phase response/biomarkers that could be useful for integrative host immunity analysis and virus surveillance.

I won't be in Singapore, but Chris is headed there. My schedule over the next weeks is pretty flexible: I'm not available on Monday Dec 9th after 2pm, Tuesday Dec 12-1pm or Thursday Dec 12th after 2:30pm. Pretty open the following week Mon Dec 16th - Thurs 19th, and I'll be challenging to get a hold of from the 23rd - Jan 1st 2020. Let me know what works for everyone and I'll try my best to accommodate a call. We can definitely chat about details for an MTA amendment with Andrew, Louise and Oliver. Generally, we will look at the sample size then project the amount of each protein/beads needed and have a price per protein created for an invoice. That will flow thru our MTA office and the Henry Jackson Foundation (HJF) will execute the invoice, and program income will tie back into our active DTRA Malaysia study.

Kind regards, Eric

Eric D. Laing, Ph.D.
Research Assistant Professor
Department of Microbiology and Immunology
Uniformed Services University
4301 Jones Bridge Road
Bethesda, MD 20814
cell:
(b) (6)
office:
(b) (6)
lab:
(b) (6)

(b) (6)

Hi Eric,

Thanks for your detailed response. I'm very glad to hear that you are interested in collaborating. All of the questions you are asking are of great interest. Some of these (e.g., SIR/SILI models, optimal surveillance approaches) are core to our research and for others we may be able to provide data to help calibrate models of serology relative to virology.

Madagascar serology is not part of PREEMPT; Cara's role in PREEMPT is focused on providing novel sequences for genotype-to-phenotype mapping, however it would be useful to compare serology from Madagascar with data from other sites. I am not familiar with the details of Cara's plans for serology, or her current collaborations (although Ali did get the information in the table directly from Cara), but I am happy to start a separate email chain so that we can follow up on this.

I think Ghana already have an MTA with you — Andrew, Olivier, Louise can add details.

Great to know about the the DTRA BTRP BAA. We will look at this. However, BOHRN sounds like a good bet right now. I have not been able to make any of the meetings due to other commitments but perhaps we can develop some ideas and take them to the POs. Another option is an NSF EEID grant focused on serology (and phylodynamics). We have been discussing a submission (with all on this email chain and also including Barbara Han for machine learning) I think we could develop a strong proposal by the deadline in 11 months.

Ina and Ed have been fantastic collaborators and Ali is working hard to develop plans for serology based out of Ina's lab. Ali has a small grant to fund multi-viral serology but we were not able to fund Australian serology on PREEMPT — although we are working hard to identify potential funding sources.

I think we could have a strong argument for a collaborative project based on the questions you stated, especially as we now have a longitudinal data set of HeV prevalence in individual bats (with known age) with paired prevalence data from under-roost sampling and a suite of covariate data on immunology, nutritional state, energetic state, body condition, co-infections etc. We now have a large repository of Hendra virus positive samples, mostly from under-roost, but enough from individual bats to make inferences about disease dynamics. The strength of our work will be in the amount of ecological/epidemiological/immunological/demographic information collected on each individual bat and and this could inform interpretation of serology.

Can we find a time to talk by Zoom videoconference to outline ideas for collaborative grants? If you are at the Nipah meeting in Singapore, you can also discuss with Vincent and Emily.

В	e	S	t,

Raina

On Dec 5, 2019, at 9:46 AM, Laing, Eric <

(b) (6) wrote:

Dear Raina,

Our research interests into virus and host ecology align with your groups', and I am interested to collaborate with everyone here. Ali helped Ian Mendenhall (Duke-NUS, SIngapore) and our group apply a mixture model for a MFI cutoff in this <u>article</u>. We are currently preparing soluble HN for 2 new *Pteropus*-hosted rubulaviruses for Ed and Ina to pair with the Menangle virus HN we previously made for biosurveillance work currently underway.

We've been developing this multiplex immunoassay with the goal in mind to collaborate with field teams and infectious disease modelers to address some of the gaps in both henipavirus and filovirus ecology (i.e. how does MFI/IgG relate time since exposure, maintenance vs non-maintenance animal hosts, using targeted serological surveillance to inform optimal windows for nucleic acid detection, SIR/SILI epi models). Development of glycoprotein antigens has been supported by DoD NMRC BDRD initially and currently DTRA BTRP. Our primary research is focused on building capacity in Peninsular Malaysia at wildlife/vet/public health gov't and academic institutions to investigate exposure to these viruses at wildlife/livestock/human interfaces thru a BTRP funded project (J. Epstein, PI). We've been validating this assay with control sera we've generated, in collaboration with Vincent and Steph (e.g. rVSV-Filo GP challenged Rousettus) and USAMRIID.

Additionally our footprint in SE Asia and India has included DTRA supported serology work with Supaporn (Chu) at TRC-EID, Bangkok and collaboratively with Ian Mendenhall/Gavin Smith (Duke-NUS, Singapore). A recent manuscript of the DTRA-supported filovirus research and capacity training in South India with Ian Mendenhall.

We're running standardized assay protocols on both BioPlex 200 or MAGPIX (Luminex xMAP-based) platforms now in Bangkok, Kuala Lumpur (3 sites), Bangalore, Phnom Penh, RML and our own lab with the intent to be able to compare MFI data across labs and geographies. Our MAGPIX is field deployable (comes with a pelican carry-case) and facilitates easy in-country testing/training if resources to purchase Luminex xMAP-based system are currently limited.

We have recently used an MTA/invoice mechanism to support our research staff and supplies (e.g. beads, G proteins) to maintain collaborative biosurveillance with groups that have not directly included us as subs and could pursue this in Australia and Ghana. However, those samples sizes are not small and we will need to figure out what we can realistically support from our end given our projected projects for the next 3 years. What we can do with Madagascar is less clear to me.

I kept in touch with Cara a little since the last CSU Bat ID meeting and we ran some samples from Madagascar over the summer that we received from her via Bucknell, but I was informed that she was working with Linfa so there wouldn't be an avenue for collaboration on Luminex serology. I've been making yearly trips to Duke-NUS since 2015 to work with Ian and Gavin and communicate with Linfa and his staff when there. I'm not aware of their development of a Luminex-based G-antigen approach. They've been developing a luciferase immunoprecipitation assay (LIPS) based on peptide antigens, which is not what we do. My last correspondence with Cara was a request for our lab to test the samples she sent us since the LIPS results were not confirming data from her most recent article. I've been kinda wondering if at some point we will be contacted to provide soluble G for that proposal.

We are on board if the work will be considered collaborative. Chris' previous email highlights our hesitation to be viewed solely as a lab source of protein; we like to maintain academic and intellectual creativity, and participate/contribute to US/international student/post-doc training. The DTRA BTRP Thrust Area 6 BAA may be an avenue to develop a collaborative IgG serology focused proposal and develop more experimental serology multiplex assays, but the four countries identified in Ali's PDF are not currently in the BAA portfolio. There might be a way to leverage Madagascar into a regional project in S. Africa, but that really depends on the scope of what Cara, PIs and Linfa have going on with their grant. We are in BORHN and most of the research we are doing hits several BOHRN objectives, collaboration makes sense. BTRP POs (Marty, Emerson, Jarrad) may be able to help steer us into a meaningful collaboration.

Kind regards, Eric

Eric D. Laing, Ph.D.
Research Assistant Professor
Department of Microbiology and Immunology
Uniformed Services University
4301 Jones Bridge Road
Bethesda, MD 20814
cell: (b) (6)
office: (b) (6)
lab: (b) (6)

On Tue, Dec 3, 2019 at 3:36 PM Raina Plowright < (b) (6) wrote: Hi Chris,

During our recent PI meeting, we discussed our approach to serologic analyses across our four field sites (Australia, Bangladesh, Ghana, Madagascar). Alison Peel (cc'd here) took the lead on summarizing the plans across teams. As you can see from the summary table she developed (below), the plans, scope, and funding for serology differ across the four sites.

PREEMPT is centered on henipaviruses but some countries have funding that overlaps with projects focused on other viruses. Ideally, we would like to compare data across sites (including age-specific data) and would include a broad panel of glycoproteins across all sites. We would also like to get your advice on controls and/or mAbs to enable comparison from one machine to another and magnetic vs plastic beads.

Serology is not funded in full across all projects and we identified serology as one of our top priorities for further funding. We understand you have an existing MTA with the institute of Zoology, London, for samples from Ghana and this is funded on PREEMPT; we also understand that Cara Brook has independent funding for serology through LinFa's lab. We are currently trying to find funding for serology for Australia and Bangladesh samples. Once we identify potential funding mechanisms, we would love to hear how we could support your contributions within these applications.

We understand that you have existing arrangements and commitments that you need to fulfill, including from within the group, and our requests must fit into this bandwidth. Please let us know how best to move forward. A videoconference call, including the team leads from each country, would be an excellent start — this would allow us to better understand how we can collaborate with you and your lab and how we can work together on funding. Around 3pm or 4pm EST works across all time zones. Let me know when you have time during that period over the next 3 weeks, or in early January. I've cc'd our program manager, Sara LaTrielle, who can help us coordinate a call.

Raina

 From:
 Munster, Vincent (NIH/NIAID) [E]

 Sent:
 Mon, 9 Dec 2019 16:41:07 +0800

To: Raina Plowright; Emily Gurley; Kwe Claude, Yinda (NIH/NIAID) [F]; Bushmaker,

Trenton (NIH/NIAID) [E]; Ausraful Islam

Subject: Meeting up with team members / RML-ICDDR,B

Attachments: IMG\_6931.JPG





Munster, Vincent (NIH/NIAID) [E] From: Sent: Mon, 9 Dec 2019 15:15:56 +0800

To: (b)(6)

Cc: Raina Plowright Re: Griffith MTA Subject:

We got Emily presenting, so we are well represented.

Btw, if you ever get questions, it would be good to specify that we are NIH so our work is supposed to support human health. Even though we are funded by DARPA there would never be any biological warfare research (nor would DARPA support this), but sometimes it is good to make that distinction,

Cheers, all well here we got Linfa, Chris B and lots of others so good to push our program a bit

From: Alison Peel <	(b) (6)		
Reply-To: "	(b) (6) <		(b) (6)
Date: Monday, December	er 9, 2019 at 11:14 A	М	
To: '	(b) (6) <		(b) (6)
Cc: Raina Plowright <		(b) (6)	
Subject: Po: Griffith MT	۸		

Subject: Re: Griffith IVI A

Hi Vincent,

Regarding being "only used for specific authorised purposes", they just want to know what they're giving approval for. e.g. at an unlikely extreme, that isolates won't be used by DARPA for biological warfare. I think they will consider all reasonable requests we have of them, and yes, they are getting lots of value out of our work, but the federal policy that they are working within states that the use of the samples must be specified.

I hope the meeting in Singapore is going well. Are you presenting?

Cheers

Ali

On Mon, 9 Dec 2019 at 11:47, Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote: I think phenotypic characterization of isolated strains (e.g. the mentioned environmental stability).

However, from my end it is not clear what "are only used for specific authorised purposes", indicates. It would be good to stress to the CVO the huge investments we are doing with regards to work they are clearly not funding. Also in my honest pov, they have a responsibility to facility advancement of science and the development of effective countermeasures, this cannot be done without access to contemporary virus isolates.

Anyway, talked with Raina a bit about all this,		(b) (4)
	Smtg they should clearly welcome.	
Now at Nipah meeting, good to discuss some	of our work.	
Hope that I'll get the DARPA money soon, its	getting at a point now that it is blocking progress,	
Cheers,		
Vincent		
From: Alison Peel < (b)	The second secon	
Reply-To: " (b) (6) <	(b) (6)	
<b>Date:</b> Saturday, December 7, 2019 at 3:40 <b>To:</b> " (b) (6) <	(b) (6)	
To: " (b) (6) <  Cc: Raina Plowright < raina.p	<sup>(b)(6)</sup> "Thruston, Jeffrey (NIH/NIAID) [E]"	
< (b) (6)	musion, Jenrey (Min/MAID) [L]	
Subject: Re: Griffith MTA		
Thanks Vincent.		
Jeff- the full name for AAHL is the CSIRO Aust Regarding the "AAHL will be notified", we ma	an and an and the artification of a state and an anti-fill and a state at the state of the state	
The concerns that the Australian CVO has rela authorised purposes. So Vincent - is there anything else that we would we	1 Allen Ann and an analysis of the second	(b) (4)
Thanks Ali		
On Sat, 7 Dec 2019 at 3:38 am, Munster, Vinc Hi Jeff,	ent (NIH/NIAID) [E] < (b) (6) wrote	e:
Quick question, would it be possible to add the	ne following language to the Griffith MTA?	
		(b) (4)
		(b) (4)
		(b) (4)
	AAHL is the government BSL4 lal	_
Australia.	70 the 10 the government BOL4 la	U 111

Let me know what you thin	ık,
Cheers,	
Vincent	

From:	Munster, Vincent (NIH/NIA	(ID) [E]			
Sent:	<b>nt:</b> Mon, 9 Dec 2019 09:49:22 +0800				
То:	b) (6) Plowright, Raina				
Subject:	Re: Follow-up testing of	(b) (4)			
Btw,					
The		(b) (4) So might be a bit easier than the other			
samples					
Cheers,					
Vincent					
From: Alison Peel <	(b) (6)				
Reply-To: "	(b) (6) <	(b) (6)			
Date: Saturday, Dece	ember 7, 2019 at 4:03 AM				
To: "Plowright, Raina	a" <	(b) (6)			
Cc: Trenton Bushmal	ker <	(b) (6) "Kwe Claude, Yinda (NIH/NIAID) [F]"			
<	(b) (6) Manuel Ruiz Aray	vena < (b) (6)			
"	(b) (6) <	(b) (6)			
Subject: Re: Follow-u	up testing of grey-headed f	lying fox Hendra positives			
Thanks everyone.					
		(b) (4)			
		do the testing on a commercial basis rather than a			
collaborative basis, I th	nink it simplifies things regard	ling co-authorship etc.			
A heads up that there	is just one week left here bef	fore everything starts to really slow down until			
January. Everyone is in	the same situation as us in t	that they try to push things through "by the end of			
		ot be able to get a response from Griffith legal before			
then, and realistically, week, but I just want t		d to wait til January. I can try to push things this			
Thanks					
Δli					

Perfect thanks V, if we get through this step, we can move forward.

On 200 0, 2013, de	9:23 AM, Munster, Vince	ent (NIH/NIAID) [E] <	(b) (6) wrote:
I'll contact Jeff and	CC you guys		
From: "Plowright,	Raina" <	(b) (6)	
Date: Friday, Dece	ember 6, 2019 at 10:19	9 AM	
To: "Kwe Claude,"	Yinda (NIH/NIAID) [F]"	(b) (6)	-
Cc: "	(b) (6) <	(b) (б) "	(b) (6)
<	(b) (6) Manuel Ruiz	Aravena <	(b) (6) Trenton
Bushmaker <	(b)	(6)	
Subject: Re: Follow	w-up testing of	(	b) (4)
I think we should			(b) (4)
	It also ad	ds more people and more comp	lexity.
your lab who could promise this (below etc.	call Jeff and ask how to	n Ali is set to push the CVOs once make the sentence below part of find out it can't be added to the	of the MTA? Ali didn't want to
	O.FO ANA V Clauda V	(AULI /AUAID) [5]	4) (6)
On Dec 6, 2019, at 8	8:58 AM, Kwe Claude, Yi	inda (NIH/NIAID) [F] <	(b) (6) wrote:
Vincent you are right		inda (NIH/NIAID) [F] <	(b) (6) wrote:
		inda (NIH/NIAID) [F] <	(b) (6) wrote:
		inda (NIH/NIAID) [F] <	

From: "Munster, Vincent (NIH/NIAID) [E]" <	(b) (6)
Date: Friday, December 6, 2019 at 4:57 AM  To: " (b) (6) <	(b) (6)
Cc: Raina Plowright <	(b) (6) Manuel Ruiz Aravena
The state of the s	Yinda (NIH/NIAID) [F]"
(b) (6) "Bushmaker, Trent	on (NIH/NIAID) [E]"
(b) (6)	
Subject: Re: Follow-up testing of	(b) (4)
Hi Ali,	
Always up for short reports. I think	(b) (4)
A	(h) (d)
Any sequencing we can do for these samples would r	nake it stronger (b) (4)
_	
Any (b) (4) would be	great to have permission to do at RML but AAHL is
fine too (but be careful not to present this as the mo	-
us getting permission) even though strain sharing bet	있다
expensive and cumbersome.	ween Ante and time is possible, it is extremely
expensive and cambersome.	
Kwe, anything you would like to add?	
So RML;	
(L) (A)	
(b) (4)	
Let me know what you think, I'll ask Steph and Eric or	n the availability of reagents for the serology
	4)/4)
Trent: can you	(b) (4)
Chaors	
Cheers,	
Vincent	
Vincent	
On Dec 6, 2019, at 00:39, Alison Peel <	(b) (6) wrote:

Hi Vincent,
(b) (4)
Regardless, I think they are worth writing up in a short note/paper.
(b) (4)
Below are the details of the individuals and some of the remaining samples that are available <image.png></image.png>
(b) (4)
I could submit to Biosecurity Queensland (the lab is literally across the road from the Griffith campus) - they could do the first two steps. If we wanted  (b) (4)
Note that we'll still keep pushing for virus isolation permission at RML, but I think it would still be good to do some of this work in Australia, regardless.
Before proceeding, I wanted to get your thoughts on what is most interesting and most valuable for the downstream analyses.
Cheers
Ali

 From:
 Munster, Vincent (NIH/NIAID) [E]

 Sent:
 Mon, 9 Dec 2019 09:29:59 +0800

To: (b) (6) Plowright, Raina

Subject: Re: Follow-up testing of grey-headed flying fox Hendra positives

Hi Ali,

Given that the actual samples has not been tested yet (b) (4)

If you like to test them in Oz, I don't really have a problem with that (other than that it likely be a little slower), given that research always moves slower than expected (and we are not getting scooped on this one) I think the timeline is realistic,

Cheers,

Vincent

From: Alison Peel < (b)(6)(b) (6) Reply-To: " (b) (6) < Date: Saturday, December 7, 2019 at 4:03 AM (b)(6)To: "Plowright, Raina" < (b) (6) "Kwe Claude, Yinda (NIH/NIAID) [F]" Cc: Trenton Bushmaker < < (b) (6) Manuel Ruiz Aravena < (b) (6) (b)(6)(b) (4) Subject: Re: Follow-up testing of

Thanks everyone.

(b) (4)

know, and I could explore testing them here. If we do the testing on a commercial basis rather than a collaborative basis, I think it simplifies things regarding co-authorship etc.

A heads up that there is just one week left here before everything starts to really slow down until January. Everyone is in the same situation as us in that they try to push things through "by the end of the year" - overloading service requests. We may not be able to get a response from Griffith legal before then, and realistically, talking to the CVOs may need to wait til January. I can try to push things this week, but I just want to set expectations

Thanks

Ali

On Sat, 7 Dec 2019 at 2:31 am, Plowright, Raina (b) (6) wrote: Perfect thanks V, if we get through this step, we can move forward. On Dec 6, 2019, at 9:23 AM, Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote: I'll contact Jeff and CC you guys (b) (6) From: "Plowright, Raina" < Date: Friday, December 6, 2019 at 10:19 AM To: "Kwe Claude, Yinda (NIH/NIAID) [F]" < (b) (6) (b) (6) < Cc: ' (b) (6) " (b) (6) (b) (6) Trenton <al (b) (6) Manuel Ruiz Aravena < (b) (6) Bushmaker < (b) (4) Subject: Re: Follow-up testing of I think we should try to isolate at RML. (b) (4) It also adds more people and more complexity. Ali, did you get in touch with Jeff yesterday? If someone from RML can help, the next step in the CVO process is finding out how to incorporate the following (pasted below) into the MTA, then Ali is set to push the CVOs once again. Vincent, anyone in your lab who could call Jeff and ask how to make the sentence below part of the MTA? Ali didn't want to promise this (below) to the CVO's and then find out it can't be added to the MTA or it is complicated etc. (b) (4) (b) (6) wrote: On Dec 6, 2019, at 8:58 AM, Kwe Claude, Yinda (NIH/NIAID) [F] < Vincent you are right! We can (b)(4)(b) (4) Kwe

From: "Munster, Vince				(b) (6)	
Date: Friday, December To: "	er 6, 2019 at	4:57 AM	(b) (6)		
Cc: Raina Plowright <	,		(b) (6) Manuel Rui	iz Aravena	
<	(b) (6)	"Kwe Claude	, Yinda (NIH/NIAID	) [F]"	
<		hmaker, Trer	nton (NIH/NIAID) [I	E]"	
<	(b) (6)			43.70	
Subject: Re: Follow-up	testing of			(b) (4)	
Hi Ali,					
Always up for short repo	rts. I think				(b) (4)
Any sequencing we can	do for these s	amples would	make it stronger		(b) (4)
					(b) (4)
Kwe, anything you would	d like to add?				
So RML;					
	(b) (4)				
Let me know what you t	hink, I'll ask St	teph and Eric	on the availability of	reagents for the se	erology
Trent: can you				(b) (4)	
Cheers,					
Vincent					

On Dec 6, 2019, at 00:39, Alison Peel < (b) (6) wrote:	
Hi Vincent,	
	(b) (4 <sub>/</sub>
Regardless, I think they are worth writing up in a short note/paper.	
	(b) (4)
Investigations could include any of the following:	(b) (4)
I could submit to Biosecurity Queensland (the lab is literally across the they could do the first two steps. If we wanted	road from the Griffith campus) - (b) (4)
Note that we'll still keep pushing for virus isolation permission at RML, to do some of this work in Australia, regardless.	but I think it would still be good
Before proceeding, I wanted to get your thoughts on what is most inte downstream analyses.	resting and most valuable for the
Cheers	

Ali

From: Munster, Vincent (NIH/NIAID) [E]
Sent: Fri, 6 Dec 2019 05:00:39 -0700

**To:** Schountz, Tony; Eric Laing; Broder, Chris (USU-DoD); Christine Carrington;

Janine Seetahal

Subject: Fwd: MS #JID-67840R1, Serological evidence for Henipa-like and Filo-like viruses

in Trinidad bats

Hi guys,

Just to let you know the paper was accepted.

Cheers,

Vincent

Begin forwarded message:

From: The Journal of Infectious Diseases <em@editorialmanager.com>

Date: December 3, 2019 at 10:53:08 MST

To: "Munster, Vincent (NIH/NIAID) [E]" < (b) (6)

Subject: Re: MS #JID-67840R1, Serological evidence for Henipa-like and Filo-like viruses

in Trinidad bats

**Reply-To:** The Journal of Infectious Diseases < jid@jidoffice.org>

CC: mshirsch@partners.org

Dear Dr. Munster,

We are pleased to inform you that your revised manuscript has been accepted for publication in a supplement to The Journal of Infectious Diseases.

In order to publish your article, our publisher, Oxford University Press (OUP), requires that you complete a license agreement online. A link to the online licensing system, and instructions on how to select and complete a license, will be provided to you by the Production Editor at Oxford University Press after your manuscript has been sent to the publisher for production.

You will receive an e-mail from OUP when your proofs are ready to be downloaded from the Internet. On return of your proofs to OUP, your paper will be scheduled for publication.

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and will have open access available upon Advance Access online publication.

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Sincerely,

Martin Hirsch, MD Editor

The Journal of Infectious Diseases 65 Landsdowne Street #412 Cambridge, MA 02139 Phone: 617-367-1848

E-mail: jid@jidoffice.org

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL:

https://www.editorialmanager.com/jid/login.asp?a=r). Please contact the publication office if you have any questions.

From: Munster, Vincent (NIH/NIAID) [E]
Sent: Thu, 5 Dec 2019 13:21:38 -0700
To: Lon Kendall; Schountz, Tony

Cc: Seifert, Stephanie (NIH/NIAID) [E]; Clifton, Dawn (NIH/NIAID) [E]; Danielle Adney

Subject: Shipment of bats from CSU to RML

Hi Lon,

Hope all is well at CSU, do you have an idea how to ship bats (per experiment) from CSU to RML?

Also, Dr. Danielle Adney (currently a vet student), would be interested in obtaining some baseline parameters of these bats, while at CSU. Let me know it this is smtg you would be able to facilitate.

It was a long haul, but we seem to have made it work (don't know about the hurricane season though)

Cheers,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: "Cisar, Alphie (NIH/OD/ORS) [E]" < (b) (6)

Date: Wednesday, November 27, 2019 at 5:13 AM

To: "Clifton, Dawn (NIH/NIAID) [E]" < (b) (6) "LaCasse, Rachel (NIH/NIAID) [E]" < (b) (6) " (b) (6) Cc: "Elkins, Randy (NIH/NIAID) [E]" < (b) (6) Heinrich Feldmann < (b) (6)

Subject: RE: zoo bats, Increase in numbers?

The cost of crates, care and transport of the Bats from Zoo Miami to CSU is \$17,525.00

They are now scheduled for arrival into CSU on 12/11, shipment was delayed a week due to request from the Zoo.

Let me know if any questions.

Alf

Alphie Cisar, LATG NHP & Large Animal Procurement Specialist and Resource Manager DVR, ORS

NIH Animal Center

Ph: (b) (6)

Fax 301-480-0644

From: Clifton, Dawn (NIH/NIAID) [E] < (b) (6)

Sent: Wednesday, November 13, 2019 10:18 AM

To: Cisar, Alphie (NIH/OD/ORS) [E] < (b) (6) LaCasse, Rachel (NIH/NIAID) [E] < (b) (6)

Cc: Elkins, Randy (NIH/NIAID) [E] < (b) (6)

Cc: Elkins, Randy (NIH/NIAID) [E] < (b) (6)

Subject: RE: zoo bats, Increase in numbers?

Thank you for the update Alphie. I will check with CSU after my morning meeting and get back to you.

As for the CAN for shipping costs, please use CAN 8041037. Could you please give us the amount when it has been decided? For our planning purposes.

Thank you so much Alf!

## Dawn

From: Cisar, Alphie (NIH/OD/ORS) [E] < (b) (6)

Sent: Wednesday, November 13, 2019 5:16 AM

To: LaCasse, Rachel (NIH/NIAID) [E] < (b) (6) Clifton, Dawn (NIH/NIAID) [E] < (b) (6) Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Cc: Elkins, Randy (NIH/NIAID) [E] (b) (6)

Subject: FW: zoo bats, Increase in numbers?

Rachel, As per our discussion CSU has confirmed they can accept all 370-400 bats. Dawn can you please confirm you have everything in place with CSU for them to receive the Bats the first week of December?

I'll also need a CAN number to charge the shipping to, cost to be confirm as I need to have transporter adjust pricing based on a single delivery to CSU now.

Please advise so I can continue moving forward with arranging transport. Alf

Alphie Cisar, LATG NHP & Large Animal Procurement Specialist and Resource Manager DVR, ORS

NIH Animal Center

Ph

(b) (6)

Fax 301-480-0644

From: Kendall,Lon < (b) (6)
Sent: Tuesday, November 12, 2019 5:30 PM

To: Cisar, Alphie (NIH/OD/ORS) [E] < (b) (6) Subject: RE: zoo bats, Increase in numbers? Yes Lon V. Kendall, DVM, PhD, DACLAM Director, Laboratory Animal Resources and Attending Veterinarian, Colorado State University 2007 Painter Center Colorado State University Fort Collins, CO 80523 Voice: (b) (6) Cell: (b) (6) Fax: 970-491-2496 (b)(6)From: Cisar, Alphie (NIH/OD/ORS) [E] < (b)(6)Sent: Tuesday, November 12, 2019 2:13 PM To: Kendall,Lon < Subject: RE: zoo bats, Increase in numbers? RML just asked if you could accept all 370-400 bats? Their space is tied up for about 4 months. Please advise, Alf Alphie Cisar, LATG 🔊 NHP & Large Animal Procurement Specialist and Resource Manager DVR, ORS **NIH Animal Center** Ph (b)(6)Fax 301-480-0644 (b)(6)From: Kendall,Lon < Sent: Friday, November 8, 2019 11:46 AM To: Cisar, Alphie (NIH/OD/ORS) [E] < (b)(6)Subject: Re: zoo bats 14 days should be good. I don't think we'll need any tests. Sent from my Verizon, Samsung Galaxy smartphone ----- Original message -----(b) (6) From: "Cisar, Alphie (NIH/OD/ORS) [E]" < Date: 11/8/19 8:40 AM (GMT-07:00)

To: "Kendall,Lon" < (b) (6)

Subject: RE: zoo bats

How long will you need after receiving the health certificate to get your permit in place. Zoo would like to issue HC with 14days prior to shipment if possible.

Will that give you enough time?

Do you request any preshipment testing for the bats?

Regarding Carollia Bats, they said that would be handled as a separate request and they will reach out to you as they may only have females available.

Please advise.

Alf

Alphie Cisar, LATG 🔊

NHP & Large Animal Procurement Specialist and Resource Manager

DVR, ORS

NIH Animal Center

Ph: (b) (6)

Fax 301-480-0644

From: Kendall,Lon < (b) (6)

Sent: Tuesday, November 5, 2019 9:26 AM

To: Cisar, Alphie (NIH/OD/ORS) [E] < (b) (6)

Subject: zoo bats

Alf.

Can we also get 30-40 Carollia bats?

Lon

Lon V. Kendall, DVM, PhD, DACLAM

Director, Laboratory Animal Resources and

Attending Veterinarian, Colorado State University

2007 Painter Center

Colorado State University

Fort Collins, CO 80523

Voice: (b) (6) Cell: (b) (6)

Fax: 970-491-2496

(b) (6)

From: Munster, Vincent (NIH/NIAID) [E]
Sent: Thu, 5 Dec 2019 13:18:15 -0700

To: Kwe Claude, Yinda (NIH/NIAID) [F]; Bushmaker, Trenton (NIH/NIAID) [E]

Cc: Plowright, Raina; LaTrielle, Sara

Subject: Re: Nov activities: BIG wins/results to report to DARPA?

Kwe can you get some lines of big wins in for Sara and Raina to pick from:

e.g.

2<sup>nd</sup> shipment of Bangladesh samples in and screening on its way, XX screened, XX nipah positive XX new paramyxoviruses from Bangladesh
2<sup>nd</sup> shipment of Oz samples in transit (or was it third)
New tentative paramyxoviruses from Jordan

ACURO approved for bat experiment

Just make a list, which Raina can use to fill the report sheets. Remember it will be crucial to report big wins and progress to maintain DARPA funding.

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: "LaTrielle, Sara" <	(b) (6)	
Reply-To: "	(b) (6) <	(b) (6)
Date: Thursday, December !	5, 2019 at 1:10 PM	
To: '	(b) (6) <	(b) (6)
Cc: "Plowright, Raina" <	(b) (6)	)
Subject: Nov activities: BIG	wins/results to report to DA	RPA?

All,

With reduced internal reporting starting this month, it is very important Raina and I receive any BIG results/updates you and your team may have accomplished in November. An informal bullet-pointed update/slide works for us- however, we can best present your results to DARPA. They are only allowing us to reduce our reporting demands if we can show we will share results with them as soon as we have them.

As usual, please make sure to fill out the google reporting doc with WG based task updates and any publications/presentations you had during November.

Thanks, Sara/Raina From: Munster, Vincent (NIH/NIAID) [E] Sent: Thu, 5 Dec 2019 09:56:42 -0700

To: Hector Aguilar-Carreno; Plowright, Raina; LaTrielle, Sara

Cc: Jamie Lloyd-Smith

Subject: Re: Next PI review meeting

July 13-14 would probably be a bit more problematic given the summer season, so June dates preferred

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology **Rocky Mountain Laboratories** NIAID/NIH

rom: Hector Aguilar-Carreno <		(b) (6)	(b) (6)	
Date: Thursday, Decem	ber 5, 2019 at	9:17 AM		
To: "Plowright, Raina" <	: "Plowright, Raina" <		"LaTrielle, Sara"	
<	(b) (6)			
Cc: Jamie Lloyd-Smith <		(b) (6) "	(b) (6)	
<	(b) (6)			
Subject: Re: Nevt Pl rev	iew meeting			

Subject: Re: Next PI review meeting

That would be great. June 29-30 also work for me. Any of the 3 dates as of now.

Hector

Hector Aguilar-Carreno

Associate Professor

Microbiology and Immunology

College of Veterinary Medicine

Cornell University

(b)(6)Office:

(b) (6) From: Plowright, Raina < Sent: Thursday, December 5, 2019 11:13 AM To: LaTrielle, Sara < (b) (6) Jamie Lloyd-Smith < Cc: Hector Aguilar-Carreno < (b)(6)(b) (6) < (b)(6)Subject: Re: Next PI review meeting

and June 29th-30th.

On Dec 5, 2019, at 8:59 AM, LaTrielle, Sara < (b) (6) wrote:

G-P team-

In looking forward to the DARPA mtg in Bozeman (likely in July 2020), Raina and I thought it would be great if the three of you could come to the meeting- and present your work to DARPA and the other 5 PREEMPT teams.

Do any of the dates work better for each of you, is this possible? July 13-14

July 1-2

Best,

Sara/Raina

From: Barbara Han < (b) (6)
Sent: Thursday, December 5, 2019 8:51 AM

To: Plowright, Raina (b) (6) LaTrielle, Sara < (b) (6)

Subject: Re: Next PI review meeting

This also works for me

On Thu, Dec 5, 2019 at 10:50 AM Plowright, Raina < (b) (6) wrote: another date to get feedback on — July 13-14th

Begin forwarded message:

From: (b)(6)Subject: RE: Next PI review meeting Date: December 5, 2019 at 7:11:00 AM MST (b) (6) 1 To: (b)(6)(b) (6) Cc: " (b) (6) < (b) (6) (b) (6) ' (b) (6) "Jean-Pierre LOMBART" (b) (6) Ariel Weinberger < (b) (6) <sup>1</sup> (b) (6) Luke Alphey < (b) (6) "Peter A Barry" < "Nuismer, Scott ( (b) (6) (b) (6) <

Good Morning PREEMPT teams,

When assessing your teams availability, let us know if July 13-14th would work as well.

Thanks,

(b) (6)

## DARPA/BTO

Original Me	ssage			
From:	(b) (6)			
Sent: Wednesd	ay, December 4, 2019 3:58 F	PM		
To:	(b) (6)		(b) (	(6)
<	(b) (6)	(	b) (6)	
<	(b) (6)			
Cc:	(b) (6)		(b) (6)	
	(b) (6) Jean-Pierre LOMBA	RT		
<	(b) (6) Ariel Wei	nberger		
<	(b) (6)		(b) (6) Luke A	lphey
<	(b) (6) Peter A Barr	y <	(b) (6)	Nuismer,
Scott (	(b) (6) <	(b) (6)		A CONTRACT A CONTRACT OF CONTRACT OF CO
Subject: Next P	I review meeting			

Hi all,

July 9-10 doesn't work for one of the PREEMPT teams.

Please respond to the DARPA team with input for the following dates...

June 29 - 30th July 1 - 2nd

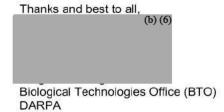
Thanks, (b) (6) DARPA/BTO

----Original Message----(b) (6) From: Sent: Friday, November 22, 2019 2:47 PM (b) (6) (b) (6) (b) (6) Jean-Pierre LOMBART (b) (6) Ariel Weinberger (b) (6) (b) (6) Luke Alphey (b) (6) Peter A Barry < (b) (6) Nuismer, Scott ( (b) (6) < (b)(6)(b) (6) (b) (6) Cc: (b) (6) Subject: next PI review meeting

Hi all,

Importance: High

I am currently looking at July 9-10, 2020 for a 2 day PREEMPT PI Review Meeting to be held at MSU in Bozeman. I am asking for your input, yet we don't have a lot of flexibility, so please reply (either way, and to my team only) to this email ASAP and let me know if for some reason these dates are not possible. ;-)



Office: (b) (6)

Work mobile: (b) (6)

Personal mobile: (b) (6)

(b) (6)

--

Dr. Barbara A. Han
Disease Ecologist
Cary Institute of Ecosystem Studies
Tel: (b) (6) ext. (b) (6)

From: Plowright, Raina

**Sent:** Wed, 4 Dec 2019 23:34:59 +0000 **To:** Munster, Vincent (NIH/NIAID) [E]

Subject: Re: SamplesOz

talk then

On Dec 4, 2019, at 1:00 PM, Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote:

Should work

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

From: "Plowright, Raina" < (b) (6)

Date: Tuesday, December 3, 2019 at 2:04 PM

To: (b) (6)

Subject: Re: SamplesOz

Does 2pm work?

On Dec 3, 2019, at 9:48 AM, Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote:

Thursday?

Good luck with the final stretches

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

From: "Plowright, Raina" < (b) (6)

Date: Tuesday, December 3, 2019 at 9:32 AM

To: " (b) (6) < (b) (6)

Subject: Re: SamplesOz

Can we talk later today or tomorrow... last day teaching today - yay.

On Dec 3, 2019, at 7:55 AM, Munster, Vincent (NIH/NIAID) [E] <

(b) (6) wrote:

Hi Raina,

Do we ever got to an conclusion about the sampling strategy in Oz? Seems to me that putting more emphasis on sampling individuals over roosts would be one way to get better fine-grained data and would also control the amount of samples a bit more.

Let me know what you are thinking,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH From: Plowright, Raina

**Sent:** Tue, 3 Dec 2019 15:36:11 +0000

To: LaTrielle, Sara

Cc: (b) (6) Cara Brook; Colin Parrish; Emily Gurley; Hamish

McCallum; Hector Aguilar-Carreno; Barbara Han; (b) (6) (6) Nita

Bharti; Olivier Restif; Peggy Eby; Peter Hudson; Schountz, Tony; Munster, Vincent (NIH/NIAID) [E];

(b) (6) McFadzen, Mary

Subject: Re: PREEMPT PI meeting (zoom and agenda links)

Attachments: PREEMPT PI mtg Dec 2019.pdf

## Hi Everyone,

Here is the PowerPoint I showed yesterday. Let us know if you have any more ideas! Meanwhile, reach out to Ali and myself before sharing results in presentations. We are happy to create aggregated/smoothed plots for presentations that show general patterns without giving away too much of the story.

The data on diet/immune status/energetic status/nutritional status/movement will start coming in over the next couple of months — exciting!!!

Raina

On Nov 26, 2019, at 4:07 PM, LaTrielle, Sara (b) (6) wrote:

All:

PREEMPT PI meeting agenda and Zoom links below, WHEN: first Monday of every month, 2-3 pm (MST).

Agenda LINK: Agenda

Zoom link: Join Zoom Meeting https://zoom.us/j 6) (6)

Meeting ID: (b) (6)

One tap mobile

+17207072699, (b) (6) US (Denver) +16465588656, (b) (6) US (New York)

Dial by your location

+1 720 707 2699 US (Denver)

+1 646 558 8656 US (New York)

Meeting ID: (b) (6)

Find your local number: https://zoom.us/u/adzPR7PsUq

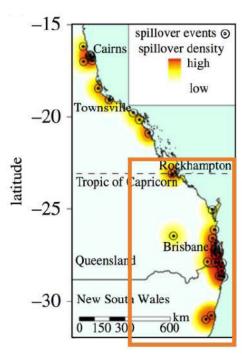
## PREEMPT PI meeting

Dec 2<sup>nd</sup> 2019

CONFIDENTIAL — DO NOT FORWARD

# What insights have we gained from the Australian field data?

### Hendra virus sampling framework

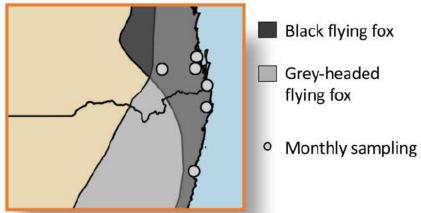


#### Under-roost:

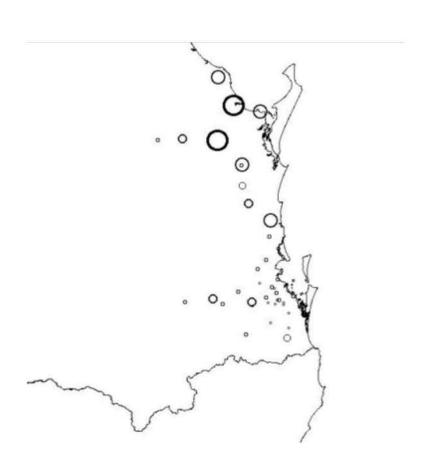
- Sampling 5 continuously occupied roosts monthly
- Sampling one southern roost sporadically (work done by volunteers)

#### Catching:

Sampling 2 continuously occupied roosts every 2-3 months



### Hendra virus sampling framework



- 2 nomadic roosts biannually (catching and under-rrost)
- Spillover response

# Hendra virus sampling framework Summary:

- Monthly under-roost 5 resident camps
- Every 2-3 months catching at 2 resident camps
- Winter & summer catching & under-roost samples in 2 nomadic camps

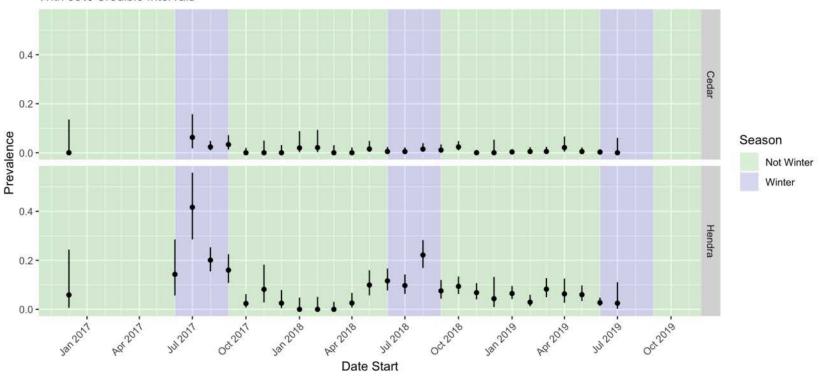
### Overall Samples

- number urine samples tested: 5091
  - 818 from catching
  - 4273 from under-roost
- number of these HeV +: 393
  - 38 from catching
  - 355 from under-roost
- From 38 HeV + from catching:
  - BFF: 36
  - GHFF: 2
- HeV + with Ct values 30 and lower: 53

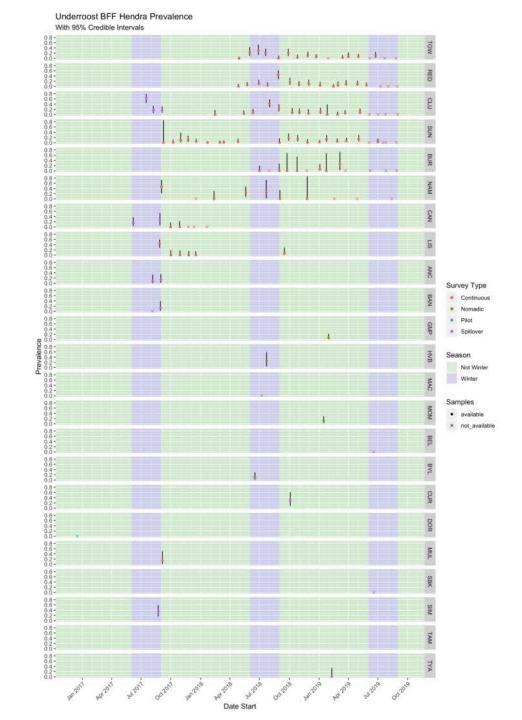
Focus on results from individual black flying foxes & under-roost samples from sheets placed under BFF or both species

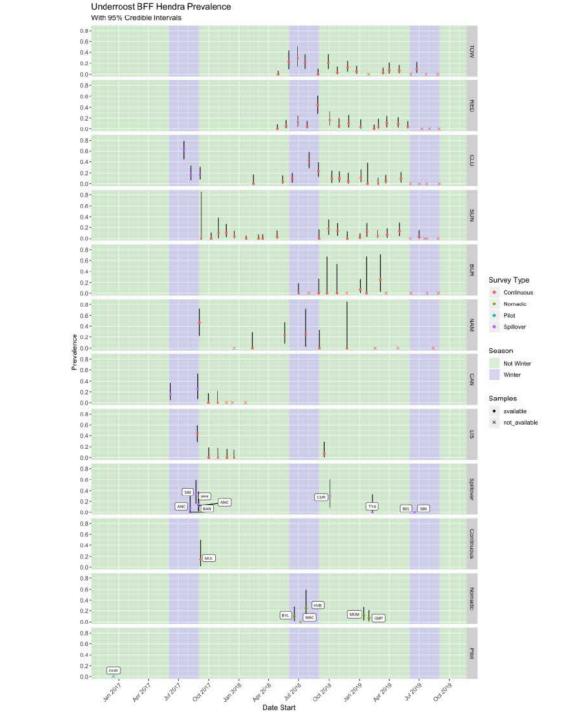
# Aggregated data

Underroost Prevalence By Month Faceted By Virus With 95% Credible Intervals

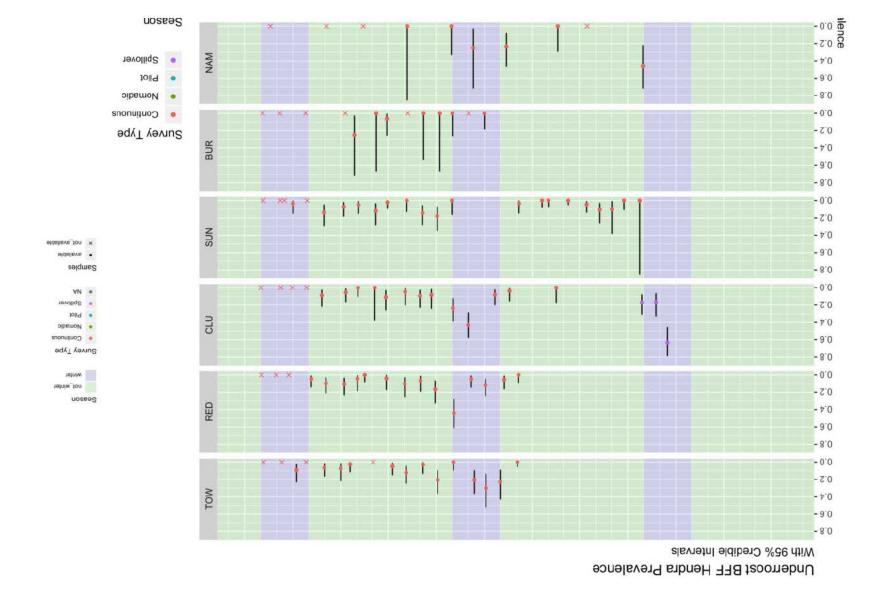


### Overall

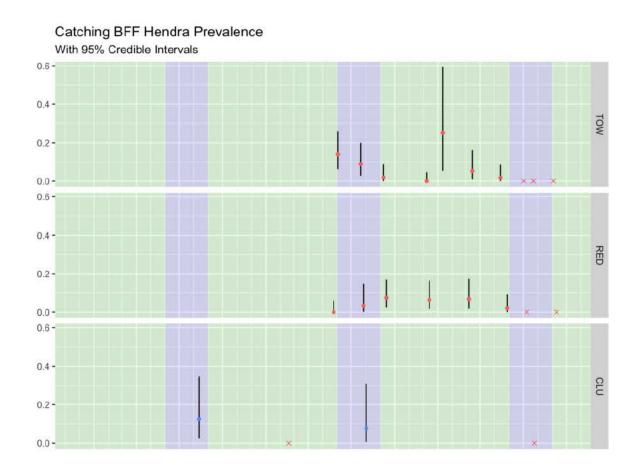




### Under-roost surveillance sites

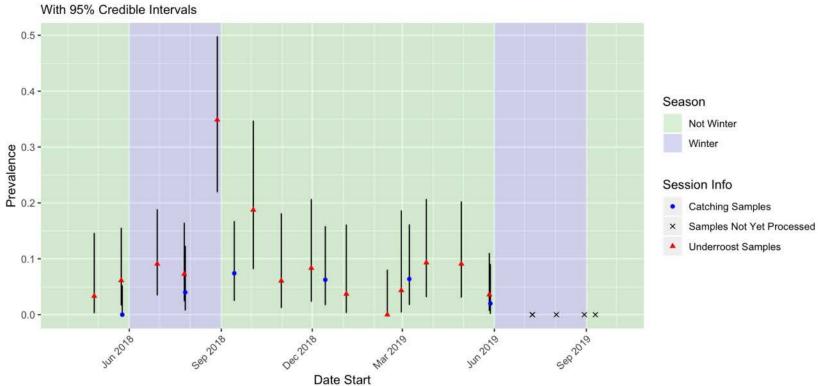


# Catching sites

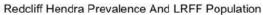


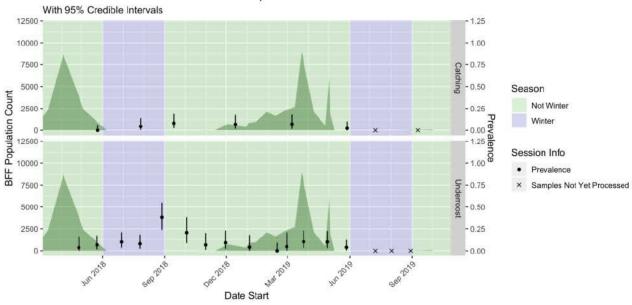


#### Redcliff Hendra Prevalence

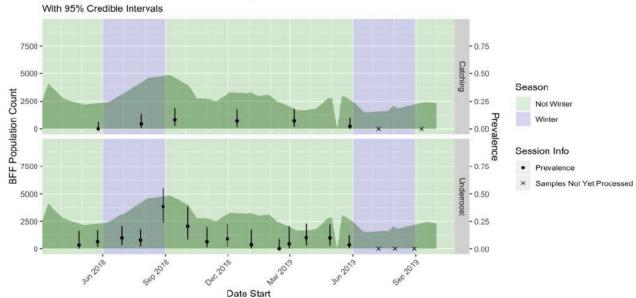


#### Other species



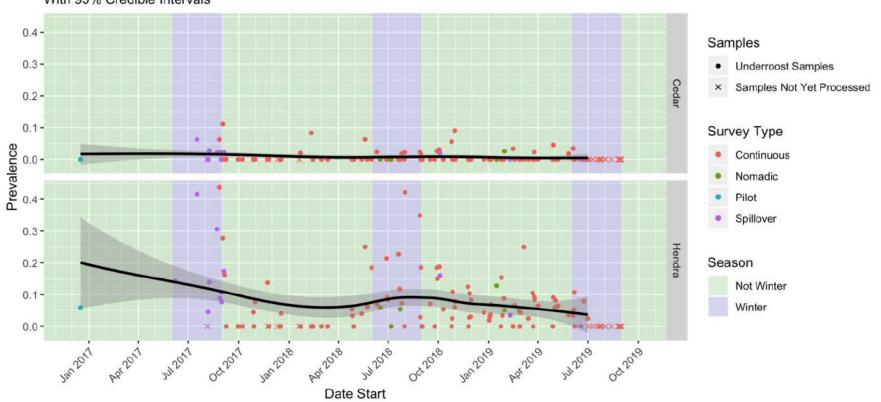


#### Redcliff Hendra Prevalence And BFF Population

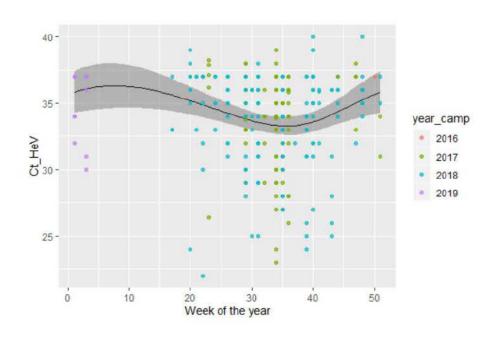


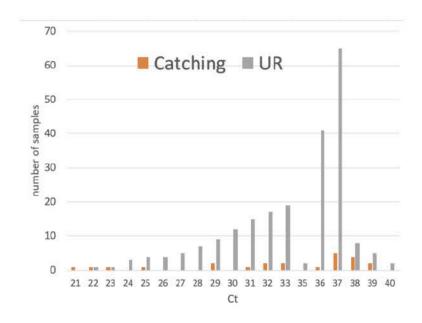
### Cedar versus Hendra

Session Prevalence Across Time Facetted By Virus Type With 95% Credible Intervals

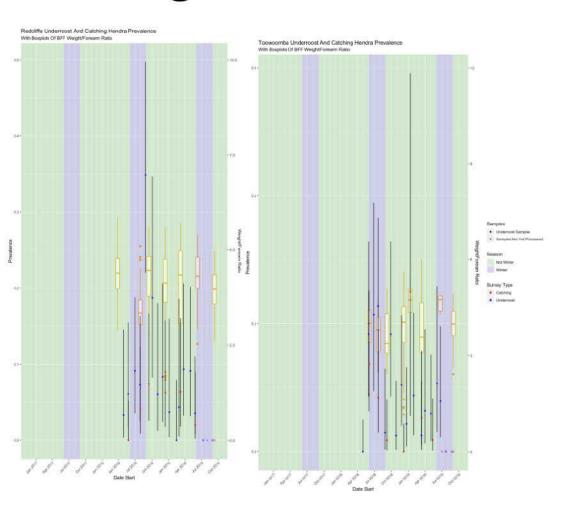


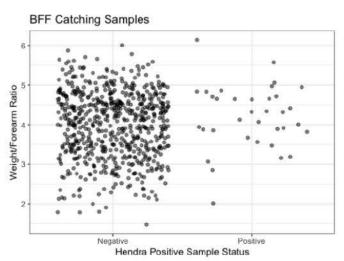
### Ct values over time



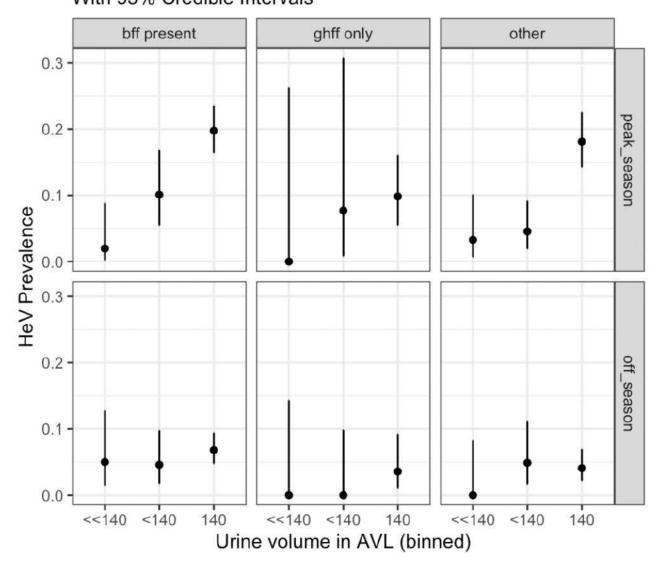


# Weight/Forearm ratios

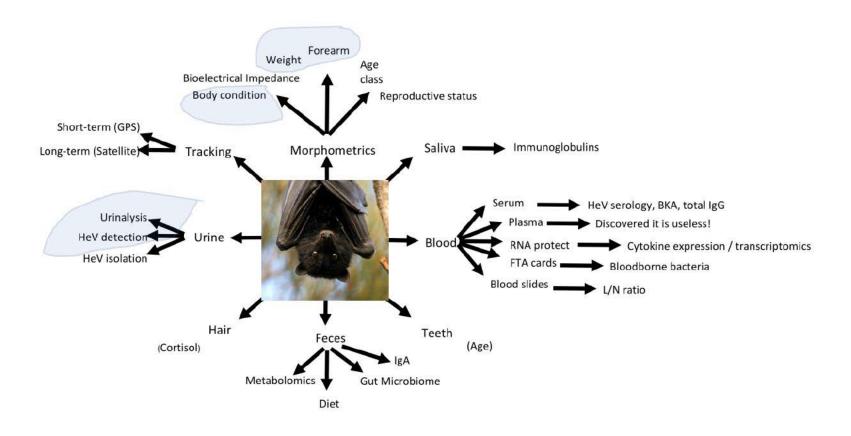




## UR HeV prevalence by volume in AVL With 95% Credible Intervals



### Covariate data to come:



From: Plowright, Raina

**Sent:** Mon, 2 Dec 2019 22:30:12 +0000 **To:** Munster, Vincent (NIH/NIAID) [E]

Cc: (b) (6) Hector Aguilar-Carreno; Emily Gurley; Jamie Lloyd-

Smith; Kwe Claude, Yinda (NIH/NIAID) [F]

Subject: Re: Kwe's first PREEMPT paper

Hey Ali this would be a perfect segue back into the conversation about viral isolation with the CVO. Also a chance to explain to the CVO that isolation is difficult be of low pathogen load in bat samples (cf horse samples)!

On Dec 2, 2019, at 3:26 PM, Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote:

Hi Ali,

Yes it would be directly sharable with the government labs, and would be a cost-effective way to do Hendra full genome sequencing on horse samples. Most details are in the paper, but we can have Kwe share a detailed protocol if labs are interested. The method would be amendable to other NSG platforms as well.

The only caveat (as with most NSG) is the relatively high copynumber you still need (as this is full long read) rather than traditional NSG which sequences a lot of very small reads

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: Alison Peel < (b) (6)

Reply-To: " (b) (6) < (b) (6)

Date: Monday, December 2, 2019 at 3:15 PM

To: Hector Aguilar-Carreno < (b) (6)

Cc: "Plowright, Raina" < (b) (6) " (b) (6)

< (b) (6) Emily Gurley < (b) (6) Jamie Lloyd-Smith

< (b) (6) "Kwe Claude, Yinda (NIH/NIAID) [F]" < (b) (6)

Subject: Re: Kwe's first PREEMPT paper

Congratulations Kwe!! Nice work!

I haven't read it yet (and may not be able to fully understand it!) but Vincent, is this something that would be good to share directly with the Australian govt labs that we were in contact with when getting

approvals to ship samples to RML? i.e. is it something of use to govt labs in Australia? If so, is there a sentence or two that you could suggest for me to use when I share it?

Thanks Ali

On Tue, 3 Dec 2019 at 08:09, Hector Aguilar-Carreno < (b) (6) wrote: Congratulations, Kwe! Well done!!!

Hector Aguilar-Carreno
Associate Professor
Microbiology and Immunology
College of Veterinary Medicine
Cornell University

Office: (b) (6)

From: Plowright, Raina < (b) (6)

Sent: Monday, December 2, 2019 3:36 PM

To: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Cc: Alison Peel < (b) (6) Emily Gurley < (b) (6) Hector Aguilar-Carreno < (b) (6) Jamie Lloyd-Smith < (b) (6) Kwe Claude, Yinda (NIH/NIAID) [F] < (b) (6)

Subject: Re: Kwe's first PREEMPT paper

Whoooo Hooooo!!! Way to go Kwe!

On Dec 2, 2019, at 1:31 PM, Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote:

Second PREEMPT paper from RML!

And 1st ACURO approved, so we are set for 2020!

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH
<Yindajiz576.pdf>

 From:
 Munster, Vincent (NIH/NIAID) [E]

 Sent:
 Mon, 2 Dec 2019 15:08:44 -0700

To: Plowright, Raina Subject: Field samples

How worried are you about TA2?

We are not on track in finding novel henipa's? We have put a very large investment in Australia, but I'm worried that it will not pay of if we don't find any novel henipa's?

I'm not quite sure whether another ~ 5000 samples is truly sustainable?

Any thoughts?

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH From: Munster, Vincent (NIH/NIAID) [E]
Sent: Mon, 2 Dec 2019 13:58:32 -0700

To: LaTrielle, Sara
Cc: Plowright, Raina
Subject: Re: DARPA \$\$-?

Nope, second installment is still not in. Smtg with government to government slowlinessssss

Final signatures should be there, so I'm hoping it will come in before the end of this year

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

From: "LaTrielle, Sara" < (b) (6)

Date: Monday, December 2, 2019 at 1:57 PM

To: ' (b) (6) < (b) (6)

Cc: "Plowright, Raina" < (b) (6)

Subject: DARPA \$\$-?

Vincent,

Just checking: did you finally get your DARPA funds, or is all in process? We want to make sure you can pay your team for all the hard work they are doing and funds are made available asap. Let us know if you need anything from us- in terms of talking to DARPA.. nudge, nudge.

Sara

From: Munster, Vincent (NIH/NIAID) [E]
Sent: Mon, 2 Dec 2019 13:31:59 -0700

To: Plowright, Raina; Alison Peel; Emily Gurley; Hector Aguilar-Carreno; Jamie Lloyd-

Smith

Cc: Kwe Claude, Yinda (NIH/NIAID) [F]

Subject: Kwe's first PREEMPT paper

Attachments: Yindajiz576.pdf

Second PREEMPT paper from RML!

And 1st ACURO approved, so we are set for 2020!

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH 
 From:
 Munster, Vincent (NIH/NIAID) [E]

 Sent:
 Mon, 2 Dec 2019 12:32:24 -0700

To: Plowright, Raina; Alison Peel; Rynda-Apple, Agnieszka

Cc: Bushmaker, Trenton (NIH/NIAID) [E]; Kwe Claude, Yinda (NIH/NIAID) [F]; Mandy

Todd; Manuel Ruiz Aravena

Subject: Re: Shipping list Dec-2019

Hi Raina,

We just figured out that the slides are methanol fixed, so they should be good to cleared directly through RML. The blood cloths are plain frozen in -80, so it would be good to have an idea what to do with these?

Thanks for all the help, especially Ali who has been very responsive. Just making sure thate everyone is aware, that there is a huge effort involved in both the front end (Oz) and back-end (RML), so it would be good that end users of samples are aware of this and that last-minute changes in shipping lists or "new" sample types can cause some confusion / sorting out,

Cheers,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

From: "Plowright, Raina" < (b) (6)

Date: Monday, December 2, 2019 at 12:25 PM

To: Alison Peel < (b) (6)

Cc: ' (b) (6) < (b) (6) Trenton Bushmaker

< (b) (6) "Kwe Claude, Yinda (NIH/NIAID) [F]"

< (b) (6) Manuel Ruiz

Aravena < (b) (6)

Subject: Re: Shipping list Dec-2019

We have no import permit for samples from bats (CDC suggested we go through RML) so slides would have to go through RML. Dan Becker was leading this part of the project but hasn't stayed involved since he left and there is no clear leader on the slides to ensure all protocols are adhered to. We really need a single 'sample tsar' to ensure all samples are cared for under the best protocols, but I think we have been understaffed in this respect and so it is messy, but everyone is stepping up and everyone is doing more than their best effort to pull it off (especially Manuel—thanks Manuel!). Thanks team for the enormous effort to get the samples away.

Raina

On Dec 2, 2019, at 12:15 PM, Alison Peel < (b) (6) wrote:

Thanks Vincent for the reminder and clarification on that. Similarly, it's quite a task on our end to get the shipments away, with requests (and last minute requests) from many people, changes to shipment lists to remove HeV-associated samples when results come in from Kwe, and many many layers of permits, agreements and approvals across multiple institutions. All good though, we can continue to refine the process.

I had it in my mind that MSU didn't have all the required import permits, but if they are obtained, then that would be much easier.

Raina- who is our best point of contact at MSU re import permits?

Thanks

Ali

On Tue, 3 Dec 2019 at 5:07 am, Munster, Vincent (NIH/NIAID) [E] < 6) (6) wrote: Thanks Ali,

This info most have been "lost" then on this end. Thanks for replying so quickly, it is quite the task with multiple shipments coming on to make sure that everything runs smoothly. Just as a reminder that this is nothing directed specifically at your team, we'll have the same scrutiny with the Bangladesh samples.

Just want to make sure, that once they are at RML, they can only be released following RML established procedures. So anything which can be routed around RML to MSU is easier for us (as every inactivation will take-up significant time of the people here).

Cheers,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

```
(b)(6)
From: Alison Peel <
                                (b) (6) <
Reply-To: "
                                                            (b) (6)
Date: Monday, December 2, 2019 at 11:59 AM
To: "
                             (b) (6) <
                                                            (b)(6)
Cc: Trenton Bushmaker <
                                                      (b) (6) "Kwe Claude, Yinda (NIH/NIAID) [F]"
                          (b) (6) Mandy Todd
                                                                            (b) (6), Manuel Ruiz
                                        (b) (6) "Plowright, Raina" <
                                                                                                  (b)(6)
Aravena <
```

Subject: Re: Shipping list Dec-2019

Hi all,

Still early here, so I or Manuel can respond more in full later on but I just wanted to say that we emailed details of the samples in this shipment on November 1st and had a discussion with Trent about the slides and the clots at that time. The slides were not sent on dry ice- just a regular box.

We should have sent the final list prior to shipment, but we did send this draft list well in advance and answered any questions posed by Trent. Let us know what else we can do for next time.

#### Cheers

Ali

On Tue, 3 Dec 2019 at 4:48 am, Munster, Vincent (NIH/NIAID) [E] < 6) 6) wrote: Hi Manuel,

You might want to consider sending the slides directly to MSU? That would make it a little bit easier from our end. If Raina can discuss this with their local IRB, if these are not considered infectious than there is no need for a CDC import permit. Also, these will not have to be shipped using a cold-chain. So they could be shipped using a regular package rather than a very expensive dry-ice shipment.

As Trent said, make sure these things are discussed well ahead of time, this would facilitate a better logistics from our end,

cheers

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

From: Trenton Bushmaker < (b) (6)

Date: Monday, December 2, 2019 at 11:26 AM

To: Manuel Ruiz Aravena < (b) (6) Mandy Todd

(b) (6) (7) (b) (6) < (b) (6)

Cc: " (b) (6) "Kwe Claude, Yinda (NIH/NIAID)

[F]" < (b) (6) "Plowright, Raina" < ra (b) (6)

Subject: RE: Shipping list Dec-2019

#### Hello,

Thank you for packing list, however Manuel I will talk with you individually because we need to have a few things to fixed on the packing list. I just want to reiterate that I need this packing list <u>before the samples are shipped</u>. This way we can discuss any discrepancies beforehand. This will delay the processing of samples and the results to you guys.

Most important for now....! will need the House Airway bill# and the Job# if you are still sending it via World Courier. I will need to track the package, we have had issues of them sending packages to different locations and via odd routes of travel.

Let me know if you have questions. Thank you again for sending the samples, can't wait to find something!

#### -Trent

Trenton Bushmaker
Biologist, Virus Ecology Unit
Rocky Mountain Laboratories
903 South 4th Street
Hamilton, MT 59840
Phone: (b) (6)
Email: (b) (6)

From: Manuel Ruiz	Aravena <	(b) (6)	
Sent: Sunday, Dece	mber 01, 2019 9:56 PM	1	
To: Bushmaker, Tre	enton (NIH/NIAID) [E] <	(b) (6)	
Cc:	(b) (6) Munster, Vince	ent (NIH/NIAID) [E] <	(b) (6) Kwe Claude,
Yinda (NIH/NIAID)	[F] <	(b) (6) Plowright, Raina <	(b) (6)
Mandy Todd <	(b	) (6)	
Subject: Shipping li	st Dec-2019		

Hi Trent,

Samples are on their way to RML!

I attach the list of samples.

Samples are packed in a way that whole boxes can be transfer to MSU without moving samples among them.

(b) (4) for Vicky's experiments are in Box AUS\_155 (Locations F01 to F04)

Details of content and destinations are below.

Regards, Manuel

(b) (4)

(b) (4)

(ъ) (4)

From: Munster, Vincent (NIH/NIAID) [E]
Sent: Mon, 2 Dec 2019 12:26:26 -0700

To: Plowright, Raina; Rynda-Apple, Agnieszka

Cc: Alison Peel; Bushmaker, Trenton (NIH/NIAID) [E]

Subject: Samples RML

#### Hi Raina and Aga,

Just to reiterate that anything which can be done to facilitate an "easier" flow of samples between Oz and MSU would be appreciated. We are having slides and blood cloths shipped here for MSU research project, but it would be good to know what downstream inactivation procedures are suitable for these types of samples.

Especially, if the slides could be shipped directly to MSU (as inactivated) than that would save my team (and Ali's) a huge amount of work. Alternatively, the samples could be inactivated in Oz and then RML would serve a clearing house. Just a reminder, that the RML bandwidth is very limited with several large PREEMPT project underway.

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH From: Munster, Vincent (NIH/NIAID) [E]
Sent: Mon, 2 Dec 2019 11:36:36 -0700
To: Plowright, Raina; Alison Peel

Cc: Bushmaker, Trenton (NIH/NIAID) [E]; Manuel Ruiz Aravena

Subject: slides

Hi guys,

On the sample list for next shipment there are included some items which need a bit clarification:

Slides (I assume bloodsmears), have these been treated somehow? Just wanting to make sure they'll still fit under inactivated, I think we discussed formalin fixation previously. Has this been done yet?

Feces: are these in ethanol? Same issue here

Blood RNA\_P, these will have to be extracted here at RML and the RNA send to MSU

Serum, these will have to be irradiated here at RML and then send to MSU

There is smtg on the list which says "clots", any more clarification of how these should be handled?

Just to reiterate that we can only releases samples which have been inactivated via approved (RML approved) protocols this will include AVL RNA extraction, Trizol, irradiation, ao% formaline inactivation and 70% EtOH. This is mandated by us by or IBC but also a prerequisite of the CDC import permit

Cheers,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH 
 From:
 Munster, Vincent (NIH/NIAID) [E]

 Sent:
 Mon, 2 Dec 2019 08:11:17 -0700

To: Plowright, Raina; Seifert, Stephanie (NIH/NIAID) [E]

Cc: LaTrielle, Sara

Subject: Re: USAMRMC DOINBC-6458.10; September 10, 2019 (UNCLASSIFIED)

Nice, good job Steph!

We can now move ahead with the bats,

Cheers,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

From: "Plowright, Raina" < (b) (6)

Date: Friday, November 29, 2019 at 3:32 PM

To: ' (b) (6) < (b) (6) "Seifert, Stephanie (NIH/NIAID)

[E]" < (b) (6)

Cc: "LaTrielle, Sara" < (b) (6)

Subject: Fwd: USAMRMC DOINBC-6458.10; September 10, 2019 (UNCLASSIFIED)

Great news!

Begin forwarded message:

From: (b) (6) <

Subject: USAMRMC DOINBC-6458.10; September 10, 2019 (UNCLASSIFIED)

Date: November 29, 2019 at 6:57:55 AM MST

CLASSIFICATION: UNCLASSIFIED

Dear Dr. Plowright:

Please see the attached correspondence from the Animal Care and Use Review Office. If you have any questions regarding this document, please contact the reviewer, (b) (6) directly either

by phone at	(b) (6) or by email at		(b) (6)	Thank you
Best Regards,				
Animal Care and U	se Review Office (ACURO)			
		(b) (6)		
CLASSIFICATION: U	INCLASSIFIED			

From: Munster, Vincent (NIH/NIAID) [E]

Sent: Wed, 27 Nov 2019 08:09:17 -0700

To: Ser Voss, Rita (NIH/NIAID) [E]; (b) (6) (b) (6)

; Plowright, Raina

Cc: Clifton, Dawn (NIH/NIAID) [E]; Kisling, Lynne (NIH/NIAID) [E]; NIAID IAMB RMS

BUDGET TEAM; (b) (6)

Subject: Re: DARPA Signature Request: XAI19001 FY20 Funds to LV/Munster

Hi (b) (6)

Do we have an update on the routing of the funds, we have now been out of DARPA funds for three months now and we are really reaching the limit of our ability to continue this project.

Kind regards,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

On 11/14/19, 6:45 AM, "Ser Voss, Rita (NIH/NIAID) [E]" < (b) (6) wrote:

Hi (b) (6) - The request for expediting this worked well! I received the attached this morning, and it is now ready for you to route so that we can accept the full year of funding as discussed. Please let me know if there are questions or if you need more information. Thank you.

Rita Ser Voss

```
----Original Message----
From: Ser Voss, Rita (NIH/NIAID) [E] < (b) (6)
Sent: Wednesday, November 13, 2019 1:53 PM
To: (b) (6)
Cc: Clifton, Dawn (NIH/NIAID) [E] < (b) (6) Kisling, Lynne (NIH/NIAID) [E] < (b) (6) NIAID IAMB RMS BUDGET TEAM
(b) (6) Munster, Vincent (NIH/NIAID) [E] < (b) (6)
```

Subject: RE: DARPA Signature Request: XAI19001 FY20 Funds to LV/Munster

Hi (b) (6) I got your message about providing full funding instead of half for FY20. That will be great, but I have re-routed our 7600 forms through the NIAID channels again for signatures. They will not accept a "pen and ink" adjustment to them. I asked them for expedited processing, so I will hope to have them available to you within the next few days. Thanks.

Rita Ser Voss

```
----Original Message----
From: Ser Voss, Rita (NIH/NIAID) [E] < (b) (6)
Sent: Wednesday, October 2, 2019 7:19 AM
To: (b) (6)

Cc: Clifton, Dawn (NIH/NIAID) [E] < (b) (6) Kisling, Lynne (NIH/NIAID) [E]
```

### (b) (6) NIAID IAMB RMS BUDGET TEAM (b) (6) Munster, Vincent (NIH/NIAID) [E]

Subject: DARPA Signature Request: XAI19001 FY20 Funds to LV/Munster

Hi Everyone - The attached agreement has been signed by NIAID as discussed below. Can you please route for signatures on your end and provide the fully signed agreement back to us along with the MIPR documents?

If you have any questions or need additional information, please let me know. Thank you.

OKRita Ser Voss
NIAID/NIH/OSMO/IAMB/RMS
Budget Analyst
Rocky Mountain Laboratories
903 South 4th Street
Hamilton, MT 59840
Phone: (b) (6)

NIAID / National Institutes of Health / DHHS The information in this e-mail and any of its attachments is confidential and may contain sensitive information. It should not be used by anyone who is not the original intended recipient. If you have received this e-mail in error please inform the sender and delete it from your mailbox or any other storage devices. National Institute of Allergy and Infectious Diseases shall not accept liability for any statements made that are sender's own and not expressly made on behalf of the NIAID by one of its representatives.

```
----Original Message----
From: Munster, Vincent (NIH/NIAID) [E] <
                                                              (b) (6)
Sent: Tuesday, October 1, 2019 9:27 AM
To:
                                                 (b) (6);
                                                                          (b)(6)
                          ; Ser Voss, Rita (NIH/NIAID) [E] <
                                                      (b) (6) Kisling, Lynne (NIH/NIAID) [E]
Cc: Clifton, Dawn (NIH/NIAID) [E] <
                 (b) (6) NIAID IAMB RMS BUDGET TEAM
                                                                        (b) (6)
Subject: Re: Please Confirm FY20 Funding Plan - IAA XAI19001
Sounds good from my end,
Regards,
Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH
On 10/1/19, 7:01 AM,
                                                                     (b) (6) wrote:
  Hi (b) (6) Rita -
  Yes, I support the PREEMPT program; however, it is transitioning to a new PM
               (b) (6) and so the new Financial POC will be
  cc'd.
```

Concur, we have \$365,702 planned for FY20. Given we are in a Continuing Resolution, we may have to send incremental funds (e.g. half in October and second half in early CY2020). Please let us know if there are any issues

```
with this.
Thanks!
R/
(b) (6)
----Original Message----
From:
                                                      (b)(6)
Sent: Monday, September 30, 2019 4:33 PM
                                                 (b)(6)
                                                      (b) (6) Kisling, Lynne
Cc: Clifton, Dawn (NIH/NIAID) [E] <
                                     (b) (6) NIAID IAMB RMS BUDGET TEAM
(NIH/NIAID) [E] <
                                              (b) (6) Munster, Vincent (NIH/NIAID) [E]
                      (b) (6) Ser Voss, Rita (NIH/NIAID) [E]
Subject: RE: Please Confirm FY20 Funding Plan - IAA XAI19001
Hi (b) (6)
Do you support PREEMPT program? Please see email below. If not, would you
please forward the email to the person who supports PREEMPT?
Thanks,
 (b)(6)
******
                (b)(6)
SETA support to DARPA/DSO
            (b) (6)
eFax (703) 741-0036
----Original Message----
From: Ser Voss, Rita (NIH/NIAID) [E] <
                                                         (b) (6)
Sent: Monday, September 30, 2019 4:08 PM
                                                     (b) (6):
                                                                   (b)(6)
To:
                                       ; Munster, Vincent (NIH/NIAID) [E]
                     (b)(6)
Cc: Clifton, Dawn (NIH/NIAID) [E] <
                                                      (b) (6) Kisling, Lynne
                                     (b) (6) NIAID IAMB RMS BUDGET TEAM
(NIH/NIAID) [E] <
                                             (b) (6)
Subject: Please Confirm FY20 Funding Plan - IAA XAI19001
Hi Everyone - Dr. Munster asked me to get a start on this as soon as
possible in FY20, so please confirm the following:
I am attaching the last fully signed modification of the agreement for your
reference.
FY20 funds to be received from DARPA: $365,701.51 (Refer to page 30 of the
attached.)
Program Official:
                                             (b) (6), DARPA/BTO;
                                                                          (b) (6)
Fax 703.741.0080;
                                        (b) (6) Funding Official:
                                      (b) (6); Fax 703.741.0059;
```

(b) (6) ALC 00008522 Component TAS: AID-97; BPOA-2019;

EPOA-2020; MAIN-0400 TAS Formatted: 97 2019/2020 0400

BPN: DODHR0011 EIN: 311575142 DUNS: 041584173

We'll appreciate having your response as soon as possible. Thank you.

Rita Ser Voss
NIAID/NIH/OSMO/IAMB/RMS
Budget Analyst
Rocky Mountain Laboratories
903 South 4th Street
Hamilton, MT 59840
Phone: (b) (6)
(b) (6)

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 From:
 Munster, Vincent (NIH/NIAID) [E]

 Sent:
 Tue, 26 Nov 2019 10:14:28 -0700

To: Raina Plowright

Cc: Manuel Ruiz Aravena; Alison Peel; Schountz, Tony; Rynda-Apple, Agnieszka;
Caylee Falvo; Dan Crowley; Benson, Evelyn; McGuire, Liam; Dale Hansen; Devin Jones; Maureen Kessler
Subject: Re: plans for exploring ketogenesis pathway and cytokine expression from

starving bats

bats

I agree, and it would get you real physiological parameters for the starving bats to link with the transcriptomics data

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

(b)(6)From: Raina Plowright < Date: Tuesday, November 26, 2019 at 10:08 AM To: ' (b) (6) < (b)(6)Cc: Manuel Ruiz Aravena < (b) (6) Alison Peel (b) (6) Tony Schountz < (b) (6) "Rynda-Apple, (b) (6) Caylee Falvo < (b) (6) Dan Agnieszka" < (b) (6) Crowley < (b) (6) "Benson, Evelyn" < "McGuire, Liam" < (b) (6) Dale Hansen < (b) (6) Devin (b) (6) Maureen Kessler < (b)(6)Jones < Subject: Re: plans for exploring ketogenesis pathway and cytokine expression from starving

Thats a good idea. We looked at iStat etc. early on but it was ~\$75 per sample — too expensive for large numbers of bats but totally worthwhile for the small number we can send for metabolomics and transcriptomics. Manuel, can you look at this? I think biochemistry needs too much blood but hematology should be doable.

On Nov 26, 2019, at 10:02 AM, Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote:

Depending on the capacity of the clinic you could run a hemavet as well, uses 20 microliter of blood and you get a complete suite of hematological parameters including WBC, platelets. Typically well equipped vet clinics should have these machines

The I-stat (handheld) would be very interesting for this as it will measure metabolic parameters such as glucose as well

https://www.abaxis.com/sites/default/files/resource-brochures/i-STAT%20Alinity%20v%20Utilization%20Guide%20ABX-00075%20R1.pdf

## http://www.drew-scientific.com/techinfo/brochures/hemavetbrochure.pdf

the only thing we then would need to think about is getting a proper referenc panel from healthy bats as well,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: Raina Plow	right <	(b) (6)		
Date: Tuesday, N	ovember 26, 2	019 at 9:55 AM		
To: Manuel Ruiz	Aravena <	(b) (6) Aliso	on Peel	
< (t	) (6) .au>, Tony	Schountz <	(b) (6)	"Rynda-Apple,
Agnieszka" <		(b) (6) Caylee Falvo <		(b) (6) Dan
Crowley <		(b) (6) "Benson, Evelyn" <		(b) (6)
"	(b) (6) <	(b) (6) "McG	uire, Liam"	
<	(b) (6)			
Cc: Dale Hansen		(b) (6) Devin Jones <		(b) (6)
Maureen Kessler	<	(b) (6)		

Subject: plans for exploring ketogenesis pathway and cytokine expression from starving bats

Hi All,

Quick update. We have a small window to adjust these sampling plans (a day maybe?), so respond urgently if you see any problems here.

Yesterday, we discussed these plans on the immunology call, then I followed up with Ali and Manuel by Zoom/phone later in the day. These are the plans as I understand them.

To ensure we have samples from starving bats during this current food shortage, Manuel will go to the Australia Zoo hospital this week to either collect samples from their freezer, or from bats coming into care during the current food shortage. Manuel has a DVM so he can get stuck in and take blood, do a PCV etc.

In an ideal scenario, we would want the following samples:

- 1) from bat not suffering from acute stress (this one is probably not possible to avoid but in the upcoming Austral winter we plan to get capillary tube samples from bats as they come out of the net)
- 2) sample taken prior to rehydration with fluids (may not be possible), definitely prior to rehydration with glucose & fluids.
- a) whole blood in RNAP (>150 microL) for PCR for cytokine expression and for transcriptomics

- b) serum for metabolomics to look for indicators of ketogenesis pathway (> 5microL for metabolomics, but >50microL for later serology would be ideal)
- c) plain urine for metabolomics (>5microL)
- d) urine in VTM for virology screening (the more the better)
- e) capillary tube of blood to run a PCV (check hydration status)

If the bat is dehydrated and Manuel/zoo staff can't get blood, then we would like:

- a) blood in capillary tube, spun down for serum (>5microL)
- b) blood in capillary tube then RNAP (whatever you can salvage)
- c) urine in VTM (whatever you can collect).

## Plans for samples:

Ideally we would run metabolomics, PCR for mRNA, transcriptomics, HeV screening, and even proteomics (Caylee to trial this as there will be a lot of troubleshooting) on the same samples. If not possible, we will just look at ketogenesis pathway (acetone assay) and untargetted mass spec; next priority would be PCR, then transcriptomes.

Let me know if I've missed anything here.

Raina

Email:

Raina Plowright BVSc MS PhD

Assistant Professor

Department of Microbiology & Immunology

Montana State University

(b) (b)

Lab website: http://bzndiseaselab.org

Phone: (b) (6)

From: Plowright, Raina

**Sent:** Mon, 25 Nov 2019 23:56:37 +0000 **To:** Munster, Vincent (NIH/NIAID) [E]

Cc: Emily Gurley; Letko, Michael (NIH/NIAID) [F]

Subject: Re: New DARPA program

And already DARPA funded! Is anyone in a position to travel on 11 Dec?

Sent from my iPhone

On Nov 25, 2019, at 4:38 PM, Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote:

I think we should send 1 or 2 people there and present a slide on:

- Large virus repository of high impact pathogens for sensitivity and specificity testing
- Large program on animal modelling with the ability to get correct samples in the right matrices (urine, blood, stool)
- Large international programs with (potential) access to human and animal samples in Bangladesh, Congo, Australia

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

From: Emily Gurley < (b) (6)

Date: Thursday, November 21, 2019 at 8:52 PM

To: "Plowright, Raina" < (b) (6) "

(b) (6)

Subject: RE: New DARPA program

Good leads - will also ask around. Am at a conference this week but back in the office next week.

From: Plowright, Raina < (b) (6)

Sent: Thursday, November 21, 2019 12:24 PM

To: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Cc: Emily Gurley < (b) (6)
Subject: Re: New DARPA program

great. keep me informed. exciting!

On Nov 21, 2019, at 9:57 AM, Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote:

Working on it,

I think Oz might still be a bit challenging, but we can discuss. I'm not sure whether they would be interested in a large wildlife component. I would probably write it as an add on, and focus largely on areas with access to human samples. It would be good to keep in the back of our minds that these designs will typically target pathogens (human), so other bat paramyxo's (like cedar) will likely not be included (so you typically won't have your multi bat paramyxo screen to look at co-infections).

Trying to see if there is interest from Ian Lipkin and/or Pardis Sabeti's groups. The majority of the task will be on the front end in the design of platforms capable of this, and we come in on the validation and field deployment side.

Let's see if we can get some people interested,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

From: "Plowright, Raina" < (b) (6)

Date: Thursday, November 21, 2019 at 9:48 AM

To: " (b) (6) < (b) (6)

Cc: Emily Gurley < (b) (6)

Subject: Re: New DARPA program

Do you know anyone doing something like this? It would be an amazing opportunity if we could deploy this in the field. If samples have to go to a lab, Australia may be out, but if diagnostics are done within Australia, that is fine (we can't detect anything *outside* of *Australia*).

On Nov 21, 2019, at 9:18 AM, Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote:

Hi Raina and Emily,

I think this is probably better approached a bit outside the scope of PREEMPT. I think to get a proposal together we would need to have a collaborator with a new platform for multiplexed pathogen detection

(given that the name is diget, I assume they would like CRISPR based technologies). What we would need is a platform (e.g. smtg with Ian lipkin or Pardis Sabetti), the testing in terms of sensitivity and specificity (lab based) and deployment in the field (largely human samples and maybe some animal (Livestock / bats).

I can see if we can put together a team based on this, I think from the preempt end it would potentially include all the field sites (but Oz will be challenging as they do not like to detect actual pathogens in their samples, whether horses or bats), additional field sites (like Congo).

Lab site: major human and animal pathogens, including arboviruses, influenza viruses, VHFs, bacterial pathogens etc. this is quite the undertaking, as they are aiming for a +100 pathogen detection system.

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: "Plowright, Raina" < (b) (6)

Reply-To: (b) (6) < (b) (6)

Date: Thursday, November 21, 2019 at 9:01 AM

To: preempt < (b) (6)

Subject: Fwd: New DARPA program

### Good Morning,

See below re: new program. If you know of anyone who could develop the diagnostic technologies proposed, we could test them in the field.

Sorry for my long silence — this semester has been brutal. Some updates coming soon. Raina

Begin forwarded message:

```
(b)(6)
From:
Subject: New DARPA program
Date: November 21, 2019 at 7:47:39 AM MST
To: Ariel Weinberger <
                                                                     (b) (6) Ashley Fennell
                              (b) (6) "Carla SALEH" <
                                                                          (b) (6) Greg Gray
                       (b) (6) Jose Garcia <
                                                                       (b) (6) Luke Alphey
                           (b) (6)
                                                                          (b) (6), Peter A Barry
                                                                           (b) (6) "Robert Huebner"
                    (b) (6) "Plowright, Raina" <
                              (b) (6)
                                            (b)(6)
                                                                                              (b) (6)
```

Dear teams,

There is a new DARPA program called DIGET which might be of interest to you and your colleagues. Below is a brief program description with some links to the SN and proposer's day.

Regards,	
(b) (6)	
DIGET - Detect it with Gene Editing Tee	chnology

The Defense Advanced Research Projects Agency (DARPA) is hosting a Proposers Day for the potential proposer community in support of a planned Broad Agency Announcement (BAA) for the DIGET (Detect It with Gene Editing Technologies) Program. The Proposers Day will be held on December 11, 2019 in Atlanta, GA.

The DIGET program aims to deliver timely and comprehensive threat detection to support overall readiness, counter the spread of disease, and promote stabilization missions. DIGET will leverage advances in gene editing technologies to develop low-cost, high-trust, rapidly reconfigurable, and fieldable diagnostic (Dx) and biosurveillance (BSV) technologies to enable detection of any threat, anytime, anywhere.

To achieve its goal, DIGET will design, develop, prototype, and deploy two novel nucleic acid detection devices for the simultaneous detection of multiple targets: 1) a disposable point-of-need diagnostic for up to 10 targets, and 2) a massively multiplexed detection (MMD) device for 1,000 or more targets. Both devices must be simple to operate, low-cost, and rapidly reconfigurable to provide high impact, high quality, trusted information that enhances decision-making. The disposable point-of-need device will improve the speed and efficacy of triage and treatment and enhance the standard of care for the military and public health domains, and the MMD device will enable early threat detection, assess disease severity, and improve situational awareness. The MMD platform will also provide actionable data for biosurveillance efforts such as characterization of known and emergent pathogens in circulation to inform countermeasure deployment.

Additional details about the DIGET program and Proposer's Day can be found here:

DIGET Press Release: <a href="https://www.darpa.mil/news-events/2019-11-15">https://go.usa.gov/xplce</a> DIGET Special Notice Announcement: <a href="https://go.usa.gov/xpkce">https://go.usa.gov/xpkce</a> DIGET Proposer's Day Registration Website: <a href="https://events.sa-meetings.com/DIGETProposersDay">https://events.sa-meetings.com/DIGETProposersDay</a>

(b) (6)

Support to Biological Technologies Office, DARPA Science and Technology Associates, Inc.
(b) (6)

 From:
 Munster, Vincent (NIH/NIAID) [E]

 Sent:
 Mon, 25 Nov 2019 13:58:39 -0700

To: Hector Aguilar-Carreno; Plowright, Raina; Alison Peel; Jamie Lloyd-Smith; Emily

Gurley

Subject: Re: Papers for PREEMPT

Took them a while to get going with this I guess, was only directly involved with the structure work with Vicky and Thomas.

Cheers,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: Hector Aguilar-Carreno < (b) (6)

Date: Monday, November 25, 2019 at 1:55 PM

To: ' (b) (6) < (b) (6) "Plowright, Raina"

< (b) (6) Alison Peel < (b) (6) Jamie Lloyd-Smith

< (b) (6) Emily Gurley <egurley1@jhu.edu>

Subject: Re: Papers for PREEMPT

Congratulations, Vince et al! This is personally super exciting, since I made these antibodies while I was a post-doc in Benhur's lab. Really nice to see that their structural epitopes are now published!

Hector

Hector Aguilar-Carreno

Associate Professor

Microbiology and Immunology

College of Veterinary Medicine

Cornell University

Office: (b) (6)

From: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Sent: Monday, November 25, 2019 3:48 PM

To: Plowright, Raina <	(b) (6) Alison Peel <	டுடு Hector
Aguilar-Carreno <	(b) (6) Jamie Lloyd-Smith <	(b) (6) Emily Gurley
(b) (6)		

Subject: Papers for PREEMPT

First paper for PREEMPT from our end (second one is accepted in JID)

https://www.pnas.org/content/early/2019/11/22/1912503116

cheers,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH From: Plowright, Raina

**Sent:** Mon, 25 Nov 2019 18:31:55 +0000 **To:** Kwe Claude, Yinda (NIH/NIAID) [F]

Cc: Alison Peel; Alison Peel; Manuel Ruiz Aravena; Bushmaker, Trenton (NIH/NIAID)

[E]; Munster, Vincent (NIH/NIAID) [E]; Madden, Wyatt

Subject: Re: Updates on HeV and CedPV screening

Thank You Kwe! I've forwarded the spreadsheet to Wyatt who can start the visualizations. Good to see a few with low CT values (though surprisingly few) but that may make more sense when we see the dates of capture.

Also, another P. poliocephalus positive — second one this study!! We appreciate all of the work that you have done to get these results. Raina

On Nov 25, 2019, at 11:24 AM, Kwe Claude, Yinda (NIH/NIAID) [F]

Hello Ali,

We have finished the screening for the last batch of samples from shipment 2. These were mostly samples in VTM. In this update we had 1381 samples: 79 HeVs and 7 CedPV positives. The spread sheet is attached.

Manuel- is there a way we can calculate how much urine was added to the VTM? This's important for calculating absolute genome copies number.

# Cheers!

--

Kwe Claude Yinda, PhD
Postdoc Fellow
Virus Ecology Unit, Laboratory of Virology
Rocky Mountain Laboratories, NIAID/NIH
903S 4th St. Hamilton, MT 59840
Email: (b) (6)
Tel: (b) (6)

<HeV-CedPV Update 11-24-2019.xlsx>

From: Sent: To: Cc: Subject:	Munster, Vincent (NIH/NIAI) Thu, 21 Nov 2019 17:45:06 - (b) (6) Raina Plowright Re: Bat1health: Future shipr	0700	
Absolutely			
On Nov 21, 2019, at 1	7:35, Alison Peel <	(b) (6) wrote:	
	ou previously said you were d be on request of specific ndra		
From: Alison Peel < Date: Fri, 22 Nov 201 Subject: Re: Bat1heal To: Sarah Britton < Cc: Plowright, Raina	9 at 10:33 am th: Future shipment and an		
Hi Sarah,			
and the second state of the second se	was a clause within the M viruses be made available t		ould be used for, and
Thanks Alison			
On Fri, 22 Nov 2019 HI Alison,	at 10:26 am, Sarah Britton	<	(b) (6) wrote:
at AAHL and Mark e	hat currently most of the vi expressed concern that if and is outside the econtrol of info that would	ne control of Australia.	(b) (4) sit (b) (4) c domain.
Kind regards			
NSW Department of Pri	f Veterinary Officer and Group mary Industries   Biosecurity a d Bag 21   Orange NSW 2800 (b) (6)	and Food Safety	



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On Fri, 22 Nov 2019 at 10:34, Alison Peel < (b) (6) wrote: Hi Sarah,

I'm expecting more feedback from the uni this morning, but to make sure we get all the information we need, can I clarify if there is a specific concern? Is it primarily about the process by which sequences would or would not be released into the public domain?

I am around today to discuss (b) (6), and will hopefully get back to you later this morning once I've heard from our legal team.

Thanks Alison

On Wed, 20 Nov 2019 at 9:11 pm, Alison Peel < (b) (6) wrote: Hi Sarah,

Many thanks for your efforts in getting that conversation to happen, and for your positive feedback. I have some understanding about the IP situation, but will clarify things with our lawyers to be certain and will get back to you by Friday.

Kind Regards,

Alison

On Wed, 20 Nov 2019 at 20:58, Sarah Britton < (b) (6) wrote: Hi Alison and Raina,

Managed to speak to both Allison and Mark today. We support the research you are doing and keen to see it progress. The question Mark had was about who owns the IP of the virus and phylogenetic data?

I can chat to you on Friday about this if suits, as I am in the field tomorrow.

Kind regards

### Sarah

Sarah Britton | NSW Chief Veterinary Officer and Group Director Animal Biosecurity NSW Department of Primary Industries | Biosecurity and Food Safety 161 Kite Street | Locked Bag 21 | Orange NSW 2800

T: (b) (6) | M: (b) (

E: (b) (6)

W: www.dpi.nsw.gov.au

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On Wed, 20 Nov 2019 at 08:46, Sarah Britton < (b) (6) wrote: Hi Alison,

I apologise for the delay in replying but have been trying to catch Allison and Mark to discuss this. I have managed to catch Allison and we need to run it past Mark- as soon as we have done that, I will contact you. It should be this week as he is away next week.

Kind regards,

#### Sarah

Sarah Britton | NSW Chief Veterinary Officer and Group Director Animal Biosecurity
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I hope to be submitting a shipment request to you later this week. We are in the process of	
getting the required MTAs finalised and it would be helpful to hear your thoughts on which o	f
the following sample testing you consider reasonable to request (further details in the previou	S
emails in this thread):	

	(b) (4)
Thanks very much,	
Alison	
On Thu, 7 Nov 2019 at 22:01, Alison Peel < (b) (c) Dear Sarah,	wrote:

Following on from my previous email, I've included some further information below on the rationale behind our request for permission to undertake virus isolation at Rocky Mountain Laboratories.



I hope this further explanation is helpful and I look forward to hearing your thoughts.
Kind Regards,
Alison
On Wed, 6 Nov 2019 at 09:15, Alison Peel < (b) (6) wrote: Dear Sarah,
Thanks for your interest in our research and for the positive feedback during our call yesterday. I have attached the spillover response pamphlet and the multiviral paper that we discussed.
(b) (4)
should we add that to our next shipment request or does this need discussion with Mark Schipp? I can provide further details on the methods if helpful. I also mentioned isolation to Allison Crook this week so it would be worth discussing if you two meet.
Regarding (b) (4) I will write a separate proposal and send to you shortly.
One last matter that was just brought to my attention is the
T. d.S.
Is this a reasonable request? It is not absolutely essential to our project but we do have a postdoc who raised the money to do the DNA extractions and PCR and it would add another layer of information into our project.
Thanks, Alison
ALISON PEEL BSc(Vet) BVSc MSc PhD
DECRA Senior Research Fellow, Griffith Wildlife Disease Ecology Group  Environmental Futures Research Institute, Sir Samuel Griffith Centre (N78) 2.23  Griffith University, Nathan Campus, 170 Kessels Rd, Nathan, QLD, 4111, Australia  Office days: Monday - Thursday  E: (b) (6) (b) (6)  W: (b) (6)  M: (b) (6)  @ali bat
www.bat1health.org www.mccallum-disease-ecology.com/alison-peel https://experts.griffith.edu.au/academic/a.peel

(b) (4)

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From: Munster, Vincent (NIH/NIAID) [E]
Sent: Thu, 21 Nov 2019 13:42:56 -0700

To: Plowright, Raina

Subject: Re: New DARPA program

#### Sounds good

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: "Plowright, Raina" < (b) (6)

Date: Thursday, November 21, 2019 at 12:34 PM

To: ' (b) (6) < (b) (6)

Subject: Fwd: New DARPA program

you free at 12 tomorrow? Want to talk with me and Blake Weidenheft — he may have something that could address the call.

# Begin forwarded message:

From: Blake Wiedenheft < (b) (6)

Subject: Re: New DARPA program

Date: November 21, 2019 at 10:35:08 AM MST

To: "Plowright, Raina" < (b) (6)

Hi Raina,

Thanks for thinking of us. I have some ideas for how we might be able to address this call. Our best shot would be for DNA detection rather than RNA, but we might be able to come up with a creative solution for RNA too.

Do I understand correctly that we would need to be ready by Dec 11? What actually needs to be done? PPT and travel? Written proposal?

I am on my way back to Bozeman now and will be home tonight. I am open between 11-3 tomorrow if you think it would be helpful to meet.

Thanks again Blake On Thu, Nov 21, 2019 at 8:49 AM Plowright, Raina < (b) (6) wrote: Hi Blake,

Is this in your wheelhouse? Do you have any emerging technologies that may be relevant? Vincent Munster and my colleagues who run our program in Bangladesh would love to do the field testing of such a device. Let me know if this is relevant.

Raina

Begin forwarded message:

```
(b) (6)
From:
Subject: New DARPA program
Date: November 21, 2019 at 7:47:39 AM MST
                                                                     (b) (6) Ashley Fennell
To: Ariel Weinberger <
                              (b) (6) "Carla SALEH" <
                                                                          (b) (6) Greg Gray
                      (b) (6) Jose Garcia <
                                                                       (b) (6) Luke Alphey
                                                                         (b) (6), Peter A Barry
                    (b) (6) "Plowright, Raina" <
                                                                           (b) (6) "Robert Huebner"
                              (b) (6)
Cc:
                                           (b)(6)
                                                                                             (b) (6)
```

Dear teams,

There is a new DARPA program called DIGET which might be of interest to you and your colleagues. Below is a brief program description with some links to the SN and proposer's day.

Regards,

.....

DIGET - Detect it with Gene Editing Technology

The Defense Advanced Research Projects Agency (DARPA) is hosting a Proposers Day for the potential proposer community in support of a planned Broad Agency Announcement (BAA) for the DIGET (Detect It with Gene Editing Technologies) Program. The Proposers Day will be held on December 11, 2019 in Atlanta, GA.

The DIGET program aims to deliver timely and comprehensive threat detection to support overall readiness, counter the spread of disease, and promote stabilization missions. DIGET will leverage advances in gene editing technologies to develop low-cost, high-trust, rapidly reconfigurable, and fieldable diagnostic (Dx) and biosurveillance (BSV) technologies to enable detection of any threat, anytime, anywhere.

To achieve its goal, DIGET will design, develop, prototype, and deploy two novel nucleic acid detection devices for the simultaneous detection of multiple targets: 1) a disposable point-of-need diagnostic for up to 10 targets, and 2) a massively multiplexed detection (MMD) device for 1,000 or more targets. Both devices must be simple to operate, low-cost, and rapidly reconfigurable to provide high impact, high quality, trusted information that enhances decision-making. The disposable point-of-need device will improve the speed and efficacy of triage and treatment and enhance the standard of care for the military and public health domains, and the MMD device will enable early threat detection, assess disease severity, and improve situational awareness. The MMD platform will also provide actionable data for biosurveillance efforts such as characterization of known and emergent pathogens in circulation to inform countermeasure deployment.

Additional details about the DIGET program and Proposer's Day can be found here:

DIGET Press Release: <a href="https://www.darpa.mil/news-events/2019-11-15">https://www.darpa.mil/news-events/2019-11-15</a>
DIGET Special Notice Announcement: <a href="https://go.usa.gov/xpkce">https://go.usa.gov/xpkce</a> DIGET

Proposer's Day Registration Website:

https://events.sa-meetings.com/DIGETProposersDay

4) (6)

(b) (6)

Support to Biological Technologies Office, DARPA Science and Technology Associates, Inc.

(b) (6)

--

Blake Wiedenheft, PhD Associate Professor Dept. Microbiology and Immunology Montana State University Bozeman MT 59717

tel: (b) (6)
fax: 406 994 4303
Wiedenheft Lab Website
Google.Scholar.Wiedenheft

 From:
 Munster, Vincent (NIH/NIAID) [E]

 Sent:
 Wed, 20 Nov 2019 14:43:16 -0700

To: Plowright, Raina

Subject: Re: Bat1health: Future shipment and analysis plans

Hi Raina,

For some reason this one went into my junk mail,

From our end there is no IP, all the date will be made freely available (after publication and deposited in genbank). In a few cases people have claimed IP on some of the application of certain human pathogens (like diagnostics). Given that these are all known pathogens, there is not much in terms of IP.

Typically within NIH, the IP will be on an invention (say the use of a certain glycoprotein in the context of a vaccine).

Does this answer your question?

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: "Plowright, Raina" < (b) (6)

Date: Wednesday, November 20, 2019 at 6:49 AM

To: ' (b) (6) < (b) (6)

Subject: Fwd: Bat1health: Future shipment and analysis plans

Mark is the national CVO. Wasn't expecting this question. What are your thoughts—at what point in downstream work does IP converge to lab? Happy to chat on phone b4 11 or 3-4pm.

Sent from my iPhone

Begin forwarded message:

From: Sarah Britton < (b) (6)

Date: November 20, 2019 at 3:58:44 AM MST

To: Alison Peel < (b) (6)

Cc: "Plowright, Raina" < (b) (6)

Subject: Re: Bat1health: Future shipment and analysis plans

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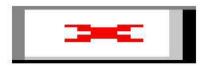
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E: (b) (6)

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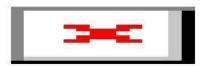
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(b) (4)	
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(b	) (4

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Thanks, Alison
ALISON PEEL BSc(Vet) BVSc MSc PhD

Environmental Futures Research Institute, Sir Samuel Griffith Centre (N78) 2.23 Griffith University, Nathan Campus, 170 Kessels Rd, Nathan, QLD, 4111, Australia

Office days: Monday - Thursday



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From: Munster, Vincent (NIH/NIAID) [E]
Sent: Tue, 19 Nov 2019 12:42:13 -0700

To: Letko, Michael (NIH/NIAID) [F]; Plowright, Raina
Cc: Kevin Olival; Seifert, Stephanie (NIH/NIAID) [E]

Subject: Re: Initial editorial feedback for manuscript NRMICRO-18-165V1

If you make it 10:15 it works for me

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: Michael Letko < (b) (6)

Date: Tuesday, November 19, 2019 at 12:36 PM

To: "Plowright, Raina" < (b) (6)

Cc: "Kevin Olival," < (b) (6)

(b) (6) "Seifert, Stephanie (NIH/NIAID) [E]" <

(b) (6)

(b) (6) wrote:

Subject: Re: Initial editorial feedback for manuscript NRMICRO-18-165V1

How does Friday at 10am (mountain time, 12pm New York time) work for everyone?

\_\_\_

Michael Letko, Ph.D
Postdoctoral IRTA
Dr. Vincent Munster Laboratory
Virus Ecology Unit, Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH
903S 4th Street
Hamilton MT 59840
(b) (6)

On Nov 18, 2019, at 10:10 AM, Plowright, Raina <

I'm available: Wed: 3-4pm Thurs: 12.30-2pm

Friday: 9-12.30 and 2.30-3.20pm

(can move things around Wed AM if necessary.)

On Nov 18, 2019, at 9:33 AM, Letko, Michael (NIH/NIAID) [F] (b) (6) wrote:

Dear co-authors,

<u>Are you available for a quick phone call this week</u> to discuss the route forward on these requested changes from the editors?

Addressing the requests should be pretty straightforward and should not take too much additional writing or time. Still, it would be nice just to make sure we are all on the same page before investing too much effort into it.

Cheers, -michael

Michael Letko, Ph.D
Postdoctoral IRTA
Dr. Vincent Munster Laboratory
Virus Ecology Unit, Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH
903S 4th Street
Hamilton MT 59840
(b) (6)

From: Kevin Olival < (b) (6)

Date: Thursday, November 14, 2019 at 9:06 PM

To: "Munster, Vincent (NIH/NIAID) [E]" < (b) (6)

Cc: "Letko, Michael (NIH/NIAID) [F]" < (b) (6) "Seifert, Stephanie (NIH/NIAID)

[E]" < (b) (6) "Plowright, Raina" < (b) (6)

Subject: Re: Initial editorial feedback for manuscript NRMICRO-18-165V1

Call next week sounds good too, let me know what times look good.

On Nov 13, 2019, at 11:03 AM, Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote:

Guess we need to increase the scope a bit, we have gotten a bit more room as well,

Kevin: the first part, viral diversity in bats, is your expertise, do you think you can come-up with smtg reasonably succinct while we start revising the other parts.

Maybe a quick call next week to discuss?

Cheers,

Vincent

From: "ursula.hofer1@nature.com" <ursula.hofer1@nature.com>

Reply-To: "ursula.hofer1@nature.com" <ursula.hofer1@nature.com>

Date: Wednesday, November 13, 2019 at 12:25 PM

To: " (b) (6) < (b) (6)

Subject: Initial editorial feedback for manuscript NRMICRO-18-165V1

Dear Vincent,

Manuscript number: NRMICRO-18-165V1

Title: Bat-borne viruses: mechanisms of spillover and emergence

Authors: Vincent Munster, Michael Letko, Stephanie Seifert, Kevin Olival, and Raina Plowright

Submission date for revisions: 13th January 2020

I hope this e-mail finds you well. Below I have provided some initial editorial feedback on your article before peer review. At this stage, my aim is to focus on the overall structure, flow and clarity of the manuscript, so my comments are intended to improve these aspects before the article is seen by referees. Please feel free to discuss any of the suggested changes with me.

I've discussed your article with Andrea and we both had expected a slightly broader scope; in particular, many of our readers won't be familiar with the diversity of viruses found in bats and what makes these animals unique host. I think this information needs to be spelled out for readers to appreciate the discussion of emergence.

My specific suggestion would be to add two new main sections: a first one right after the introduction that discusses viruses found in bats. You mention some that have spilled over to humans in the introduction. Can you expand on that? Are there other viruses with the potential to infect humans? Do bats have more diverse viruses than other animals? How well do we understand the diversity of bat viruses? To complement this section, you could add a table on bat viruses with subsections, e.g. on viruses directly emerged from bats, indirectly emerged, with proposed links to bats (e.g., I seem to remember some discussion of ZIKV in bats) etc.

After this section on diversity, I would suggest to have a section on virus infection bats, which would include the section you already have on innate immunity and add more details (is there more to say about the IFN pathways in bats?). In addition, is there anything to say about adaptive immunity? Also, you could mention recent literature describing the role of metabolism and flight in relation to immunity and viral infection. Finally, it would be good to then link immunity and metabolism to viral persistence and shedding. You could have a schematic figure for this section that highlights some of the unique features of bat immunity (e.g., something like the figures in this review: https://www.mdpi.com/1999-

## 4915/11/2/192).

I realise that this means quite a bit of new text and I'm fine with extending the word limit to ~5500. You could also streamline the spillover/barrier sections a little, e.g. by shortening or removing the knowledge gap and limitations sections (some of the things like need for better models, systems and reagents are mentioned repeatedly; instead of having all these sections on limitations you could mention this once in the bat model box or in the conclusions).

Finally, to reflect this broader scope, I'd suggest changing the title to 'Bat-borne virus diversity, spillover and emergence'.

I hope all of this makes sense! I'd be happy to give you a call if that would be helpful.

I would be grateful if you could return a revised version of the article to me by 13th January 2020.

If at any time you think you will be unable to meet this deadline, please contact me at your earliest convenience to discuss a new date.

Please use the following link to upload your revised manuscript:

https://mts-nrmicro.nature.com/cgi-

bin/main.plex?el=A5Z2CNM2A7TyV6J2A9ftd9SfKV5ozalV07IZDg5exPwZ

Thank you very much for all your hard work on this piece so far. Please don't hesitate to contact me if you have any questions or wish to discuss any points in this letter. Finally, I would be very grateful if you could acknowledge receipt of this e-mail and confirm whether you will be able to return your revised draft by the suggested date.

Best wishes, Ursula

Ursula Hofer, MD PhD Chief Editor, Nature Reviews Microbiology 4 Crinan Street London N1 9XW

e-mail:ursula.hofer1@nature.com tel: +44 (0)20 7014 6648

http://www.nature.com/nrmicro

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From: Munster, Vincent (NIH/NIAID) [E] Sent: Wed, 13 Nov 2019 11:57:14 +0100 To: Plowright, Raina; Alison Peel Cc: Subject: (b) (4) Re: Yes would be interested, but have to think about capacity (currently lacking). Need to think a bit about available assays or whether we need to develop a completely new assay (single test). (b) (4) How many targets are we generally looking for? Obviously, I have to look into assays and actually lab-bandwidth, we are currently swamped with (b) (4) work, as everybody seems to be coming to us for their respective projects (not necessarily a bad thing though \,\[ \], but the timeline could be quite longer as we need to make sure that the gateway criteria of PREEMPT are met). Let's set-up a call soon, now at WHO in Geneva and then onwards to African CDC, Cheers, Vincent From: "Plowright, Raina" < (b) (6) Date: Wednesday, November 13, 2019 at 4:50 AM (b)(6)To: Alison Peel < (b) (6) (b)(6)Cc: ' (b) (6) < (b)(4)Subject: Re: A great summary Ali! Yes, a positive chat with the CVO. She trusts us and sees the value of the research for managing disease. She definitely seems willing to go into bat for us (the wooden kind of bat)! Raina

On Nov 11, 2019, at 3:36 PM, Alison Peel < (b) (6) wrote:

Hi Vincent,

Not sure if you've spoken with Raina, but we had a good chat with the NSW CVO, Sarah Britton, last

week about our progress so far and future plans. She is open to broader PMV work, though it would need to be put forward as a case to the Australian CVO, Mark Schipp. She thinks there is a much greater likelihood of getting clearance to look at known PMV than unknowns, but we may be able to get approval to do family-level PMV PCRs to target our more specific screening.

It would be good to hear your thoughts on a whole range of things (rough brainstorm below)

<ul> <li>what your primary interests are if we had greater scope in this area (keeping in mind</li> </ul>	that
detecting novel viruses is going to be more contentious than	(b) (4)
what capacity you and your team have to take on    (b) (4) (I've he	eard that
this is not as sensitive, so we would likely miss positive samples if we were to only do specific testing on the samples that were positive on the family-level PCR. Perhaps it suited to identifying sessions (b) (4) then targeting those sessions more specifically? What are you thoughts on this?).	may be
<ul> <li>whether you still have an interest in this if the sequencing cannot happen in the US</li> </ul>	(b) (4)
	(1) (1)
whether you have interest in/capacity to expand	(b) (4)
I am working with Ina Smith and Lee McMichael at the moment We had planned to do this back in	(b) (4) Australia.
Essentially, what are your interests and capacity and what opportunities do you envisage?	
This overlaps to a degree with the (b) (4) by the Sydney Uni/Ina S	mith, so
there is still the possibility of doing the more politically sensitive work with them or AAHL.	
If it's easier to chat through this over a zoom call than back and forth emails, I'd be happy to week sometime.	chat next
Cheers	
Ali	

From: Plowright, Raina

**Sent:** Fri, 8 Nov 2019 14:42:19 +0000

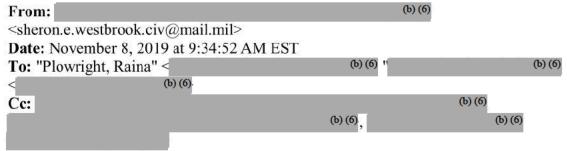
To: Munster, Vincent (NIH/NIAID) [E]; Seifert, Stephanie (NIH/NIAID) [E]
Subject: Fwd: IACUC protocol 2019-038-E, proposal DOINBC-6458.10, Award

DA18AC00031

Great news! It should move quickly now.

Sent from my iPhone

Begin forwarded message:



Subject: IACUC protocol 2019-038-E, proposal DOINBC-6458.10, Award DA18AC00031

Good morning Dr. Plowright and Dr. Seifert,

The protocol titled, "Experimental Nipah and Hendra virus infection in Artibeus jamaicensis bats," IACUC protocol 2019-038-E, proposal DOINBC-6458.10, Award DA18AC00031, is currently under review for compliance with Federal and Department of Defense regulations and guidelines pertaining to the use of animals.

After completion of preliminary review, the following information or clarifications are requested.

- 1) Appendix 5, Personnel: I do not see the protocol PI listed in this section of the AUCRO Appendix. Is it correct to assume this individual is not an animal handler?
- 2) Appendix 5, Personnel: All personnel listed in this section of the Appendix do not appear to be listed as approved personnel in the IACUC approved protocol submitted to ACURO for review. Please provide IACUC communication to confirm all personnel listed in the Appendix are approved to handle funded animals.
- 3) Appendix 10.a, Regulated Species: This section is checked no for "does the protocol involve Animal Welfare Act-regulated species?" Is this a typographical error? It is my understanding that the funded bats are purpose bred which would categorize them as a regulated species.
- 4) Protocol Page 5, Temperature Transponder Placement: When is the temperature transponder

placed in relation to study procedures?

- 5) Protocol Page 5, Anesthetic Monitoring and Recovery: Please describe intraprocedural monitoring used to ensure DOD funded animals will be maintained at an appropriate anesthetic plane during procedures and please briefly describe monitoring procedures employed during the anesthetic recovery period from completion of the procedure(s) to the animal becoming ambulatory.
- 6) Protocol Page 7, Humane Endpoints: Weight loss is listed as early removal criteria, please identify how often animals will be weighed.]
- 7) Protocol Page 7, P/D Category: Two bats are assigned to p/d category C when it appears that all bats undergo cardiac puncture under anesthesia prior to euthanasia as described on protocol page 4. Is cardiac puncture under sedation performed prior to euthanasia? If so, please provide communication from your IACUC that cardiac puncture is a procedure that is considered a USDA p/d category C procedure.

Please keep in mind that no DOD funded animal work may be performed until approved by the ACURO. Please do not hesitate to contact me with any questions or concerns.

The Animal Care and Use Review Office is experiencing a high volume of protocol submissions. As a result, the time it takes to review your submission or respond to your message could be longer than you may be accustomed to. ACURO expects this decreased staffing to lengthen review times throughout the next several months. We apologize for any inconvenience.

Thank you for your patience and understanding through this review process.

Thank you,

Sheron

(b) (6)
Office of Research Protections (ORP)
US Army Medical Research and Development Command (USAMRDC)
Animal Care and Use Review Office (ACURO)
(b) (6)
Phone: (b) (6)
Fax: (301)619-4165
(b) (6)

 From:
 Munster, Vincent (NIH/NIAID) [E]

 Sent:
 Thu, 7 Nov 2019 13:50:02 -0700

To: Letko, Michael (NIH/NIAID) [F]; Seifert, Stephanie (NIH/NIAID) [E]; Kevin Olival,;

Plowright, Raina

Subject: FW: Receipt of Review for Nature Reviews Microbiology - NRMICRO-18-165V1

Lets hope we get some good reviews back!

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: "a.dutoit@nature.com" <a.dutoit@nature.com>
Reply-To: "a.dutoit@nature.com" <a.dutoit@nature.com>

Date: Thursday, November 7, 2019 at 1:43 PM

To: ' (b) (6) < (b) (6)

Subject: Receipt of Review for Nature Reviews Microbiology - NRMICRO-18-165V1

Dear Dr Munster,

Thank you for submitting your Review entitled "Bat-borne viruses: mechanisms of spillover and emergence" to Nature Reviews Microbiology.

Your Review has been assigned the following tracking number: NRMICRO-18-165V1.

We will be in touch again as soon as we have had a chance to look through your submission. In any communication about your manuscript, please quote this manuscript tracking number: NRMICRO-18-165V1.

You may track the status of your submission by clicking on the link below. Once you have logged in, you should access your "Live Manuscript" folder and then click on the "Check Manuscript Status" link.

# HOME LINK:



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Dr. Andrea Du Toit Senior Editor Nature Reviews Microbiology

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From: Plowright, Raina

**Sent:** Wed, 6 Nov 2019 23:34:00 +0000 **To:** Letko, Michael (NIH/NIAID) [F]

Cc: Kevin Olival; Munster, Vincent (NIH/NIAID) [E]; Seifert, Stephanie (NIH/NIAID)

[F]

Subject: Re: Nat rev microbiology

Attachments: 2 NRM DRAFT 10\_24\_19 VM\_ML\_KJO\_RKP.docx

Mike — paper is fantastic! Such an interesting read and addresses key issues in this field. Full of information that would be impossible to get from any other single source. I hope this flies through review.

I got to the end and then went back to the paragraph on 'one health' to write a few sentences to round this out (I think the root cause of bat-virus spillover, as usually being habitat/resources/environmentally driven is missing from this section...) but I have to run to my next flight now (and I still have to write a talk for tomorrow so need to spend the next flight doing this). take a read and if you think this section fits into the paper, I'll craft it...& if I get my talk done in time I'll shoot you something from my cell phone.

Thanks again for including me.

Raina

On Nov 6, 2019, at 12:55 PM, Plowright, Raina < (b) (6) wrote:

Mike — On flight now and will get it to you on other side. Sorry my schedule this week has been impossible.

Raina

Sent from my iPhone

On Nov 4, 2019, at 3:21 PM, Letko, Michael (NIH/NIAID) [F] < (b) (6) wrote:

Awesome. I like your re-write of the conclusion and have incorporated the changes.

Michael Letko, Ph.D
Postdoctoral IRTA
Dr. Vincent Munster Laboratory
Virus Ecology Unit, Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH
903S 4th Street
Hamilton MT 59840

(b) (6)

From: Kevin Olival < (b) (6)

Date: Monday, November 4, 2019 at 1:12 PM

To: "Munster, Vincent (NIH/NIAID) [E]" < (b) (6) "Letko, Michael (NIH/NIAID) [F]" (b) (6)

Cc: "Plowright, Raina" (b) (6) (NIH/NIAID) [F]" < (b) (6)

Subject: Re: Nat rev microbiology

Michael and all,

Great job on this! ATTACHED MY EDITS AND FINAL COMMENTS!

Cheers, Kevin

## Kevin J. Olival, PhD

Vice President for Research

EcoHealth Alliance 460 West 34th Street – 17th floor New York, NY 10001

(b) (6) (direct) (b) (6) (mobile) 1.212.380.4465 (fax) www.ecohealthalliance.org

EcoHealth Alliance leads cutting-edge research into the critical connections between human and wildlife health and delicate ecosystems. With this science we develop solutions that promote conservation and prevent pandemics.

On Nov 4, 2019, at 10:34 AM, Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote:

Thanks guys, hope you're feeling better Kevin!

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: "Plowright, R	laina" <	(b) (6)		
Date: Monday, Nov	rember 4, 2019 at 8:3	1 AM		
To: "Kevin Olival," <		(b) (6)		
Cc: "	(b) (6) <	(b) (6)	Michael Letko	
<	(b) (6) "Seifert, Step	hanie (NIH/NIAID) [F]	]" <	(b) (6)
Subject: Re: Nat rev	/ microbiology			
Good plan. I read thre Kevin, hope you are f	75.0 50 54	nk it doesn't need mud	:h work, so I'll try not	t to hold you up.
On Nov 4, 2019, at 8:	28 AM, Kevin Olival <		(b) (6) wrote:	
I'll try and get to this	today and provide som	otop that needed repai ne light edits. Raina, pro send our comments fo	obably best we just v	work
Cheers, kevin				
On Nov 4, 2019, at 10	:20 AM, Munster, Vind	cent (NIH/NIAID) [E] <		(b) (6) wrote:
Hi guys,				
Let us know what the	status on this is, we w	ould like to get this sul	bmitted by Wednesd	lay,
Cheers,				
Vincent Munster, PhI Chief, Virus Ecology S	Section			
Laboratory of Virolog Rocky Mountain Labo	58M			
	NO ACTUAL MANAGEMENT			

NIAID/NIH

## 1 Title:

2 Bat-borne viruses: future perspectives on the mechanisms of spillover and emergence

3

- 4 Future perspectives on bat virus ecology, molecular mechanisms of zoonosis and
- 5 surveillance.

6 7

## Authors:

8 Letko, M., Seifert, S., Olival, K.J., Plowright, R.K., Munster, V.

9

### 10 Abstract

- 11 Most viral pathogens in humans have animal origins and arose through cross-species
- 12 transmission. Over the past 50 years, viruses including Ebola, Marburg, Nipah, Hendra
- 13 SARS-CoV and MERS-CoV have all been linked back to various bat species. Despite
- 14 decades of research into bats and the pathogens they carry, the fields of bat-virus ecology
- and molecular biology are still nascent, with many questions largely unexplored, hindering
- our ability to predict the next viral outbreak. Here we review the latest advancements and
- 17 understanding of bat-bo rne viruses, reflect on current knowledge gaps and outline
- 18 potential routes forward.

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### Introduction

- 21 Bats have been identified as natural reservoir hosts species for several emerging
- 22 infectious diseases capable of inducing severe pathology in humans, including RNA
- 23 viruses such as Marburg virus, Hendra virus, Sosuga virus, Nipah virus, and Severe

Commented [PR1]: What is a 'future perspective'? I would keep it simple "Bat-borne viruses: mechanisms of spillover and emergence"

Commented [MOU2]: Not convinced any of these are the right title that captures this review, but took a stab at some ideas. I think it should reflect the specific focus of moving from the discovery phase of bat research, into the "future" that includes understanding the molecular basis for zoonotic spillover, and turning data into something relevant to public health action. Depending on this exact focus, I can help add another section on the future of understanding bat-human interactinos (e.g. behavioral risk work) and maybe Raina, Vincent and I could flesh out a "future of" bat viral ecology/dynamics section a little more.

Commented [MOU3]: "anticipate and prepare for"? Not just about prediction, but in helping prepare for by developing treatments, vaccines etc (for molecular biology component)

Commented [MOU4]: Bit vague.

Commented [MOU5]: Just expanding the list, feel free to

Acute Respiratory Syndrome Coronavirus (SARS-CoV). In addition to direct isolation of these human pathogens from bats, accumulating evidence strongly suggest that other related viruses such as Ebola viruses and Middle East Respiratory Coronavirus (MERS-CoV) also originate in bats1-3. Across mammals, bats are known to harbor a higher overall viral diversity and proportion of viruses that are zoonotic than other orders - flagging them as an important taxonomic group for global viral discovery and zoonotic disease surveillance efforts<sup>4</sup>. These efforts, ultimately aimed at predicting and preventingidentifying and mitigating against future bat-borne disease emergence events, have resulted in thousands of novel bat-derived viral genomic sequences published over the last decade. However, little progress has been made toward translating sequence data from novel viruses into a risk-based framework to quantify zoonotic potential and elicit public health action. Further confounding this effort is an incomplete understanding of the animals themselves, their distributions, behaviors, and interactions with the environment and the epidemiological processes that allow contact with humans. Here we review the current state and knowledge gaps of bat-virus ecology and the molecular barriers to zoonotic disease emergence; we also review advances and challenges in pandemic preparedness and provide a framework for addressing critical deficits in our understanding of bat-borne viruses.

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Box 1: Bat ecology

Bats are the second most diverse mammalian Order on earth, comprising approximately

22% of all named mammal species, with populations on every continent except Antarctica

5. Significant gains have been made in understanding bat viral ecology over the last two

Commented [MOU6]: I think best to save this WHO R&D blueprint for discussion?

Commented [LM([7R7]: Agreed

Commented [PR8]: Their distributions, behaviors, and interactions with the environment and the epidemiological processes that allow contact with humans.

Commented [LM([9R9]: Nice!

Commented [PR10]: Deleted bc was repetitive with previous sentence

Commented [LM([11R11]: agreed

Commented [MOU12]: Wonder if this is best served as a "box" or if we should also/instead integrate more ecological framework in the main text. As it stands, the text is largely molecular mechansims of infection (which is great, and something not covered as much in previous reviews) – just something to think of for the abstract and title of paper.

Commented [LM([13R13]: I think we should keep it as a box for now.

Commented [MOU14R13]: OK!

decades, yet this knowledge remains limited to a handful of species, and the extremely diverse ecology, biology, and life history traits of bats pose a challenge when extrapolating data from any one species or population to bats more broadly. Beyond the within-host process that can limit susceptibility and viral shedding, ecological factors can facilitate or inhibit virus spill over spillover. The most revealing ecological studies thus far have employed hypothesis-driven field-sampling schemes, critically targeting specific reservoir hosts through time and space Data from these targeted, longitudinal studies, combined with mathematical modeling, have revealed that the frequency and synchronization of reproduction in a reservoir species can influence the prevalence and persistence of viruses within and between bat populations<sup>7,8</sup>, as can change in land-use. particularly when such changes lead to nutritional stress9. Longitudinal datasets have revealed seasonal patterns in spill-overspillover or shedding of Nipah virus in Bangladesh<sup>10</sup>, Hendra virus in Australia 11-13, Marburg virus in Uganda<sup>7</sup>, and Ebola virus spill-overspillover events in Central Africa<sup>14</sup>, though the ability to predict spill-overspillover events on a finer scale remains elusive. Recent efforts to develop rigorous statistical models to prioritize surveillance for bat species most likely to serve as reservoir hosts for key viral groups of interest 4.15-17 may provide the insight necessary to maximize sampling efforts and increase the impact of field studies. While environmental and host ecological factors certainly influence the risk of cross species transmission, little is known about the fine-scale host-pathogen interactions of bats and viruses and how variation in host species and viruses at the molecular level influence broader patterns of zoonotic spillover<sup>18</sup>.

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Commented [MOU15]: I typically don't hyphenate "spillover". Depends on how it's being used, or personal pref. Check throughout.

Commented [PR16]: If you don't have reference limits, we just wrote a paper on exactly this topic.

Plowright R.K., D. J. Becker, H. McCallum & Manlove, K. 2019 Sampling to elucidate the dynamics of infections in reservoir hosts. *Philosophical Transactions of the Royal Society B: Biological Sciences*. (DOI:10.1098/rstb.2018.0336).

#### Commented [LM([17R17]: added

Commented [PR18]: Hayman's paper is just a model — there is not field data and the model is based on assumptions that are unlikely to be true. I wouldn't perpetuate the message. I think the Amman paper is excellent. But there is an issue — the field studies show shedding is synchronous with breeding but they don't tell you anything about persistence. Models will give us some inference about persistence. Best modeling paper on this is Peel et al. Birth Pulses. Replace Hayman with Peel.

Peel, A., Pulliam, J., Luis, A., Plowright, R., O'Shea, T., Hayman, D., Wood, J., Webb, C. & Restif, O. 2014 The effect of seasonal birth pulses on pathogen persistence in wild mammal populations. *Proceedings of the Royal Society B: Biological Sciences* 281, 20132962.

#### Commented [LM([19R19]: replaced

Commented [PR20]: "have revealed seasonal patterns in spillover"

Commented [LM([21R21]: changed

Commented [PR22]: References:

### Best one:

Páez, D., Giles, J., McCallum, H., Field, H., Jordan, D., Peel, A. & Plowright, R. 2017 Conditions affecting the timing and magnitude of Hendra virus shedding across pteropodid bat populations in Australia. *Epidemiology & Infection* **145**, 3143-3153.

#### If room for more:

Plowright, R. K., Eby, P., Hudson, P. J., Smith, I. L., Westcott, D., Bryden, W. L., Middleton, D., Reid, P. A.,

#### Commented [LM([23R23]: Added

Commented [PR24R23]: If you add word SPILLOVER as Kevin suggests, then the refs I suggested are not correctThe only paper that examines spillover patterns is Plowright et

Commented [MOU25]: Please also cite:

https://www.nature.com/articles/nature22975 and https://www.biorxiv.org/content/10.1101/732255v2

Commented [LM([26R26]: Done

Commented [PR27]: We wrote a paper on this that I think will be useful for this review:
Plowright, R. K., Peel, A. J., Streicker, D. G., Gilbert, A.

Commented [LM([28R28]: added

## Viral entry as a barrier to cross-species transmission

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All viruses, regardless of classification or origins, must be able to subvert and overcome various molecular factors within the host in order to replicate and spill over into a new species. Every stage of the viral life cycle relies on numerous protein interactions with the host-cell, including viral binding and entry, recruitment of host factors essential for viral replication, suppression of antiviral host factors, assembly and egress from the cell and evasion of the host immune system (Fig. 1)19. Viral-host protein interfaces have been shown, through functional and structural studies, to be remarkably specific and involve multiple points of contact<sup>20</sup>. Even single amino acid variations in the same protein between different species can dramatically impact or totally abrogate a viral-host protein interaction between different species and form a molecular block, or species barrier, to viral replication 21-26. The complexity of these viral-host protein interactions is compounded by number of sites. Recent proteomics studies have identified at least 194 protein interactions between Ebola virus and the host cell<sup>27</sup>, 198 virus-host protein interactions for Zika virus<sup>28</sup>, 101 for Nipah virus<sup>29</sup>, and over 300 virus-host interactions for iInfluenza A virus<sup>30</sup>. Given that even small perturbations in these complex networks of virus-host interactions can mean the difference between a dead-end infection or viral emergence in a new host species, it is likely the majority of animalbat-borne viruses fail to infect novel species as a result of within-host barriers<sup>31</sup>.

90 Trends in zoonotic viral entry. One of the first major virus-host protein interactions that 91

occurs during the course of infection is at the level of viral entry, when the virus interacts with the host receptor to facilitate release of viral components into the cytoplasm. Commented [M[29]: So i think the introduction needs to be reformatted quite a bit, i think will be essential to move from currently known bat diversity, e.g. xx virus families, xx viruses and then make the link to known spillovers in the intro. E.g. rabies, filo's henipa's etc

Commented [M[30]: its written a bit generically for emerging viruses in general, try to focus on bring it back to bat-orne viruses, are they different from e.g. rodent or birdborne infections?

Commented [MOU31R31]: Agree, good thing to consider in each section. If we can dig up more bat-borne virus examples, better yet, though I suspect for some fields we highlight not much known.

Commented [LM([32R31]: Nothing about species barriers is really "unique" to bat viruses except how little we know about species barriers and bat viruses - which is a big point of this whole section

Commented [PR33]: Our Nature Reviews paper: Plowright, R. K., Parrish, C. R., McCallum, H., Hudson, P. J., Ko, A. I., Graham, A. L. & Lloyd-Smith, J. O. 2017 Pathways to zoonotic spillover. Nature Reviews Microbiology 15, 502.

Commented [MOU34]: Wondering if we should add a Stage 5 to Fig 1 (after 4. Assembly and egress) that is focused on what the host immune system does after the virus leaves the cell. This could be a way to schematic what is known about bat immunity? Could get complex, but something to consider.

Commented [LM([35R35]: Updated the figure

Commented [PR36]: Another good one is Parrish: Parrish, C. R., Holmes, E. C., Morens, D. M., Park, E.-C., Burke, D. S., Calisher, C. H., Laughlin, C. A., Saif, L. J. & Daszak, P. 2008 Cross-species virus transmission and the emergence of new epidemic diseases. Microbiology and Molecular Biology Reviews 72, 457-470.

Commented [PR37]: "can impact or abrogate" would be stronger IMO (less drama makes it more dramatic!) ©

Commented [PR38]: Not sure what this means

Commented [PR39]: Really cool stuff!

Commented [PR40]: This would be the case with the majority of ALL viruses (because of a series of barriers, not just virus host interactions). We discuss this towards the end of this paper:

Plowright, R. K., Parrish, C. R., McCallum, H., Hudson, P. J., Ko, A. I., Graham, A. L. & Lloyd-Smith, J. O.

Commented [PR41]: How these interrupt flow of pathogen between species would depend on how many of these interactions are species specific. Many interactions

Commented [MOU42]: Change to: "Current understanding of bat-borne and other zoonotic virus cellular entry"? Not sure these are "trends"?

Commented [MOU43]: Cell entry?

Depending on the virus, this process can involve one or more viral proteins, one or more host components, and encompass multiple steps occurring at either the cell surface or from within an internalized membrane.

It is not surprising that many bat-borne zoonotic viruses have evolved to use highly conserved host molecules for cell entry that have little genetic variation between different species. Henipaviruses bind to the ephrin family of signaling proteins<sup>32-34</sup>, Filoviruses bind to the cholesterol transporter, Niemann-pick C1 (NPC1)<sup>35,36</sup>, and Betacoronaviruses have been shown to bind various common cell-surface proteases, including angiotensin-converting enzyme 2 (ACE2) in the case of SARS-CoV<sup>37</sup> and dipeptidyl peptidase IV (DPP4) in the case of MERS-CoV<sup>38</sup>. Indeed, these receptors are nearly identical, at least in the regions that interact with the virus, between various bat species, intermediate host species such as camels and palm civets and humans.

Total blocks to cell entry are not easily overcome by viruses. For example, wildtype mice are completely resistant to infection with MERS-CoV because of differences in murine DPP4 glycosylation from human DPP4<sup>39</sup>. Despite great effort from the animal disease-modelling community, to date there is no MERS-CoV isolate capable of utilizing wild-type murine DPP4; likely because too many viral adaptations are necessary. Partial blocks to cell entry, however, are more easily overcome. Recently, it has been shown that MERS-CoV can rapidly acquire single point mutations to increase compatibility with different bat species' DPP4<sup>26</sup>. Some MERS-related CoVs discovered in bats, which appear nearly identical to MERS over most of the genome, have mutations at key binding sites across the receptor-binding spike glycoprotein and are thus unable to bind to the DPP4 receptor and likely pose a low zoonotic risk<sup>40</sup>. Similar types of viral adaptation have been observed

Commented [MV([44]: Intermediate host species? Like palm civets and dromedary camels?

Commented [M[45]: so conceptually, there is need for explaining the viral diversity in bats, this is obviously one mechanism that relatively little adaptations are needed to allow replication in another bat host and it would be onward to new lineage of viruses. The link could be amde with all the different mers-cov-like or SARS-like viruses found in bats.

Commented [SS46R46]: This is a minefield, the topic of global patterns of taxonomic diversity has been discussed for ages; explaining the mechanism for the latitudinal diversity gradient (which bats and viruses typically follow) is one of the most hotly debated questions in biogeography. I don't think we should blunder into the field with a poorly developed hypothesis given how restrictive this manuscript is on space – we cannot answer this question well in a couple of sentences and any more than that will be incongruous with the rest of the manuscript.

for other zoonotic viruses such as SARS-CoV41, parvoviruses42, and avian influenza A virus<sup>43</sup>. Taken together, the ability to use conserved host receptors and quickly adapt to small variation between species are two characteristic hallmarks of viruses which have spilled over into the human population. The genetic diversity of many RNA viruses can be attributed to high mutation rates, short generation times, and the strong selective pressure of the host environment; however, positive stranded RNA viruses, including SARS-CoV and MERS-CoV have relatively low mutation rates associated with 3'-5' exoribonuclease proofreading activity. The rapid evolution of coronaviruses to the host environment is largely driven by high rates of genetic recombination which facilitates the acquisition of multiple mutations in a single event, which can have dramatic effects on viral adaptation to new host environments. Recent phylogenetic analyses have revealed that the variation in MERS-CoV circulating in camel populations is largely driven by recombination<sup>44-47</sup>. While SARS-related coronaviruses (SARSr-CoVs) have been identified and isolated from bats, no single batisolate perfectly matches the human strains. For example, some SARSr-CoV have been shown to utilize the human receptor but vary drastically from SARS-CoV in the 3-prime end of their genome, while other SARSr-CoVs are nearly identical to SARS in this region but fail to interact with the human receptor<sup>48</sup>. In further support of these findings, the entire SARS-CoV genome has now been sequenced across multiple separate but related viruses circulating in bats, strongly suggesting the human virus is a recombinant form of these ancestral elder variants<sup>49</sup>. The ability of these SARSr-CoVs to recombine and emerge in human populations is supported by recent serological findings showing human exposure to SARSr-CoVs in rural communities in China occurring after the 2003 SARS

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Commented [SS47]: Adaptation implies selection, mutations occur regardless of selective pressures.

Commented [MV([48]: Ancestral? Or variants circulating in the bat populations?

Commented [PR49]: This is super interesting!

Commented [PR50]: How does serological finding give evidence for recombination? Evidence for emergence --yes. I may be missing something -- why this is evidence for recombining—does the serology tell you it is a recombined form?..

outbreak<sup>50</sup>. Outside fo the coronaviruses, recombination in the rabies virus glycoprotein was shown to facilitate cross-species transmission from bats to skunks and raccoons<sup>51</sup>. Thus, in addition to the rapid mutation rate characteristic of many RNA viruses, recombination provides an additional mechanism to rapidly overcome barriers in novel host species.

Knowledge gaps in viral entry. The biggest limitation to studying entry of novel, animal-derived viruses is identifying cell lines that are permissive for viral infection. For example, isolation of bat-derived coronaviruses has been challenging as most bat-derived coronavirus viruses do not infect the due to a limited ability to infect standard, typically primate-derived, cell lines used for virus isolation 40,52,53. Further, even cell lines derived from the same bat species that the viruses were originally sequenced from also often may fail to support replication, likely due to loss of expression of the host receptor 54. Thus, there is an urgent need for more cell culture reagents that can better support virus isolation. Additionally, the bat-host species themselves also need better genetic characterization through whole genome sequencing and annotation, in order to pinpoint genetic factors responsible for viral replication phenotypes. Viral passaging studies in new host species also provides a clear an approach to assessing how viruses adapt and how these adaptations may lead to spill-over. Ultimately, this work will expand our predicative capacity for which animal viruses have the potential to spread to new species.

Post-entry cellular barriers to cross-species transmission

Commented [MOU51]: Wang et al. 2018. doi: 10.1007/s12250-018-0012-7

Commented [SS52]: Herpes viruses are DNA-based, orthomyxos typically reassort rather than recombine (different mechanisms). Might be a citation we can omit for space?

Commented [PR53]: Is there evidence for this in any other bat viruses (or i? Is it something we should look for in particular groups of viruses? The paragraph needs a sentence to put the concept into broader context.

Commented [MOU54R54]: I always assumed that recombination was something conserved at a viral family level, or viral genus?, but agree would be good to give some context on that w bat-borne virus families.

Commented [PR55]: Grammar issue

While our understanding of viral entry as a species barrier is becoming clearer for many emerging zoonotic viruses, cellular blocks beyond entry are more elusive and remain largely unknown. However, research over the past 20 years with well-studied zoonotic pathogens such as lentiviruses including HIV and its evolutionary predecessor SIV, and ilnfluenza A virus which includes aAvian ilnfluenza A vVirus (AIV), has led to the identification of numerous intracellular species barriers in the form of dependency factors, which these viruses rely on to replicate, and restriction factors, which are antiviral proteins expressed at a basal level<sup>55</sup>. For example, the capacity for the SIV accessory protein Vif to antagonize the host restriction factor APOBEC3 is vital in determining potential host breadth in nonhuman primates 56,57. The AIV accessory protein PB1-F2 disrupts mitochondrial antiviral signaling more efficiently in the avian host than the truncated PB1-F2 common in mammalian influenza A viruses<sup>58</sup>. While the post-entry species barriers which limit host breadth for lentiviruses and influenza viruses are likely to differdifferent from those which limit host breadth for the emerging batborne infectious diseases, the research framework for these well-studied host-pathogen systems can serve as a road-map in moving forward with research into bat-borne hostpathogen systems.

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Recent advances with understanding post-entry barriers in bat-borne viruses.

Recent experimental infection studies in bats provided evidence of species-level postentry barriers, suggesting that the some bat-borne viruses are likely host specificic and
may have limited ability to transmit between certain bat species. For example, EBOV and
WIV1-CoV are capable of using the cellular receptors from Rousettus aegptiacus bats to

Commented [MOU56]: We don't actually call out the methods that would be useful for bat virus studies, or specifically how we'll do this. Although I suppose that's in the next section! So maybe a better transition if we get to this next. Maybe "has served as a road map for recent advances in understanding post-entry barriers in bat viruses.."

enter cells, but both viruses fail to replicate efficiently in the case of EBOV or replicate at all in the case of Nipah virus for these this particular animals<sup>25,59,60</sup>bat species<sup>25,59,60</sup>.

While transcriptomics studies have identified various immune signaling pathways that are activated differently in human versus *Rousettus* cells<sup>61,62</sup> other studies have taken more direct approaches to identify post-entry barriers to replication. Mass-spectrometry has pinpointed the host E3-ubiquitin ligase, RBBBP6, as a negative regulator of EBOV transcription that functions by binding VP30, a viral protein that is key in replication<sup>27</sup>. A similar study identified that the key EBOV protein involved in antagonizing the host interferon pathway, VP35, forms an essential interaction with host TRIM6 protein in order to carry out its function, and that disruptions in this interface reduce viral replication<sup>63</sup>. Additionally, tetherin<sup>64-66</sup> and ITFITM host proteins<sup>67</sup>, which have been identified to inhibit lentiviruses and influenza A virus, respectively, have been shown to have broader antiviral effects against EBOV and SARS-CoV. Unfortunately, in contrast to the transcriptomic studies, these more directed approaches only look at post-entry blocks within the context of human cells, so whether or not these proteins play a role in viral replication within bats and how that may translate to pathogen spillover into other species remains to be determined.

Knowledge gaps in post-entry species barriers. Shortly after the 2014 west African Ebola outbreak, several groups identified mutations in the viral glycoprotein (GP) from patient samples<sup>68-70</sup>. Pseudotyped assays revealed that these mutations, alone, enhanced viral entry into human cells and it was concluded that EBOV was further adapting to humans, potentially contributing to the severity of the outbreak<sup>68,70</sup>. However,

Commented [MOU57]: You say NiV here, but ref WIV1-CoV above... need correct one.

Commented [MV([58]: So EBOV actually does replicate, but very inefficient. The wording needs to reflect this

Commented [LM([59R59]: Good point I like the adjusted wording.

Commented [PR60]: "pathogen spillover into other species"

Commented [PR61]: Really enjoying this paper – learning so much! Its going to be a great addition!

Commented [MOU62]: Just realized we should probably spell out somewhere before this (in the intro?) that EBOV is likely bat-borne? With one sentence and some refs. Can cite Leroy et al. Science, and also my review with David Hayman for a summary (although 5 years old now!). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4014719/

Commented [LM([63R63]: Done

the GP mutations were also coupled with several other mutations elsewhere in the viral genome, which were excluded from these studies. When these additional mutations were tested in reverse genetics experiments with full, replication-competent EBOV, the effect of increased entry was diminished and the mutant viruses replicated similar to wild type strains from previous outbreaks<sup>69</sup>. Further, viral isolates from the 2014 outbreak replicated no differently and exhibited no difference in pathology in non-human primates compared to previous viral isolates71. Thus, the true role of these GP and other genomic mutations during infection is likely more complex than initially appreciated. Unfortunately, current work characterizing mutations in emerging viruses is often centered on entry primarily because it is one of the better understood virus-host interactions. This reductionist approach may leave mutations elsewhere in viral genomes understudied. The roles of the majority of non-structural proteins for emerging viruses are still unknown, much less what host factors they may interact with. Therefore, it is crucial to identify and characterize these interactions in order to understand how these viruses adapt-to, replicate-in and transmit-between new hosts. Compared to more well-studied viruses with a zoonotic origin, e.g. iInfluenza A virus and HIV, there is still much to uncover for post-entry species barriers of emergent, bat-derived viral pathogens. Large-scale CRISPR/Cas9-mediated knock out and activation screens in human cells have recently identified specific host-factors that are essential to

flaviviruses 72-74, HIV75, Epstein-Barr virus76, and iInfluenza A virus77.78. While these

screens have been valuable in identifying human proteins involved in viral infection, they

have yet to be applied to other host species, including bats. Given that an annotated

transcriptome is now available for the Rousettus aegyptiacus bat<sup>79</sup>, similar screens could

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Commented [PR64]: Because it is relatively easy to study in vitro?

Commented [PR65]: Because this requires in vivo work that is harder, more expensive, and more difficult to interpret?

Commented [MOU66]: Bit strong?

Commented [PR67]: Another great paragraph! So interesting.

Commented [MV([68]: Think its also available for the Artibeus bats

Commented [LM([69R69]: Let's just keep it with the Rousettus for now as more species genomes are sure to be apportated.

be performed in *Rousettus* cells to elucidate factors involved in filovirus infection, for example. The ambitious Bat1K project has begun the process of generating genome sequence data for all extant bat species<sup>80</sup>, the results of this effort will undoubtedly be an invaluable resource in elucidating specific bat-pathogen interactions.

Classic restriction factors for lentiviruses such as the APOBEC3 family of cytidine deaminsases, tetherin and Trim5a were identified by comparing permissive and non-permissive cells from the same species; in some cases derived from the same parental cell line<sup>81-85</sup>. In contrast, EBOV is capable of replicating in all *Rousettus* cell lines generated to date, hindering efforts to identify cellular factors that may be responsible for inhibiting viral replication in *Rousettus* bats. Isolating more cell lines that are non-permissive to viral infection would greatly increase the toolbox used to identify novel species barriers.

While large scale proteomics studies using mass-spectrometry have identified hundreds of viral-host protein interactions for emerging viruses, there is still a lack of downstream assays to identify which interactions are the most crucial for replication. Additionally, the choice of cells used for these studies may also influence the outcome, as many cell lines are irregular in their gene expression profiles compared to the natural target cells for these viruses.

### Current understanding in bat innate immunity

While viruses such as Nipah and Marburg have been shown, experimentally, to replicate and shed efficiently from their bat host species, a striking feature of these infections is that the bats do not exhibit overt signs of pathology<sup>86-89</sup>. This suggests that the classical

Commented [PR70]: Paragraph coherence: I didn't understand this... above you talk about cell lines, then need to identify factors that can inhibit replication...so I'm not sure which cell lines you are referring to – a new type of cell line that inhibits viral replication?

Commented [MV([71]: What does large-scale mean, typically still limited amounts or replicates, cell types, viruses?

Commented [PR72]: Important point. How much research do we need to view with skepticism because it is done on immortalized cells?

Commented [LM([73R73]: I did not want to explicitly make any statements on this because I think it will upset a lot of people.

Commented [PR74R73]: Fair enough! © I think you state this subtly and perfectly as is.

Commented [MOU75]: Is it "species bariers" or should this be more general, i.e. Current knowledge of bat immunity?

Commented [LM(|76R76]: Current knowledge is more accurate. Changed.

Commented [PR77]: The infection experiments with NiV at AAHL didn't show efficient shedding... I guess depends on your definition of 'efficient'. You may run into less problems with reviewers if you state "have been shown, experimentally, to replicate and shed from their bat ..."

pathology caused by over-activation of the immune system in response to viral infection that is seen in humans and laboratory animal models is not occurring in bats. Thus, the lack of pathology observed in these species is likely coming from a combination betweenof differences in tissue tropism and their immune responses. High Vviral replication and shedding in bats in combination with an apparent lack of disease may allow for efficient maintenance and dissemination of these viruses. Immune signaling pathways have been shown to vary in their level of activation between bat and human cells in response to infection<sup>61,62,90,91</sup>, particularly with filoviruses. How these differences play a role in overall pathology in bats is still to be determined. A notable finding common to all of these studies is that, regardless of the host species, all of the bat cell lines tested support filovirus infection, suggesting that the innate immune pathways assessed in these cell culture assays do not form significant barriers to infection. Broader characterizations of bat innate immunity, in general, have provided some insights into the differences between bat and human immune responses. For example, Pteropus spp. bats have a significantly smaller type I interferon genomic locus compared to other mammals, yet they have constitutive basal expression of their IFN-a genes, regardless of stimulation<sup>92</sup>. Additionally, compared to Rousettus bats, which have a more diverse type I interferon locus and strongly induce type I interferon in response to viral infection<sup>93,94</sup>, Pteropodid bats mount a stronger type III interferon response<sup>95</sup>. Knowledge gaps in bat innate immunity. The studies described above provide mounting evidence that the bat innate immune system and its response to viral infection

varies from other mammals, and also between two closely related bat genera in the family

Pteropodidae: Rousettus and Pteropus. However, given that there are 21 bat families,

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**Commented [MOU78]:** What about non human primates or other animal models?

Commented [LM([79R79]: Included

Commented [MV([80]: Define high, lot of viruses are actually not really shed very high as opposed to the shedding/replication observed in humans. Seems to be a fine-tuned mechanism of shedding sufficient for transmition and limited activation of the immune reponse so no disease

Commented [LM([81R81]: Maybe better to avoid using that word at all. It's kind of arbitrary and opens us up to further questions.

Commented [PR82R81]: Good call.

Commented [MOU83]: Bat cell lines?

Commented [LM([84R84]: Clarified.

Commented [PR85]: I went back to this paper to check but hard to tell which experiments were done on lightly passaged cells vs immortalized kidney cells. Given the different finding in Rousettus, should we be skeptical that results may be influenced by the genetic changes that occur during immortalization?

Commented [LM([86R86]: I agree that the difference may be an artifact of cell culture. I call attention to this issue in the knowledge gaps section but refrained from calling out this paper directly.

Commented [PR87R86]: Good idea.

and over 200 genera and 1400 extant species of bats, conclusions regarding general features of bat immunity should be reserved. Most bat immunology studies to date have relied on cell culture systems using transformed, commonly available cell lines - often derived tissue-specific fibroblasts, which are not considered the initial target cell type of the viruses studied. Thus, there is a need for cell lines that are more reflective of the natural course of infection in bats, and in otherwise developing bat-specific reagents for immunology studies. Filoviruses, for example, are believed to initially infect dendritic cells and macrophages during early infection, which have only rarely been studied from bats96. One common cell line used as a surrogate for human kidney cells in these filovirus immunity studies includes 293T cells - a human embryonic kidney derivative that has also been shown to express neuronal tissue markers97, and contain massive chromosomal rearrangements, deletions and polyploidy98. How these abnormalities influence the transcriptional regulation of immune genes in response to infection is unknown, but they likely provide an incomplete picture of natural infection. Furthermore, as the host reservoirs for many filoviruses have yet to be identified, selecting cell lines from a single or very few bat species based on partial surveillance data1,16 is not sufficient for drawing broad conclusions. A major problem facing all studies of bat-derived virus cell biology is the lack of available reagents and animal models (see Box 2), compounded by the enormous taxonomic diversity of these animals. Moving forward, it is the existing repertoire of available cell lines should be expanded to include a broader range of bat species, tissue origins and cell types. In addition, organoid systems withincorporating their-multiple cell-types within a three-dimensional architecture to reproduce-and tissue-specific functional properties

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Commented [MOU88]: The most up to date taxonomy is Nancy Simmons new website/list. batnames.org

Commented [PR89]: Have you tried to isolate these cells from bats? My colleague Diane Bimczok at MSU works with these cell types in humans. Would be cool to get these for hats

Commented [LM([90R90]: We have not tried to isolate dendritic cells yet, but have a postdoc starting soon who will try!

could potentially facilitate the translation from in vitro single cell-type data into more organ—specific host-pathogen interaction studies. FurtherLastly, live animal models will also be crucial to understanding how the molecular findings in bat cells play a role in the course of infection in the natural host.

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## Box 2: Bats as animal models

While a growing number of laboratories are studying emerging infectious diseases from bats in laboratory settings, there are few examples of bat species being successfully established as animal models. This is in part due to unique handling requirements for volant animals, challenges with keeping many insectivorous bats fed and healthy, and difficulties in meeting complex behavioral adaptations (e.g. hibernation for temperate bats). These challenges are compounded by limited availability of breeding stock, regulations on importation of live animals, and the high costs of maintaining animals in BSL 3 or 4 facilities. Nonetheless, several bat species have been established as animal models, including Pteropus spp. for Nipah and Hendra virus, Eidolon helvum for African Henipaviruses, Rousettus aegyptiacus for MARV, Artibeus jamaicensis for Zika, MERS-CoV and Rabies, and Myotis lucifigus for white nose syndrome 59,86,99-102. These studies have led to valuable discoveries, for example showing that Rousettus aegyptiacusthe Egyptian fruit bat from which Marburg virus was isolated, are refractory to infection with many other viruses that are associated with other bat reservoir species 14,59,60,87,89, raising the question of their broad utility in disease pathology modeling. Beyond the technical challenges of working with these animals, a bigger issue with bats as animal models lies in our fundamental approach to disease modelling: almost all current established animal

Commented [PR91]: It would be good to emphasize the importance of in vivo studies in bats (given incongruous findings such as constitutive expression of INFa in one cell line but not another cell line from another spp.). could also mention the difficulty of getting bats and expense of keeping them in BSL4 where need to do these experiments.

Commented [MOU92R92]: Bat behavior is also not conducive to captivity, never mind the cost and BSL requirements. Could be a point worth noting – hard to keep volant animals in small spaces!

Commented [LM([93R92]: 1 like the changes!

Commented [PR94R92]: Good point. Artibeus may be one of only spp where this is relatively easy (small size, fruit eating, non hibernating).

Commented [MOU95]: Maybe cite Tony Schountz review from 2014 in this section? <a href="https://www.mdpl.com/1999-4915/6/12/4880">https://www.mdpl.com/1999-4915/6/12/4880</a>, see section 5.1

## Commented [MOU96]:

https://www.sciencedirect.com/science/article/pii/S00219 9750700031X

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https://www.ncbi.nlm.nih.gov/pubmed/22049055

Commented [MOU97]: e.g.

https://www.ncbi.nlm.nih.gov/pubmed/31401962

Commented [MOU98]: And other North American species for White Nose Syndrome experimental work.

Commented [LM([99R99]: Added

Commented [MV([100]: Seitching from Rousettus to Egyptian fruit bat?

Commented [LM([101R101]: Corrected. Let's keep the full names throughout.

Commented [PR102]: "With many other viruses that are associated with other bat reservoir species"

Commented [LM([103R103]: Changed

Commented [MOU104]: I think of disease "modeling" a different way, i.e. in silico!

Commented [LM([105R105]: Clarified

models in virology are centered on severe disease phenotypes and high levels of viral replication. This is in contrast to our current understanding of bat-virus biology, where it is presumed that bats exhibit minimal pathology and likely low levels or short temporal bursts, of viral replication. Especially, rRecent experimental infection studies with Tacaribe virus and Lagos bat virus in their respective natural reservoir bat species 103,104, which both showresulted in severe disease and mortality, showing that the often communicated paradigm that bats are resistant to highly pathogenic viruses should be addressed on the level of specific host-pathogen interactions rather than a generalization towards a complete animal order. Comparative immunological, pathological and systems biological studies between animal models offer human disease and bat animal models are needed to understand the mechanistic differences and similaritiesmechanisms responsible for minimal vs the severedifferences in disease phenotypesseverity of batborne viruses observed in the natural reservoir and spillover host species.

Commented [MV([106]: Ref van Tony Schountz, amd ref Suu-Ire: pathogenesis of bat rabies in a natural reservoir

Commented [LM([107R107]: Added.

Commented [MOU108]: GREAT!

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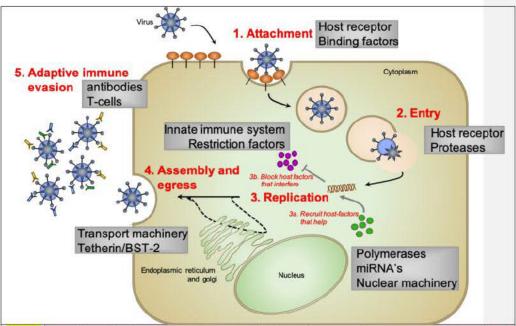


Fig. 1. Overview of molecular host species barriers. Viruses rely on numerous interactions Commented [MOU109]: Made a comment earlier, but with host cell machinery in order to replicate and transmit.

Current virus discovery efforts

The discovery and isolation of SARSr-CoV<sup>53,105</sup>, Nipah virus 106-108 and MARV<sup>14</sup> from bats, in combination with the ever decreasing cost of next generation sequencing technologies, has spawned the current era of viral discovery efforts. Worldwide consortiums such as the USAID PREDICT program, in addition to many independent academic laboratories, have used a combination of consensus PCR screening and deep sequencing to characterize viral genomes from samples taken from healthy bats. This has led to the identification of viruses and genomic sequences closely related to SARS-CoV<sup>53</sup>, MERS-CoV<sup>109</sup>, Rabies virus<sup>110</sup>, Nipah and Hendra virus<sup>111</sup>, and EBOV<sup>112,113</sup> in various bat

Commented [MOU109]: Made a comment earlier, but wondering if we could couple this with a figure showing some basic mechanisms of bat immune response to viral infection, i.e. what happens after Stage 4 when the virus leaves the cell?

Commented [LM([110R110]: Added a step 5 for adaptive immune responses

Commented [MV([111]: Wondering whether we should say smtg about syndromic as well, as the initial mers-cov case was identified by deep sequencing. I wonder whether this is the virus human pathogen, in addition you might then include PEDV here as well?

Commented [LM([112R112]: We could mention that but I don't think it will add much to the concept.

Commented [M]113]: so we are missing half the part here, going from molecular interaction, to cellular intercations but completely missing the in vivo part. special emphasis should be on comparative pathogenicity (this could potentially be in a box format too, this would adress questions of how bats deal with viruses differently than humans (or animal models) in a more hollistic way. Ranging from molecular, tissue tropism, cellular immunity to shedding and transmision.

Commented [LM([114R114]: I added a bit in the bats-asmodels box about how these viruese inherently behave differently in bats with repsect to pathology.

species. Many of these novel viruses are phylogentically related to pathogens of interest 347 348 to public health, however the capacity for these novel viruses to cause future outbreaks 349 remains unresolved. In addition, recent syndromic pathogen discovery in humans and 350 livestock has directly to the identification of novel bat-borne pathogens, such as MERS-351 CoV and PEDV, with significant public and veterinary health and wider socio-economic 352 impact (ref). 353 With viruses isolated directly from bat samples and molecular approaches including viral 354 pseudotype studies and reverse genetics, researchers have been able to demonstrate 355 the potential of novel viruses to replicate in human cells or use human receptors for entry 52,53,114. The discovery and subsequent studies withinvestigations of a novel non-356 pathogenic henipavirus 115, Cedar virus, related to Nipah virus and Hendra virus, from an 357 358 urine sample collected under a flying fox colony in Australia 115, have proved invaluable in revealing the genetic determinants of pathogenicity in henipaviruses. 359 Identification of viruses related to Ebola virus in various bat species, including the novel 360 361 Bombali virus, in bats has provided additional support for bats as the reservoirs for 362 Ebolaviruses even though, though further research is needed to confirm host species 363 range and potential for human infection, a specific host species or set of host species has 364 yet to be confirmed. Ancestral variants of zoonotic coronaviruses similar to SARS-CoV 365 and MERS-CoV have been identified from bats, with some viruses related to SARS-CoV 366 even being capable of directly using the human receptor, ACE2. While both SARS-CoV and MERS-CoV have also been directly isolated from "intermediate" hosts, palm civets116 367 and camels<sup>117</sup>, respectively, it is possible that these two virueses may have can be directly 368 transmitted to humans from bats. 369

Commented [MOU115]: I feel as this is our central hypothesis, at least one of them for this review. We call it out in the intro nicely, so may want to think about keeping that as the main theme throughout and maybe move this section up so we aren't repetitive?

Commented [PR116]: And a range of ecological, epidemiological, and molecular studies would be required to fully understand the likelihood of zoonotic spillover (Plowright et al. 2017 Nrmicro).

Commented [MOU117R117]: YES!

Commented [LM([118R117]: We hit on this in the ecology section, right? | also added an extra line saying this in the proceeding knowledge gaps section.

Commented [MV(|119]: Refs, first mers paper and pedv, any other recently identified unknown true bat pathogens?

Commented [MOU120]: We don't describe all these techniques before, and not sure we should take for granted that every reader is familiar with them. Maybe this is where we ref the Fig 2 process and add to that figure.

Commented [LM([121R121]: Rephrased a bit for clarification. I want to avoid depicting specific approaches in figure 2 because it will be too cramped and isn't so important yet.

Commented [PR122]: It falls a bit flat to say it is invaluable...but not to explain why. A sentence saying how it differs from Niv/HeV and what is current thought on why not pathogenic (lack of v/w that inhibits innate response, diff receptors).. recent paper from Broder gp probably good reference. Extra sentence will give reader more to chew.

Commented [MOU123]: Ref: https://www.nature.com/articles/s41564-018-0227-2

Commented [MOU124]: We already go in detail on this on Page 5 and 6 above, but maybe we want to move the ref on SARS-CoV serology in Yunnan China here, showing that indeed direct spillover may still be happening w SARSr-CoVs! 371 Knowledge gaps in viral discovery. New viral sequences are constantly being 372 discovered across a wide geographic range and in countless host species, however there 373 374 are far fewer downstream studies aimed at functionally characterizing these viruses or the ecological and epidemiological factors of their hosts that may or may not facilitate 375 376 zoonosis (Fig. 2). Thus, it remains unknown which of these new sequences can jump species barriers and start the next human outbreak. Deep sequencing is becoming more 377 378 cost-effective and efficient at producing full-length genomes of novel viruses. Still, many 379 virus discovery efforts focus on family-level consensus PCR methods to identify close 380 relatives of known human pathogens then sequence only a small, conserved region of 381 the genome. While these datasets provide valuable information for evolutionary studies, they offer little in terms of functional characterization. Focusing exclusively on Further, 382 preferentially targeting discovery to -relatives of highly pathogenic viruses limits our ability 383

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Surveillance and outbreak control

Even knowing the taxonomic family of a novel pathogen causing an outbreak can help medical staff and epidemiologists narrow down control and treatment strategies. Novel diagnostic platforms such as the GeneExpert allow for rapid, multiplexed detection of a wide panel of human pathogens and are constantly being improved to increase sensitivity and pathogen coverage. Virus discovery efforts, though in their infancy, are producing a

to discover the next unexpected zoonotic pathogen. For example, before SARS-CoV, few

had considered betacoronaviruses as a serious pandemic public health threat.

Commented [M[125]: do we need to say smtg about global distribution of the surveillance efforts and underserved parts?

Commented [LM([126R126]: Virus discovery papers are rapidly coming out left and right from all over the world, so I don't think we should make this a big point. By the time this review publishes, even more holes in the "virus sampling map" will be filled.

Commented [M[127]: maybe contextualise this with surveillance, how to move further than just stam collecting? even if we know the zoonotic potential, do we then need the underlying intrinsic host-pathogen relationship to determine what areas would be at risk? E.g with the bactrian camel story?

Commented [MOU128R128]: Agree. As I said above, this is really one of the main take home messages, that we have viral sequences from 1000s of bat-borne viruses, but how can we better understand risk by applying the specific molecular/host-pathogen investigations we describe in this paper, along with more ecology and epi. This whole section could be moved up, or keep it as a key conclusion and consodiate earlier language about this.

Commented [LM([129R128]: I want to keep this section focused on lack of functional assays for newly discovered viruses. If we turn the focus to ecology and epi needs, then it's no different than the other sections.

Commented [PR130]: And it is so much more than sequence that determines spillover. Ecological & epidemiological are also key. See our nrmicro paper.

Commented [MOUI31R131]: Exactly, I think we can flesh out this and conclusion sections with more on ecol and epi, and behavioral risk - human-bat contact. There are many gaps in our understanding in these areas, just depends how much we want to go into this, but it should be addressed.

Commented [LM([132R131]: I added a line but we should really try to keep each section focused or we'll just end every section the same.

Commented [PR133]: Good paragraph. Makes a clear point and you were right to keep it focused.

Commented [M[134]: start with the surveillance, how often does a priori knowledge result in effective countermeasures?

Commented [LM([135R135]: | re-structured this whole

On that note, with the exception of rabies, probably not

Commented [M[136]: continue to couple it back to bats, don't make it a generic emerging infectious disease review. use small conting sentences to bring it back to bats and not

Commented [SS137R137]: Added a sentence

Commented [LM([138R137]: The re-structuring should help keep it more bat-focused

Commented [MOU139]: Trademarked name? Ref?

wealth of genome sequence data which are then made publicly available through online data repositories. Targeted sampling of bats, in particular, have yielded sequences of novel coronaviruses, filoviruses, lyssaviruses, influenza viruses, and henipaviruses. The resulting datasets provide insight into the existing variation in viral families, allowing for the development of diagnostic and surveillance assays broadly targeting virus clades. For example, Bombali ebolavirus was initially discovered in bat samples using a consensus PCR assay<sup>113</sup> developed to target a region of the viral genome for which the nucleic acid sequence is conserved between related viruses. Broadening our ability to rapidly characterize a-novel pathogens should be a priority in the coming years.

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predict Ebola virus spill-overspillover events could allow for targeted prophylactic vaccination campaigns or intervention strategies to minimize contact between bats the reservoir and humans. For example,s—targeted Ebola virus vaccination of high-risk populations—reducing the frequency of interacting with wildlife to prevent Ebola virus outbreaks rather than responding to them after spillover, or educational campaigns to teach local communities how to live safely around bats and reduce direct contact.

The identification of keya reservoir species and the development of better models to

Next-generation vaccine technologies have been shown to be broadly and rapidly adaptable for different types of viral pathogens. Importantly, several of these platforms are built on genetically modified viruses that can mount efficient immune responses in both humans and animals, such as the <u>VSV and ChadOx1 platformsvector</u>, which has been shown to form protective immunity in humans, mice, guinea pigs, nonhuman primates and livestock<sup>118-120</sup> to a number of pathogens, including bat-borne Ebola virus and Nipah virus. Vaccine efficacy in a variety of animals, including livestock and other

Commented [MOU140]: I know we can't fit it all in here, but would be worth mentioning "Serology chip" methods too!

Commented [PR141]: To really round this out you could add a comment on the root cause of spillover – generally habitat destruction. We are tyring to reverse spillover by regenerating the habitat pathes required to keep nomadic bats nomadic. Some sentence along lines of 'or prevention of the environmental degradation or ecological chage that brings bats into increasing contact with humans". Can't think of a good reference. Maybe Kessler et al. 2018. Is closest out there.

Kessler MK, Becker DJ, Peel AJ, Justice NV, Lunn T, Crowley DE, Jones DN, Eby P, Sánchez CA, Plowright RK. 2018. Changing resource landscapes and spillover of henipaviruses.

Ann NY Acad Sci 1429;78-99.

--postnote -- this would be better below where talk about one health.

#### Commented [MOU142]: e.g.

https://www.ecohealthalliance.org/living-safely-with-bats https://www.ecohealthalliance.org/wpcontent/uploads/2018/10/Living-Safely-with-Bats\_download.pdf

Commented [MOU143]: Explain more? Relevant to bat viruses?

Commented [LM([144R144]: Added some clarification to this section

peri-domestic animals may even allow for proactive measures to reduce cross-species transmission of bat viruses to humans. Depending on the point-route of transmission, advanced therapeutics may not be necessarypreemptive control strategies would allow for low-cost countermeasures. For example, Nipah virus is believed to be transmitted to humans through date palm sap collection containers that have been contaminated with virus-containing urine from visiting fruit bats<sup>121</sup>. One proposed intervention strategy has been to cover the containers to prevent bat feeding and contamination with bat urine<sup>122</sup>. Likewise wildlife and livestock mortality surveillance, such as the great ape EBOV carcass surveillance in the Republic of the Congo, could function as an early warning system preceding spillover in the human population<sup>123</sup>.

While still nascent and only in early clinical trials, novel platforms such as DNA-based

While still nascent and only in early clinical trials, <u>novel platforms such as DNA-based</u> and <u>mRNA</u> vaccines offer <u>the potential for</u> an incredibly rapid response time from pathogen discovery to therapeutic intervention, with very little to no side effects. Using these is technologies, researchers were able to test the first Zika vaccine in mice and nonhuman primates within 3.5 months of the initial outbreak in 2015<sup>124</sup>. Other platforms based on VSV or adenovirus are already in clinical trials and have been shown to be effective in multiple species and for most of the major emerging viruses identified, to date.

### Challenges to outbreak control.

One-health approaches involve addressing zoonosis at both the human, and animal and environmental levels. One of the most significant hurdles to preventing zoonosis at the animal level is the feasibility of wildlife vaccination. Given that filoviruses and coronaviruses are likely hosted in a variety of different animal populations, including bats

Commented [MOU145]: This can be part of addressing some of the non-virological factors in a stand alone section on next steps in understanding but virus ecology and epi?

Commented [LM(|146R146]: | have kept it vague on this subject because I really am not an expert here. If somebody else wants to add in something on this, go ahead.

Commented [PR147]: Talk to Emily about this. It has been hard to implement. She may have a reference for this. Like the Hendra vaccine, changing people's behaviors proves to be very difficult.

Commented [LM(|148R148]: Addressed Hendra horse vaccination issues in the proceeding "challenges" section

Commented [MV([149]: Ref Kuisma et al

Commented [LM([150R150]: Added.

Commented [PR151]: Real one health approaches would address the environmental root causes...comments above would probably be better here. Wish I had a good reference for this (we are working on it!). Kessler et al. best for now.

and other mammals, covering large geographic regions, current vaccination delivery methods are impracticable and likely insufficient to induce effective herd immunity. While effective vaccines are now in development for Ebolavirus, Hendra and rabies, there are no currently effective vaccines available for both human and animal use. Some progress has been made on this front, for example in the form of oral vaccine delivery for rabies in dog populations<sup>125</sup> and bats<sup>126</sup> as well as plague in black-tailed prairie dogs<sup>127</sup>. Applying similar efforts to bats and other mammals will require a greater understanding of host ecology and behavior.

After it was discovered that horses are susceptible to Hendra virus and can serve to amplify the virus and lead to spill overspillover intoinfect humans, the Australian government invested in developing a highly effective vaccine that could be given to horses 128. It was hoped that reducing transmission of the virus to horses would reduce transmission to humans. However, vaccination efforts in Australia have been hindered by antivaccination sentiment, the public perception of the vaccine being too costly for such a rare pathogen and by anecdotal evidence of unwanted side effects. This lack of adoption in Hendra vaccination has allowed for sporadic Hendra outbreaks in horses to continue 129, which may eventually again spread to humans threatening human health.

The geopolitical climate represents an even bigger challenge to outbreak prevention. Despite the existence of multiple, experimental therapeutic options, the latest EBOV outbreak in the Democratic Republic of Congo has been stymied by civil war breaking down the healthcare system and militant groups targeting healthcare workers and outbreak response teams 130. While the rVSV-EBOV vaccine has been successfully employed in response to Ebola virus outbreaks—, the pre-IND approval limits potential

Commented [MV([152]: Check on the correct name of the

Commented [LM([153R153]: Added the little "r" – that's what MERCK is calling it now

broadscale application as a prophylactic countermeasure that not been widely used to prevent spill-over events. The full licensure of the VSV vaccine would allow for a broader preemptive rather than a reactive vaccination approach and would mark the first licensure of a human vaccine for a bat-borne infectious disease. Another example of geopolitical disruption was seen during the emergence of SARS-CoV in China in 2002, when the Chinese government delayed reporting the health crisis to the international community well after the outbreak had begun to spread<sup>131</sup>. Thus, even with all of the steps of a multifaceted one-health approach in place, a significant hurdle to overcome is human nature.

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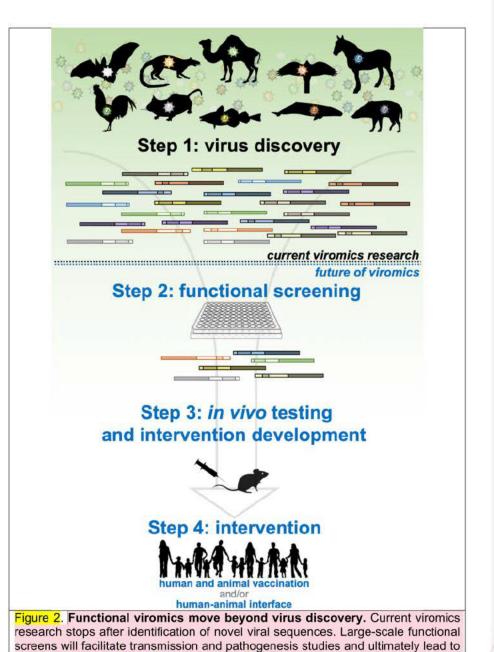
Commented [M[154]: although completely true, not very relative in the context of the review?

Commented [SS155R155]: I disagree, it supports continued research in basic science rather than putting all our research eggs into the vaccine basket.

Commented [PR156R155]: Doesn't it suggest investing in the sociological research to ensure that countermeausres are used and are effective? Same story with Hendra vaccine in horses. It isn't being used bc of antivax narratives.

Commented [PR157]: I would argue this isn't as multifacelted as it needs to be.

Commented [PR158]: Here is where you could add a more holistic approach. As the root cause of many bat virus spillover problems is a change in the .....ugh I have to run to my next flight. Will send you a couple of sentences.



the development of preventative one health intervention strategies.

Commented [MOU159]: I like this figure, and we could add in some more steps here probably. Isnt' there a gap between step 3 and 4? Ideally we lay out a few concrete ways that data/info can lead to interventions and action. Once we have in vivo studies, how can we take this to public health officials?

 $\begin{tabular}{ll} \textbf{Commented [LM([160R160]: Updated the figure with a bit more detail)} \end{tabular}$ 

# BOX 3. The future of bat virus research

There is a growing anxiety in the field that merely identifying all of the novel animal-derived viruses will do little to prevent the next outbreak. This is in part due to the near total lack of downstream assays to functionally characterize these viruses at the scale in which they are being discovered. Thus, most studies have focused on animal viruses that already bear close resemblance to known human pathogens. One avenue for future research efforts should focus on the development of scalable tools that can functionally assess important questions related to viral zoonosis, such as whether or not these-novel bat viruses can infect human cells or use known human receptors. With the cost of gene synthesis decreasing as the technology advances, novel viral glycoprotein sequences could be synthesized in bulk and tested *in vitro*, for example.

Beyond functional studies, disease ecology and modelling are essential to determine the true risk of cross-species transmission 132. Recent advances in the miniaturization of GPS and camera technology have allowed for smaller GPS trackers and more efficient, higher resolution camera traps and will certainly help improve our understanding of host species distribution and key host-environment-interactions in at the humanbat-human-environment-animal interface. These devices are slowing being deployed in the field to increase our understanding of bat migratory patterns and bat-environment interactions. Additionally, nNew weather and environmental satellites are providing finer resolution of global climate trends, urbanization and development. In addition, open-access datasets of host-virus associations combined with new analytical approaches, e.g. machine learning, are expanding our understanding of virus host range beyond the limits of current surveillance data. Collectively, such information will greatly is

Commented [PR161]: I vote for this being 'future of bat virus research' and adding a cohesive summary that rounds the paper out. I'm happy to do a good round of editing if someone can take a stab at the first draft.

Commented [LM([162R162]: Done. This is now box 3 and there is a new conclusion section.

Commented [MOU163]: Cite GVP and anit-GVP studies?

Commented [MOU164]: Nice!!

Commented [LM([165R165]: Thanks

Commented [MOU166]: Need a transition here that points first to the general need for more disease ecology and modeling. These investigations can be supported by new technological advances. We also need more expertise and collaboration with good old'fashion ecologists and taxonomists. See our recent paper that touches on these collaborations and win-win examples: <a href="https://www.mdpi.com/1999-4915/11/3/240/htm">https://www.mdpi.com/1999-4915/11/3/240/htm</a>

Commented [LM([167R167]: added

Commented [MOU168]: Lots of refs to add here. Some from Han et al, Drake, and my Nature paper

advancinge our ability to pinpoint potential hotspots of zoonotic spill over hot-spets and identify new host reservoirs.

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# Conclusions

Disease X, or the as-of-yet unknown pathogen poised to cause the nexta global pandemic, poses the greatesta grand challenge in outbreak prevention and response. Bats represent an important, but largely uncharacterized, source of known human pathogens, implying they are likely a source of future unknownwon human pathogens. Despite having only a limited understanding of bats, the viruses they carry and the molecular and ecological forces driving zoonosisviral spillover, the tools to develop nextgeneration vaccines and antiviral technologies are maturing to the point where researchers will be able to respond to the next outbreak with unprecedented speed. However, a penultimate goal of bat-virus research is to transition from reactionary responses to proactive preventions. In order to transition bat virus research from reactive to achieve predictive redictive with the ability e capacity to determine for which pathogens represent the greatest threat to global health, vast advancements are need to be made across a multitude of disciplines. Broadly, an Here we have identified significant progress made in the last decade and significant gaps remaining inimproved our understanding the ecology of these animals and a greater appreciation of theirof bat-virus ecology, -genetic diversity, and -molecular mechanisms underlying zoonotic infection and immunity. The emergence and re-emergence of zoonotic bat pathogens demonstrates the inextricable link between the health of humans, animals, and the environment. Therefore e≣fforts to Commented [MV([169]: should we include a final statement on that that all is meaningless if our ability to deploy countermeasures remains limited?

Commented [LM([170R170]: Let's keep it optimistic since we are already pretty negative throughout the review. Also, the pre-licensing of all the various EBOV vaccines during the outbreak suggests that countermeasure deployment is getting better.

Commented [MOU171]: Took a stab at rewriting this conclusion to make it more punchy.

Commented [MOU172]: Reference WHO R&D blueprint paper?

to mitigate the public health impacts of bat-borne viruses zoonotic pathogens must
integrate research across these disciplines, applying a one-health approach, from field to
lab, to address the problem.
The future of bat virus research lies in a combined and concerted effort to will be essential
to evaluateing the molecular and macro-ecological risk of factors of zeonotic
transmission, clarifying the molecular mechanisms underlying zoonosis will shine light on
which viruses carry the potential to transmitspill over, and conduct large-scale,
longitudinal -surveillance which will allow for the deployment and evaluation of next
generation interventions. The emergence and re-emergence of zeonotic bat pathogens
demonstrates the inextricable link between the health of humans, animals, and the
environment. Efforts to mitigate the public health impacts of zoonotic pathogens must
integrate-research across-disciplines, applying a one-health approach, to address the
problem.

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 **From:** Munster, Vincent (NIH/NIAID) [E] **Sent:** Wed, 6 Nov 2019 13:27:52 -0700

To: Plowright, Raina; Letko, Michael (NIH/NIAID) [F]
Cc: Kevin Olival; Seifert, Stephanie (NIH/NIAID) [F]

Subject: Re: Nat rev microbiology

Awesome,

Safe travels!

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

From: "Plowright, Raina" < (b) (6)

Date: Wednesday, November 6, 2019 at 12:56 PM

To: Michael Letko < (b) (6)

Cc: "Kevin Olival," < (b) (6) '

< (b) (6) "Seifert, Stephanie (NIH/NIAID) [F]" < (b) (6)

Subject: Re: Nat rev microbiology

Mike — (b) (6) Sorry my schedule this week has been

impossible. Raina

Sent from my iPhone

On Nov 4, 2019, at 3:21 PM, Letko, Michael (NIH/NIAID) [F] < (b) (6) wrote:

Awesome. I like your re-write of the conclusion and have incorporated the changes.

--

Michael Letko, Ph.D
Postdoctoral IRTA
Dr. Vincent Munster Laboratory
Virus Ecology Unit, Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH
903S 4th Street

# Hamilton MT 59840 (b) (6)

From: Kevin Olival < (b) (6)

Date: Monday, November 4, 2019 at 1:12 PM

To: "Munster, Vincent (NIH/NIAID) [E]" < (b) (6) "Letko, Michael (NIH/NIAID) [F]" < (b) (6) "Seifert, Stephanie (NIH/NIAID) [F]" < (b) (6) "Seifert, Stephanie (NIH/NIAID) [F]"

Subject: Re: Nat rev microbiology

Michael and all,

Great job on this! ATTACHED MY EDITS AND FINAL COMMENTS!

Cheers, Kevin

# Kevin J. Olival, PhD

Vice President for Research

EcoHealth Alliance 460 West 34th Street – 17th floor New York, NY 10001

(b) (6) (direct) (b) (6) (mobile) 1.212.380.4465 (fax)

www.ecohealthalliance.org

EcoHealth Alliance leads cutting-edge research into the critical connections between human and wildlife health and delicate ecosystems. With this science we develop solutions that promote conservation and prevent pandemics.

On Nov 4, 2019, at 10:34 AM, Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote:

Thanks guys, hope you're feeling better Kevin!

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories

NIAID/NIH

From: "Plowright, Ra	ina" <	(b) (6)		
Date: Monday, Nove	mber 4, 2019 at 8:3	1 AM		
To: "Kevin Olival," <		(b) (6)		
Cc: "	(b) (6) <	(b) (	<sup>6</sup> Michael Letko	
<	(b) (6) "Seifert, Steph	hanie (NIH/NIAID) [	F]" <	(b) (6)
Subject: Re: Nat rev r	nicrobiology			
Good plan. I read throu Kevin, hope you are fee	77.0	nk it doesn't need m	uch work, so I'll try no	ot to hold you up.
On Nov 4, 2019, at 8:28	3 AM, Kevin Olival <		(b) (6) wrote:	
Sorry Vincent and all. I I'll try and get to this to independently to not h	day and provide som	ne light edits. Raina, p	probably best we just	work
Cheers, kevin				
On Nov 4, 2019, at 10:2	20 AM, Munster, Vinc	ent (NIH/NIAID) [E] <		(b) (6) wrote:
Hi guys,				
Let us know what the s	tatus on this is, we w	ould like to get this s	ubmitted by Wednes	day,
Cheers,				
Vincent Munster, PhD				
Chief, Virus Ecology Sec	ction			
Laboratory of Virology				
Rocky Mountain Labora	atories			

From: Munster, Vincent (NIH/NIAID) [E]
Sent: Wed, 6 Nov 2019 11:13:23 -0700

To: Plowright, Raina
Subject: Re: Pushing ACURO

Great, just forwarded it to Monica (and Cc-ed you). The VA meeting went well?

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

From: "Plowright, Raina" < (b) (6)

Date: Wednesday, November 6, 2019 at 11:10 AM

To: ' (b) (6) < (b) (6)

Subject: Re: Pushing ACURO

YES excellent timing. I have it on my list to reach out to you. I'll ask for one expedited ACURO approval. Tony just got his protocols approved BTW.

On Nov 6, 2019, at 11:06 AM, Munster, Vincent (NIH/NIAID) [E] (b) (6) wrote:

Hi Raina,

You mentioned being able to push ACURO, is this still possible. We have a tentative date of starting the Artibeus Nipah and Hendra studies in January. Any delay would likely result in postponing the study due to losing available slot in the BSL4.

Let me know what you think,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

 From:
 Munster, Vincent (NIH/NIAID) [E]

 Sent:
 Wed, 6 Nov 2019 09:38:14 -0700

**To:** Matson, Jeremiah (NIH/NIAID) [F]; Offei Owusu, Irene (NIH/NIAID) [F]; Avanzato, Victoria (NIH/NIAID) [F]; Kwe Claude, Yinda (NIH/NIAID) [F]; Jyothi Purushotham; Letko,

Michael (NIH/NIAID) [F]

**Subject:** FARE award and other awards

Just a reminder, make sure you always apply for the NIH awards,

We have had good success over the years, it is not about the award money but about your ability to build a resume. As science is extremely competitive, you should take any opportunity to gain a competitive edge. It is unclear why certain people have not applied for this award, but it is really in your best interest to apply (as typically 1 in 4 gets the FARE).

That includes the Norm Salzman award, which is a little bit more advanced.

Also make it a habit to point this out to your (new) fellow lab mates,

Cheers,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

From: Munster, Vincent (NIH/NIAID) [E] Sent: Wed, 6 Nov 2019 08:20:12 -0700 To: Broder, Chris (USU-DoD) Cc: Seifert, Stephanie (NIH/NIAID) [F] Subject: Re: Conflict of Interest Disclosure Form for the Rousettus NiV manuscript Sorry Chris, This must have been overlooked by us, otherwise we definitely would have changed it. Again, sorry for not having noticed / failed to change this Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology **Rocky Mountain Laboratories** NIAID/NIH From: "Broder, Christopher" < (b) (6) Date: Wednesday, November 6, 2019 at 8:07 AM (b) (6) To: ' (b) (6) < (b) (6) Cc: "Seifert, Stephanie (NIH/NIAID) [F]" < Subject: Re: Conflict of Interest Disclosure Form for the Rousettus NiV manuscript Seifert / Vincent Why did you not accept my changes to the author line? v/r Chris (b) (6) wrote: On Fri, Aug 2, 2019 at 1:51 PM Broder, Christopher < sorry i have been traveling. my comments are on top of Eric's version. thanks

thanks Chris

On Thu, Aug 1, 2019 at 1:50 PM Munster, Vincent (NIH/NIAID) [E] < 60 60 wrote: In addition, if you send us an email reply with OK, we can generated the coi statement on your behalf,

Cheers,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

From: "Seifert, Steph	anie (NIH/NIA	(b) (6)		
Date: Thursday, Augu	ust 1, 2019 at 1	1:26 AM		
To: Michael Letko <		(b) (6) Trenton Bushmaker <		(b) (6) Eric
Laing <	(b) (б) "Sat	urday, Greg (NIH/NIAID) [E]" <	(b) (6)	"Meade-
White, Kimberly (NIH	/NIAID) [E]" <	(b) (6)	Neeltje van Doremalen	
<	(b) (6)	"Broder, Chris (USU-DoD)" <		(b) (6)
11	(b) (6) <	(b) (6)		

Hi all,

I have attached the "final draft" of the Rousettus NiV manuscript for submission to the JID NiV special Issue. In order to submit, I need each coauthor to read and sign the ICMJE form for Disclosure of Potential Conflicts of Interest and return to me. | promise it's short, 5 min tops!

Thank you again for all of the help in putting this manuscript together.

Cheers, Steph

--

Christopher C. Broder, Ph.D.
Professor and Chair
Department of Microbiology and Immunology
Uniformed Services University, B4152
4301 Jones Bridge Rd, Bethesda, MD 20814-4799

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USU is "America's Medical School"
Email: (b) (6)
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https://www.usuhs.edu/national/faculty/christopher-broder-phd

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Lucille Washington

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fax - 301-295-3773

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disclosure or distribution is prohibited. If you are not the intended recipient, please contact the sender by replying to this e-mail and destroy all copies of the original message. (Uniformed Services University)

From: Munster, Vincent (NIH/NIAID) [E]
Sent: Wed, 6 Nov 2019 07:58:23 -0700

To: (b) (6) Bushmaker, Trenton (NIH/NIAID) [E]; Kwe Claude, Yinda

(NIH/NIAID) [F]

Cc: Raina Plowright

**Subject:** Re: ASAP: Virus isolation and virus survival studies.



Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

From: Alison Peel < (b) (6)

Reply-To: ' (b) (6) < (b) (6)

Date: Tuesday, November 5, 2019 at 4:02 PM

To: Trenton Bushmaker < (b) (6) "Kwe Claude, Yinda (NIH/NIAID) [F]"

< (b) (6)

Cc: ' (b) (6) < (b) (6) Raina Plowright

< (b) (6)

Subject: ASAP: Virus isolation and virus survival studies.

Hi Trent/Kwe,

I will be submitting the formal request for virus isolation to the CVOs shortly. Can you please write up one (not too technical) paragraph that describes:

- the value of virus isolation for obtaining whole genome sequences for improved phylogenetic resolution
- the planned approach for virus aerosolation and virus survival studies in the ?Goldburn drum. Include an emphasis on this equipment being highly specialised, (i.e. indicating that we couldn't do this research in Australia)

Thank you!

Cheers

Ali

 From:
 Munster, Vincent (NIH/NIAID) [E]

 Sent:
 Tue, 5 Nov 2019 12:06:52 -0700

To: Schountz, Tony; Seifert, Stephanie (NIH/NIAID) [F]

Subject: Re: 26 Artibeus

Sounds good!!!

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: Tony Schountz < (b) (6)

Date: Tuesday, November 5, 2019 at 11:51 AM

To: ' (b) (6) < (b) (6) "Seifert, Stephanie (NIH/NIAID)

[F]" < (b) (6)

Subject: Re: 26 Artibeus

Sure can. We're expecting a new ultrasound in the coming weeks so we should be able to send you non-pregnant females (as well as males) if you want them.

Τ.

Tony Schountz, PhD
Associate Professor
Arthropod-borne and Infectious Disease Laboratory
Department of Microbiology, Immunology and Pathology
College of Veterinary Medicine
Colorado State University
3185 Rampart Road
Fort Collins, CO 80523-1692
(b) (6)

From: "Munster, Vincent (NIH/NIAID) [E]" < (b) (6)

Date: Tuesday, November 5, 2019 at 11:49 AM

To: "Schountz,Tony" < (b) (6) "Seifert, Stephanie (NIH/NIAID) [F]"

(b) (6)

Subject: 26 Artibeus

Hi Tony,

We are finally gearing-up with a bats study planned in January. We will need 26 Artibeus, so we will need to figuring out shipment etc.

The first study will be a filovirus one, and then the second (May-ish) will be a Nipah / Hendra one. Both studies will take 26 bats, hopefully we will have the bats from Florida at CSU by that time, but otherwise will you be able to support these two studies?

Hope all is well,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH 
 From:
 Munster, Vincent (NIH/NIAID) [E]

 Sent:
 Tue, 5 Nov 2019 08:59:37 -0700

To: van Doremalen, Neeltje (NIH/NIAID) [E]

Cc: Letko, Michael (NIH/NIAID) [F]

Subject: Re: drosten data

# Couple of modifications:

Middle East Respiratory Syndrome coronavirus (MERS-CoV) was first detected in the human population in 2012 and has continued to cause human cases in the Middle East as a result of frequent spillover from dromedary camels to humans and subsequent nosocomial transmission. MERS-CoV strains from different geographic regions and human or dromedary camel origin exhibit genetic variation in all open reading frames, including nonsynonymous mutations and deletions. While some of these MERS-CoV variants have been characterized at the molecular level, it is still unclear how viral variation influences pathogenicity and environmental stability. Here we compare the environmental stability, replication kinetics and pathogenicity of several diverse strains of MERS-CoV, isolated from humans, camels, different geographic regions and spanning the entire duration of the current outbreak, from 2012 to 2018. While most of the MERS-CoV strains performed similarly in our tests, one isolate was significantly different in replication, environmental stability, whereas another was significantly different in pathogenicity. Taken together, these findings underscore the importance of continual surveillance in humans and camels together with genetic and phenotypic characterization of novel MERS-CoV strains. In addition, it shows that the ongoing, natural mutation of MERS-CoV results in different viral phenotypes. Thus, it remains possible that ongoing MERS-CoV evolution will drive the emergence of MERS-CoV strains with enhanced epidemic potential.

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

From: Neeltje van Doremalen < (b) (6)

Date: Monday, November 4, 2019 at 5:17 PM

To: ' (b) (6) < (b) (6)

Cc: Michael Letko < (b) (6)

Subject: RE: drosten data

Hi Vincent,

Please find the abstract of the virus strain comparison manuscript below. Let me or Michael know if you have any questions.

#### Abstract

Middle East Respiratory Syndrome coronavirus (MERS-CoV) was first detected in the human population in 2012 and has since maintained a continual outbreak in the Middle East as a result of frequent spillover from dromedary camels to humans. Viral strains isolated and sequenced from humans and dromedary camels and from different geographic regions exhibit genetic variation in all open reading frames, including nonsynonymous mutations and deletions. While some of these variants have been characterized at the molecular level and indeed alter viral replication and innate and adaptive immune evasion, it is still unclear how viral variation influences pathogenicity and environmental stability. Here we compare the replication kinetics, environmental stability and animal model pathogenicity of several diverse strains of MERS-CoV, isolated from humans, camels, different geographic regions and spanning the entire duration of the current outbreak, from 2012 to 2018. While most of the stains performed similarly in our tests, one isolate was significantly different in replication, environmental stability, whereas another was significantly different in pathogenicity. Taken together, these findings underscore the importance of continual monitoring of MERS-CoV strains and show that the ongoing, natural mutation of MERS-CoV results in different viral phenotypes. Thus, it remains possible that the current outbreak may be able to shift to new environments and gain enhanced global spread.

From: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

**Sent:** Friday, October 25, 2019 8:47 AM

To: van Doremalen, Neeltje (NIH/NIAID) [E] < (b) (6)

Cc: Letko, Michael (NIH/NIAID) [F] < (b) (6)

Subject: Re: drosten data

Your right

On Oct 25, 2019, at 16:35, van Doremalen, Neeltje (NIH/NIAID) [E]

(b) (6) wrote:

They would all have to see it again then, so I would wait until we have the final data. That will only be a few weeks later.

From: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

**Sent:** Friday, October 25, 2019 8:28 AM

To: van Doremalen, Neeltje (NIH/NIAID) [E] < (b) (6)

Cc: Letko, Michael (NIH/NIAID) [F] < (b) (6)

Subject: Re: drosten data

Maybe send it to co-authors without the HAE data? That would speed it up a bit

On Oct 25, 2019, at 16:25, van Doremalen, Neeltje (NIH/NIAID) [E]

(b) (6) wrote:

I don't think so.

I think EID will be really good for it. Let's aim to have a good abstract on Nov 8?

Neeltje

From: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Sent: Friday, October 25, 2019 8:23 AM

To: van Doremalen, Neeltje (NIH/NIAID) [E] < (b) (6)

Cc: Letko, Michael (NIH/NIAID) [F] < (b) (6)

Subject: Re: drosten data

No other then it's circulating in KSA, our KSAs not recombinanten? He also found a lot of orf4 deletion variants from Africa.

He is not doing animal work, so we are good still on that end. If we have a good draft/abstract I can start to pitch it. Still EID? Or you guys want to try a different journal?

All well here,

Vincent

On Oct 25, 2019, at 16:14, van Doremalen, Neeltje (NIH/NIAID) [E]

(b) (6) wrote:

Hey,

Do you know anything more about the recombinant strain?

Jon has everything planned to be done early December, and Michael and I have set up a schedule for completion of the paper. Figures are done already (except GCs), M&M and results are fully written. We expect to have the manuscript finished Mid-December.

# Neeltje

From: Munster	Vincent (NIH/NIAID) [E] <	(b) (6)	
Sent: Friday, Oc	tober 25, 2019 4:20 AM		
To: Letko, Michael (NIH/NIAID) [F] <		(b) (6) van Doremalen, Neeltje (NIH/NIAID) [E]	
< (b) (6)			
Subject: droste	n data		

Christian has data in HAEs and explants from a recombinant strain circulating in KSA which typically has an increased replication for about a log.

No animal data though, but definitely a competitor. We only need to do the HAEs right? Probably get the draft ready, so we only have to plug in the final data

Cheers,

Vincent

From: Munster, Vincent (NIH/NIAID) [E]
Sent: Mon, 4 Nov 2019 10:52:03 -0700

To: Plowright, Raina Subject: Re: Spring Admits

I think the tuition will be paid by Trent, yhere is no mechanism in place that the NIH can pay his tuition as he will continue to work as a technician.

Might take a bit to sort this out, but you can contact Trent directly

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: "Plowright, Raina" < (b) (6)

Date: Monday, November 4, 2019 at 9:41 AM

To: ' (b) (6) < (b) (6)

Subject: Re: Spring Admits

Great. Is there a finance person there I can connect to our front office?

From: "Munster, Vincent (NIH/NIAID) [E]" < (b) (6)

Date: Monday, November 4, 2019 at 9:39 AM

To: "Plowright, Raina" < (b) (6)

Subject: Re: Spring Admits

So we would keep him on salary here, and then pay tuition to MSU

Cheers,

Vincent Munster, PhD
Chief, Virus Ecology Section
Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH

From: "Plowright, Raina" < (b) (6)

Date: Monday, November 4, 2019 at 9:13 AM

To: ' (b) (6) < (b) (6)

Subject: Fwd: Spring Admits

How do you want to organize Trent's salary? Do you have a finance person we should talk to? You could have money come through MSU, or you could keep him on salary there and just pay tuition to MSU. MSU admin are hassling me about this pretty consistently now:)

#### Begin forwarded message:

From: Ileana Yates-Johnson < (b) (6)

**Subject: Spring Admits** 

Date: October 28, 2019 at 12:25:32 PM MDT

To: "Plowright, Raina" < (b) (6) Cc: "McFadzen, Mary" < (b) (6)

Hi Raina,

I need to get Troy and Trent admitted for the Spring term, but need to know what you would like to offer them.

#### Stipend -

Insurance –See chart below. They would be joining in the spring, so \$2,727.28 each would cover for spring and summer months.

Additional Pay (\$130/month during 10 month academic year) – required Tuition and fees -

# DEADLINES, COVERAGE PERIODS AND PREMIUM COSTS

	Fall New/Returning	Spring Returning	Spring New
Waiver deadline	the end of the 15th day of classes	the end of the 15th day of classes	the end of the 15th day of classes
Dates Covered	08/01/2019 to 01/31/2020	02/01/2020 to 07/31/2020	01/01/2020 to 07/31/2020
Student Rate	\$2,337.50	\$2,337.50	\$2,727.28

Sincerely,

Ileana Yates-Johnson

Graduate Program Coordinator

Department of Microbiology & Immunology

(b) (6)

Sent:	Thu, 31 Oct 2019 15:06:58 -0600	
To: Cc:	Alison Peel Bushmaker, Trenton (NIH/NIAID) [E]; Ploy	wright, Raina: (b) (6)
Manuel Ruiz Aravena	<u> </u>	
Subject:	Re: (b) (4)	
Hi Alli,		
See response below:		
Hi Vincent,		
be working with our appropriate. Given o	to look over our SOPs. We don't have any for University Biosafety Committee (UBC) to dev ur general lab inexperience, and in particular as just looking for guidance on things to cons	relop ones that everyone feels are with developing lab SOPs for (b) (4)
We have a		(b) (4)
have to look through moment.  • In brief, I this	ever, with the larger number of samples now, the link you provided in more detail, but this nk our protocols should be to store o some calculations on freezer space).	57-7
•		(b) (4)
(or under the we have one catalog/shift	All of those samples wolving re-cataloguing everything. I think that led direct supervision of) the field team leader freezer that is 'untested samples', let's chat all negative tested samples at the same time person responsible for this would limit potent	(or Manuel at this point). Manuel - if about whether it makes sense to re-
I assume the	re are	(b) (4)
		300 - 000
0		(b) (4)
Sounds reasonable, a	again depending on the decision of the UBC	

o For the samples that will require manipulation	(b) (4)
I will need Adrienne to look into ways this can hap compromising (b) (4) This sounds like a big job to navigate point where she'll be analysing samples.  I agree, this will obviously the most challenging part. Remind yourself too that there might on how you are allowed to ship samples (b) (4) E.G. in the US this will clied Cat A shipment which is extremely cumbersome with closed chains of custody and specific shippers.	to get to the be restrictions would be a so-
• I also need to communicate to the UBC how long we intend on holding the samples say until the end of current funding (b) (4) but for ongoing management, I'm thinking an annual review of the usage/storage plans for the samples, and an inventory che of a random portion of samples. (I know RML needs to do every single sample, but if that's necessary here, or whether we will have the human resources for that).  Sounds good, for a whole slew of reasons annual (or even bi-annual) assessment of samples good idea. When you store them long term, you can spot check the box and seal it. Typically do not need to have to be checked in our system.  I'm going to meet with Kim Halpin from AAHL next Friday when she happens to be in the an Michelle Baker when I'm in Canberra on the 13th. I have no intention of promising any sam (particularly before we've had further conversations with CVOs about virus isolation etc), be interested to canvass ideas for future collaborative work based on the samples we'll have he Australia. There was a recent funding opportunity for collaborative grants with AAHL, but I application in on time. They're interested in discussing ideas for a pilot study that could suppear's round though. Anyway, let me know if you have any thoughts on that.	ing perhaps ck - perhaps I'm not sure s would be a y sealed boxes rea, and aples out would be nere in didn't get an apport next
I think more collaboration within and between groups in Oz and beyond is always welcomed navigate the waters as their might be some political sensitivities etc.	d, but I let you
Thanks for your input on this.	(b) (4)
I'll try and move forward with disc the UBC. We're also pushing to get a shipment away in late Nov/early Dec, so there's alway :)	
Cheers	
Ali	
From: Munster, Vincent (NIH/NIAID) [E]  Sent: 30 October 2019 06:52:33 (UTC+10:00) Brisbane  To: Alison Peel  Cc: Bushmaker, Trenton (NIH/NIAID) [E]; Raina Plowright  Subject: (b) (4)	

Hi Alison,

We can have a look over your current SOPs and provide guidance. However, it will be crucial that you talk to your institutional biosafety people. In addition, make sure that current SOPs, storage etc are in line with the regulations within Australia. It might not be very useful to include our biosafety into this discussion, as they will not look upon the current situation very favorably (remind yourself they are US and government).

Within the US, our biosafety is mandated by the CDC in the context of an institutional biosafety committee, and useful recourses are:

https://www.cdc.gov/safelabs/resources-tools.html

typically, I would suggest to	(b) (4) (depended whether you have those) to
appropriate biocontainment level to preven	ent any unintentional handling of these samples outside
proper containment.	

Let me what your thoughts are,

Cheers.

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH From: Munster, Vincent (NIH/NIAID) [E]
Sent: Tue, 29 Oct 2019 09:01:08 -0600
To: Lon Kendall; Schountz, Tony

Subject: FW: Zoo Miami Bat Meeting - Outcome

See email form Alphie,

We seem to have succeeded.

Tony, contact them directly if you still would like Carolia as well

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology Rocky Mountain Laboratories NIAID/NIH

Subject: FW: Zoo Miami Bat Meeting - Outcome

Houston we have lift off!! See the great news below. I'll be in contact with Transporter and Zoo Miami and start working the logistics out.

Dr. Kendall and Rachel, can you please confirm the time line in which you could receive the bats at your facilities, I'm working with 60 for RML and 300 for CSU? Please confirm this is correct.

Please advise, Alf

Alphie Cisar, LATG NHP & Large Animal Procurement Specialist and Resource Manager DVR, ORS

NIH Animal Center

Ph: (b) (6)

Fax 301-480-0644

From: Ridgley, Frank (MDPR) < (b) (6)

Sent: Monday, October 28, 2019 4:22 PM

To: Cisar, Alphie (NIH/OD/ORS) [E] < (b) (6) Watkins Rogers, Rachel (MDPR) < (b) (6)

Cc: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Subject: RE: Zoo Miami Bat Meeting - Outcome

Hi Alphie,

I finally harassed the last needed people from our IACUC and there were no animal welfare concerns expressed and the study has been approval. Our Chief of Animal Science also consulted the head of the AZA Animal Ethics committee and got a verbal approval for the transfer. She is waiting on a written statement but that is just a formality at this point. It appears all the hurdles have been cleared on our end to proceed with the transaction. I will leave it up to you an Rachel to continue talking to move forward.

Thanks,

#### Frank

Frank Ridgley DVM, Zoo Conservation and Veterinary Services Manager Conservation and Research Department Zoo Miami
Miami-Dade Co. Parks, Recreation & Open Spaces Dept.

12400 SW 152<sup>nd</sup> St. Miami, FL 33177
Phone: (b) (6) Ext. (b) (6)

# miamidade.gov

# zoomiami.org

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From: Cisar, Alphie (NII	H/OD/ORS) [E] [mailto	(b) (6)
Sent: Wednesday, Octo	ber 23, 2019 9:09 AM	
To: Ridgley, Frank (MDF	PR) <	(b) (6) Watkins Rogers, Rachel (MDPR)
<	(b) (6)	
Cc: Munster, Vincent (N	IIH/NIAID) [E] <	(b) (6)
Subject: RE: Zoo Miami	Bat Meeting - Outcome	
S Managar Millingar and Communication		
EMAIL RECEIVED FRO	OM EXTERNAL SOURCE.	

Alphie Cisar, LATG 🔊

NHP & Large Animal Procurement Specialist and Resource Manager

DVR, ORS

NIH Animal Center

Ph:

(b) (6)

Fax 301-480-0644

From: Ridgley, Frank (MDPR) < (b) (6)

Sent: Tuesday, October 22, 2019 3:05 PM

To: Watkins Rogers, Rachel (MDPR) < (b) (6) Cisar, Alphie (NIH/OD/ORS) [E]

(b) (6)

Cc: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Subject: Re: Zoo Miami Bat Meeting - Outcome

Hi Sophie,

We haven't forgot about you. It has just been difficult to get the IACUC members together due to some vacations. Once I hear back from everyone, I'll be back in touch!

Thanks,

Frank

# Get Outlook for Android

From: Watkins Rogers, Rachel (MDPR) < (b) (6)

Sent: Tuesday, October 22, 2019 11:57:37 AM

To: Cisar, Alphie (NIH/OD/ORS) [E] < (b) (6) Ridgley, Frank (MDPR)

(b) (6'

Cc: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Subject: RE: Zoo Miami Bat Meeting - Outcome

Good morning Alphie,

I know Frank is here today and I know they started the review, but I am not sure at what point we are. I will let Frank respond to you about this IACUC review.

Thanks for your email!

Thank you, Rachél

New Days off: Wednesday/Thursday

From: Cisar, Alphie (NIH/OD/ORS) [E] [mailto] (b) (6) Sent: Tuesday, October 22, 2019 11:30 AM To: Ridgley, Frank (MDPR) < (b) (6) Watkins Rogers, Rachel (MDPR) Cc: Munster, Vincent (NIH/NIAID) [E] < (b) (6) Subject: RE: Zoo Miami Bat Meeting - Outcome EMAIL RECEIVED FROM EXTERNAL SOURCE. ? Please advise, Alf Alphie Cisar, LATG 🔊 NHP & Large Animal Procurement Specialist and Resource Manager DVR, ORS NIH Animal Center Ph: (b)(6)Fax 301-480-0644 From: Cisar, Alphie (NIH/OD/ORS) [E] Sent: Monday, October 7, 2019 2:21 PM (b)(6)Cc: Watkins Rogers, Rachel (MDPR) < (b) (6) Munster, Vincent (NIH/NIAID) [E] Subject: RE: Zoo Miami Bat Meeting - Outcome Dr. Ridgley, After some internal discussions and review, I've attached the requested document for your review. Please let us know if you have any questions or would like to discuss any details by phone. We look forward to your response. Alf Alphie Cisar, LATG 🔊 NHP & Large Animal Procurement Specialist and Resource Manager DVR, ORS NIH Animal Center Ph: (b)(6)Fax 301-480-0644 From: Watkins Rogers, Rachel (MDPR) < (b)(6)Sent: Friday, August 30, 2019 12:18 PM

(b) (6)

To: Cisar, Alphie (NIH/OD/ORS) [E] <

Subject: RE: Zoo Miami Bat Meeting - Outcome

#### Hello Alphie,

I spoke to Frank and he is willing to talk with you about some details he can give you about the process. Today he is trying to move to a new house before the hurricane hits. I filled him in on your concerns and he does have some feedback for you.

Dorian made a change at the 11:00 AM update:

https://www.nhc.noaa.gov/refresh/graphics at5+shtml/145103.shtml?gm track#contents

Thank you, Rachél

# New Days off: Wednesday/Thursday

From: Cisar, Alphie (NIH/OD/ORS) [E] [mailto (b) (6)

Sent: Thursday, August 29, 2019 12:13 PM

To: Watkins Rogers, Rachel (MDPR) < (b) (6)

Subject: RE: Zoo Miami Bat Meeting - Outcome

EMAIL RECEIVED FROM EXTERNAL SOURCE.

Alphie Cisar, LATG 🔊

NHP & Large Animal Procurement Specialist and Resource Manager

DVR, ORS

NIH Animal Center

Ph: (b) (6) Fax 301-480-0644

From: Watkins Rogers, Rachel (MDPR) < (b) (6)

**Sent:** Tuesday, August 27, 2019 4:30 PM

To: Cisar, Alphie (NIH/OD/ORS) [E] < (b) (6)

Cc: Bezjian, Marisa (MDPR) < (b) (6) Traverse, James (MDPR)

(b) (6) Keenan, Heather (MDPR) 
 Myers, Gwen (MDPR) 
 (b) (6) Johnson, James (MDPR)
 (b) (6) Kruse, J. Carol (MDPR) 
 (b) (6) Ridgley, Frank (MDPR)
 (b) (6) Flacke, Gabriella (MDPR) 
 (b) (6)

Subject: Zoo Miami Bat Meeting - Outcome

Good afternoon Alphie,

Today we had a very deep discussion about the Jamaican fruit bat transfer to NIH labs and found the current process was not the appropriate one to follow. We will need to complete this review under a different process by our IACUC instead of our regular Animal Science Department Animal Transactions approval process.

- Due to the need to evaluate the research project these bats will be used in, this will need to go through our IACUC to be in line with our procedures for approval.
- I have attached a form we use for federally funded grants that we feel will meet your needs better than the AZA form.
- · If you can please run this through your approval process we would really appreciate it.

# For submission of the form please email it to the contact below:

Frank Ridgley DVM, Zoo Conservation and Veterinary Services Manager Conservation and Research Department /Zoo Miami 12400 SW 152<sup>nd</sup> Street, Miami, FL 33177

P: (b) (6), Ext. (b) (6); E: (b) (6)

Please let me know if I can help you with any questions or concerns.

Respectfully, Rachél

Rachél Watkins Rogers, Zoo Registrar and Records Coordinator

New Days off: Wednesday/Thursday

Zoo Miami 12400 SW 152 Street, Miami, FL 33177-1402

P: (b) (6); F: 305.378.6381/E: (b) (6)

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From: Munster, Vincent (NIH/NIAID) [E]
Sent: Fri, 25 Oct 2019 20:05:55 +0200

To: Kevin Olival

Cc: Letko, Michael (NIH/NIAID) [F]; Plowright, Raina; Seifert, Stephanie (NIH/NIAID)

[F]

Subject: Re: Nature Reviews Microbiology manuscript draft

As usual wayyyyyy past the deadline (my fault).

Cheers,

Vincent

On Oct 25, 2019, at 19:55, Kevin Olival < (b) (6) wrote:

Thanks Michael, received. When do you need comments by, I'm sure ASAP, but want to see how many days we have. Thanks.

Kevin

On Oct 24, 2019, at 4:54 PM, Letko, Michael (NIH/NIAID) [F] < (b) (6) wrote:

#### LAST CALL!

Attached is the "final" version of the manuscript. Please look over it one more time, let us know if anything needs to be changed and then we will send it off to Nature Reviews.

I've gone over everyone's comments and have tried to address them.

#### What's new:

- 1. Another new title
- 2. A lot of re-structuring to make it more bat-focused
- 3. Added an abstract and conclusion
- 4. Both figures have been updated with new details
- 5. Added lots of references
- 6. Vincent gave it a final look and added some new parts as well

Thank you, -michael

--

Michael Letko, Ph.D
Postdoctoral IRTA
Dr. Vincent Munster Laboratory
Virus Ecology Unit, Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH
903S 4th Street
Hamilton MT 59840
(b) (6)

tomorrow.

From: "Plowright, Raina" < (b) (6)
Date: Monday, September 16, 2019 at 10:58 PM
To: Kevin Olival < (b) (6)
Cc: "Letko, Michael (NIH/NIAID) [F]" < (b) (6) "Munster, Vincent (NIH/NIAID)
[E]" < (b) (6) "Seifert, Stephanie (NIH/NIAID) [F]"
(b) (6)
Subject: Re: Nature Reviews Microbiology manuscript draft
Benediction # Burg 1994 is a rest of a substitution of the control
No I'm at a mtg in Berlin.
Sent from my iPhone
On Sep 17, 2019, at 6:06 AM, Kevin Olival (b) (6) wrote:
Received. And entoute now, Turkey to Poland. Raina, you going to be at the DTRA Warsaw meeting?
Received. And entoute now, furkey to roland. Rama, you going to be at the DTRA warsaw meeting:
Kevin
On Sep 16, 2019, at 11:25 PM, Plowright, Raina < (b) (6) wrote:
Here it is. Great paper — it will be a useful addition!
I'm happy to do more on the intro and conclusion (if you decide to do a separate conclusion, which I
support!) and abstract. My jet lag just set in so best to hand it to Kevin now and I'll let Michael send me
the next version for more help on those summary sections. If you catch me as I fly home next Sunday
morning European time I can get edits back quickly so you can meet the nrmicro deadline.
Thanks again for including me.
Raina
On San 16, 2010, at 7.56 DM. Blauwight Bains
On Sep 16, 2019, at 7:56 PM, Plowright, Raina < (b) (6) wrote:

Ha! Sitting in a vegan restaurant in Berlin working on this right now. I'm behind on schedule bc of a flaw in my plan... leaving for a meeting with no talk written. Hope to get this to you later today or

Sent	from	my	iPh	one
OCITE	110111	1117	11 1	10116

Michael Letko, Ph.D
Postdoctoral IRTA
Dr. Vincent Munster Laboratory
Virus Ecology Unit, Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH
903S 4th Street
Hamilton MT 59840
(b) (6)

From: Kevin Olival < (b) (6)

Date: Sunday, September 15, 2019 at 12:30 AM

To: "Letko, Michael (NIH/NIAID) [F]" (6) (6)

Cc: "Plowright, Raina" < (b) (6) "Munster, Vincent (NIH/NIAID) [E]" < (b) (6) "Seifert, Stephanie (NIH/NIAID) [F]" <

Subject: Re: Nature Reviews Microbiology manuscript draft

Micheael,

I've been coordinating w Raina. She should finish her edits on Sunday, and I'll pick it up and edit at that point. We thought it would make sense to do this sequentially. I have a flight Monday so will try to work on this enroute, otherwise should be able to carve out some time while at my next meeting next week.

Cheers, Kevin

On Sep 10, 2019, at 12:28 AM, Letko, Michael (NIH/NIAID) [F] < (b) (6) wrote:

Hi Raina,

The editor said we are limited to "about 140 references." So we have room to add more.

Cheers, -michael

Michael Letko, Ph.D
Postdoctoral IRTA
Dr. Vincent Munster Laboratory
Virus Ecology Unit, Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH
903S 4th Street
Hamilton MT 59840
(b) (6)

From: "Plowright, Raina" < (b) (6)

Date: Monday, September 9, 2019 at 10:05 AM

To: "Letko, Michael (NIH/NIAID) [F]" < (b) (6)

Cc: Kevin Olival < (b) (6) "Munster, Vincent (NIH/NIAID) [E]"

< (b) (6) "Seifert, Stephanie (NIH/NIAID) [F]" < (b) (6)

Subject: Re: Nature Reviews Microbiology manuscript draft

Hi Michael,

Do you have a reference limit, and if so, are you at the limit?

It will help me to know if I should suggest 3 or 4 refs for some concepts or just choose a single best pick. Raina

On Aug 27, 2019, at 2:11 PM, Letko, Michael (NIH/NIAID) [F] < (b) (6) wrote:

Dear co-authors,

Attached is our draft of the bat-virus manuscript for Nature Reviews Microbiology. Please take a look at the manuscript and make changes wherever you see fit. If you want to include any references, just paste the PMID where you want and we will add them in through EndNote.

Ideally, we would like to submit the finalized manuscript to the editors sometime in the 3<sup>rd</sup> or 4<sup>th</sup> week of September (around 16<sup>th</sup>-27<sup>th</sup>).

In general, our review briefs through several contemporary areas of bat-virus research, then highlights the knowledge gaps in those areas and poses ways to address them. This larger scope and forward-thinking perspective is where our review is different from other bat-virus reviews. There are 3 sections:

- a. Lines 20-41: **Ecology section/box** (the editors suggested we keep it shorter but it could still use some expansion)
- b. Lines 47-273 Molecular section (species barriers and immunity)
  - a. With a figure of the types of cellular species barriers viruses must overcome
  - b. followed by a box on bat-animal models (lines 278-290)
- c. Lines 301-422: Virus surveillance and one health section
  - a. With a figure on the future of virus discovery
  - b. Followed by a box on the future of bat virus research (lines 428-459)
    - i. Alternatively, we can form this box into a conclusion paragraph, which also fits

#### In general, the current manuscript will benefit from the following:

- 1. <u>Preferably from the senior authors (Kevin, Raina, Vincent)</u>: broad-strokes statements in the introduction and conclusion, to help contextualize within the field.
- 2. More bat-virus-specific examples, where necessary
- 3. Transition statements to help link core concepts
- 4. Additional figures if you can think of any. We have 2 right now and 2 or 3 boxes, but most of the editor's ideas did not make sense (like a phylogenetic tree of all viruses) or have been done a thousand times over by every other review (factors influencing spillover).

Let us know if you have any questions or issues. It has been a team effort and we are excited to finally close in on submitting this review!

We look forward to your additions and changes!

Best, -michael

\_\_

Michael Letko, Ph.D
Postdoctoral IRTA
Dr. Vincent Munster Laboratory
Virus Ecology Unit, Laboratory of Virology
Rocky Mountain Laboratories
NIAID/NIH
903S 4th Street
Hamilton MT 59840

(b) (6)

<NRM DRAFT 8 27 19.docx>

<NRM DRAFT 8\_27\_19\_RP.docx>
<2 NRM DRAFT 10 24 19 VM ML.docx>

From: Schountz, Tony

Sent: Thu, 24 Oct 2019 18:58:10 +0000

To: Munster, Vincent (NIH/NIAID) [E]

Cc: van Doremalen, Neeltje (NIH/NIAID) [E]

Subject: Number of Aj bats on DARPA project

Hi Vinnie,

I realize (b) (6) so I'm cc'ing Neeltje on this in case she can help. I have comments from ACURO for the bat colony and one of them is a request for the total number of bats that will be used. I have the number we will use for our VLP inoculation study, so I only need the total number you have in your submitted ACURO protocol. Can you or Neeltje provide that information in the next few days?

Thanks,

Tony

\_

Tony Schountz, PhD
Associate Professor
Arthropod-borne and Infectious Disease Laboratory
Department of Microbiology, Immunology and Pathology
College of Veterinary Medicine
Colorado State University
3185 Rampart Road
Fort Collins, CO 80523-1692

(b) (6)

(b) (6)

 From:
 Munster, Vincent (NIH/NIAID) [E]

 Sent:
 Fri, 18 Oct 2019 10:10:46 -0600

To: Schountz, Tony; Raina Plowright; Alison Peel; Rynda-Apple, Agnieszka

Subject: immunology

Hi Tony,

One of the discussion we need to have, is what we are actually allowed to "share" outside RML based o our standing CDC agreement. This is a discussion we have had with Raina and Ali, but CDC does not directly allow us to share non-inactivated samples outside RML regardless whether they contain Hendra or not.

As discussed with Raina and Ali, that some of the analyses are "easier" to be done in Australia.

Let's discuss this a bit more so that we are all on the same page, what can actually be done,

Cheers,

From: Edward Holmes

**Sent:** Thu, 17 Oct 2019 22:06:06 +0000 **To:** Munster, Vincent (NIH/NIAID) [E]

Subject: Re: Phylodynamics / phytogeography Hendra

Hi Vincent.

Sounds like great data. The virus flow question will be simple enough to answer. Trivial in fact.

What might be harder is dating any of this evolution - that will depend on the extent of temporal structure in the data. All we can do is look and test. You know how smelly molecular clocks can be...

Cheers,

Eddie

#### PROFESSOR EDWARD C. HOLMES FAA FRS

ARC Australian Laureate Fellow

#### THE UNIVERSITY OF SYDNEY

Marie Bashir Institute for Infectious Diseases & Biosecurity, Charles Perkins Centre, School of Life & Environmental Sciences and Sydney Medical School, The University of Sydney | Sydney | NSW | 2006 | Australia

T (b) (6) (b) (6)

On 18 Oct 2019, at 1:53 am, Munster, Vincent (NIH/NIAID) [E] < (b) (6) wrote:

So we are currently working on trying to full genome sequence ~100 Hendra positive bat urine samples collected in 2017, 2018 and 2019 (and still collecting),

They are from 5 different roost sites in NSW and Queensland, we should have good spatiotemporal coverage. It would be interesting to see whether there is virus flow between populations and how this would relate to spillover (we are trying to get the virus from the most recent spillover sequenced as well, Kim Halpin at AAHL).

Let me know what you think, interestingly there are very few Hendra genomes available (even though quite extensively sampled over the years)

(b) (6) From: Edward Holmes <

Date: Wednesday, October 16, 2019 at 2:25 AM

To: " (b) (6) < (b)(6)

Subject: Re: Phylodynamics / phytogeography Hendra

Hi Vincent,

Of course, happy to help. Sounds like unique data.

One thing though: are all these viruses sampled from the same time point (more or less)? If so, it will be tricky to do some things.

Cheers,

Eddie

#### PROFESSOR EDWARD C. HOLMES FAA FRS

ARC Australian Laureate Fellow

#### THE UNIVERSITY OF SYDNEY

Marie Bashir Institute for Infectious Diseases & Biosecurity, Charles Perkins Centre, School of Life & Environmental Sciences and Sydney Medical School, The University of Sydney | Sydney | NSW | 2006 | Australia

T E

(b) (6) wrote: On 16 Oct 2019, at 9:06 am, Munster, Vincent (NIH/NIAID) [E] <

Hi Eddie,

Was wondering whether you would be interested in helping me a bit in analyzing Hendra bat data. Running a program with Raina Plowright, Ali Peel and Peter Hudson. Have analyzed 5000 bat samples, ~300 Hendra positives and I'm hoping to tease out ~80-100 full genomes.

Let me know what you think,

From: Plowright, Raina

**Sent:** Thu, 17 Oct 2019 05:28:06 +0000 **To:** Munster, Vincent (NIH/NIAID) [E]

Subject: Fwd: Spring 2020 Admits

Great he got in! A few things to sort out. I assume u will keep his RML salary going. Talk later.

Sent from my iPhone

Begin forwarded message:

From: Ileana Yates-Johnson < (b) (6)

Date: October 16, 2019 at 12:17:47 PM MDT

To: "Plowright, Raina" < (b) (6) (Cc: "McFadzen, Mary" < (b) (6)

Subject: Spring 2020 Admits

Hi Raina,

I want to confirm with you the terms of accepting Troy Koser and Trent Bushmaker which I will build into their offer letters.

Monthly stipend: \$1,833.33 (Based on what you are currently paying others)

Additional Payment (required): \$130/month (10 month academic year)

Tuition and fees: 6 or 6+ credits (you can just do 6 as a guarantee but can always offer more if needed or

you can indicate 6+ now)

Health Insurance: \$2,727.28 (covers spring and summer) and then \$\$2,337.50 per term (current rates) Date you would like them to arrive (they will start getting paid on 1/2/20, but classes don't' start until

1/13/20

Sincerely,

#### Ileana Yates-Johnson

Graduate Program Coordinator

Department of Microbiology & Immunology

(b) (6)

(b) (6)

From: Schountz, Tony

**Sent:** Mon, 14 Oct 2019 22:53:22 +0000

To: Rynda-Apple, Agnieszka

Cc: Hector Aguilar-Carreno; Olivier Restif; Munster, Vincent (NIH/NIAID) [E]

Subject: Re: Power Point

Thanks Aga.

Sent from my iPhone

On Oct 14, 2019, at 4:07 PM, Rynda-Apple, Agnieszka < (b) (6) wrote:

Hi All,

I added up again to the presentation on slides 12, 13, and 14, so please use this version v2.1 to modify further.

Looking forward to seeing everyone on Wednesday and travel safe!

Cheers, Aga

From: Hector Aguilar-Carreno < (b) (6)

Date: Monday, October 14, 2019 at 2:50 PM

To: "Schountz,Tony" < (b) (6) Olivier Restif < (b) (6)

"Munster, Vincent (NIH/NIAID) [E]" < (b) (6)

Cc: "Rynda-Apple, Agnieszka" < (b) (6)

Subject: Re: Power Point

Hi all,

Tony, I have added our hamster data to your presentation. Please let me know if you need anything else. I am putting the Genotype to Phenotype group presentation together, so I don't think I will have time to help you with more, but if I do, I will let you know. Any specific questions are welcome.

See you soon!

Hector

Hector Aguilar-Carreno

Associate Professor

Microbiology and Immunology

College of Veterinary Medicine

Cornell University

Office:	(b) (6)
O IIII CO.	

From: Schountz,Tony < (b) (6)

Sent: Sunday, October 13, 2019 11:55 AM

To: Olivier Restif < (b) (6) Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Hector Aguilar-Carreno < (b) (6)

Cc: Rynda-Apple, Agnieszka < (b) (6)

Subject: Power Point

Hector, Vincent and Olivier,

Attached is a Power Point file we're supposed to populate for the meeting this week.

Hector, can you add your data/comments to it and send to Vincent? Then Vincent can send to Olivier, then finally back to me. We need to get it to Sara by Tuesday sometime. I arrive in Bozeman early that morning.

Thanks,

Tony

Tony Schountz, PhD

Associate Professor

Arthropod-borne and Infectious Disease Laboratory

Department of Microbiology, Immunology and Pathology

College of Veterinary Medicine

Colorado State University

3185 Rampart Road

Fort Collins, CO 80523-1692

(b) (6)

(b) (6)

<PREEMP 2019 Immuno Experimental report v2.1 .pptx>

From: Schountz, Tony

**Sent:** Sun, 13 Oct 2019 15:55:49 +0000

To: Olivier Restif; Munster, Vincent (NIH/NIAID) [E]; Hector Aguilar-Carreno

Cc: Rynda-Apple, Agnieszka

Subject: Power Point

Attachments: PREEMP 2019 Immuno Experimental report.pptx

Hector, Vincent and Olivier,

Attached is a Power Point file we're supposed to populate for the meeting this week.

Hector, can you add your data/comments to it and send to Vincent? Then Vincent can send to Olivier, then finally back to me. We need to get it to Sara by Tuesday sometime. I arrive in Bozeman early that morning.

Thanks,

Tony

\_

Tony Schountz, PhD
Associate Professor
Arthropod-borne and Infectious Disease Laboratory
Department of Microbiology, Immunology and Pathology
College of Veterinary Medicine
Colorado State University
3185 Rampart Road
Fort Collins, CO 80523-1692

(b) (6)

(b) (6)

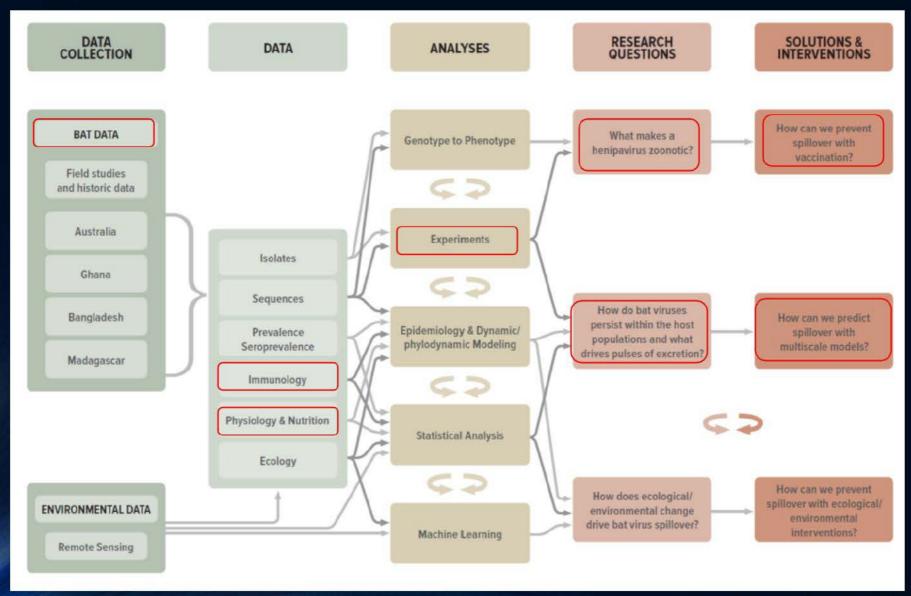
# Work Group Immunology/Bat Experiments

Tony Schountz, Colorado State University

Agnieszka Rynda-Apple, Hector Aguilar-Carreno, Vincent Munster, Olivier Restif, Dan Crowley, Caylee Falvo, Evelyn Benson, Elinor Jax, Juliette Dean

PREEMPT YEAR-1 SUMMARY MEETING SESSION 1 WORK GROUP REVIEW TALKS B BAR, TOM MINER BASIN OCTOBER 16-18, 2019

## Immunology/Bat Experiments work group's role in PREEMPT



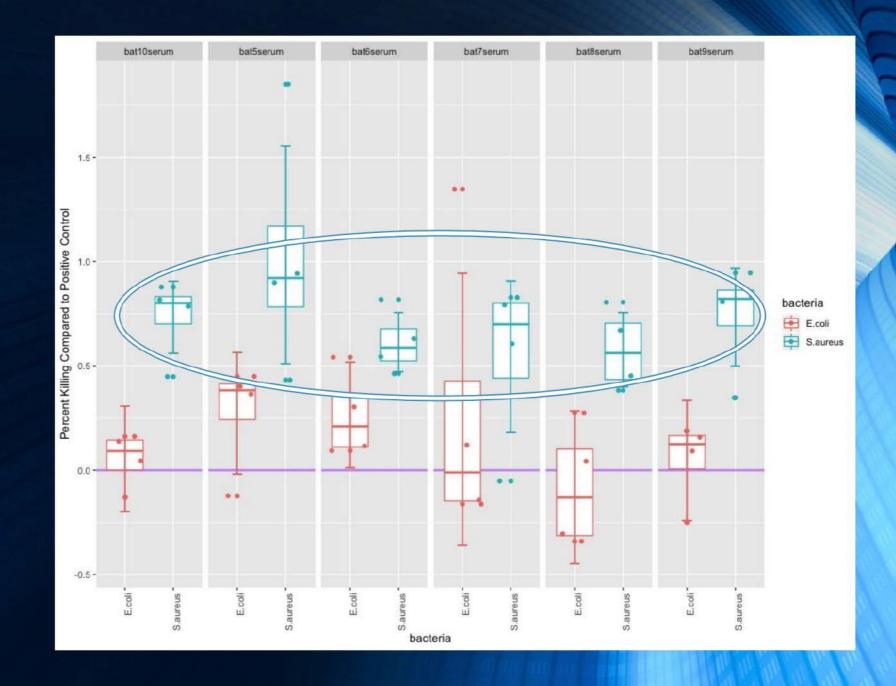
## Science Summary: What we learned ("BIG WINS") in PREEMPT yr 1

- ACURO approved for MSU and Cornell
- IACUC approvals for CSU and RML but awaiting ACURO
- Optimized conditions for lab-based assays: BKA and qPCR
- Optimized conditions for sample collections and handling for multiple subprojects
- VLP selection and optimization well under way

- Demonstrated susceptibility of Aj bat primary kidney cells to CedV, NiV and HeV
- Showed CedV does not suppress innate response in Aj bat kidney cells whereas NiV and HeV do
- Developed proteomics method for detecting Aj bat cytokines using mass spec

# Bat BKA Results

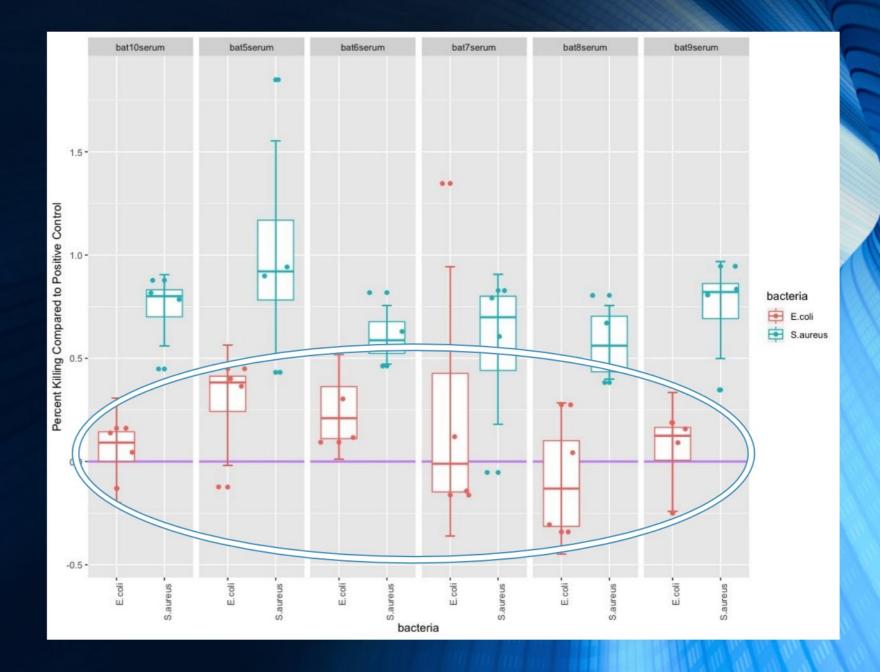
• S. aureus consistently killed by bat serum



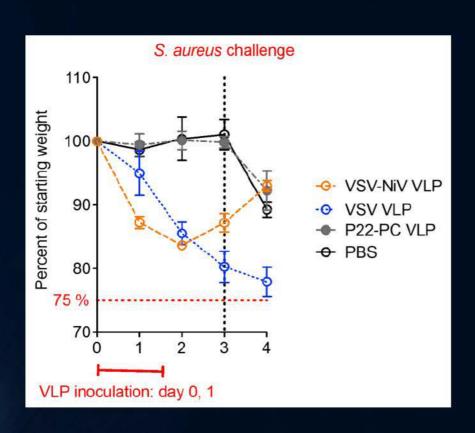
## Bat BKA Results

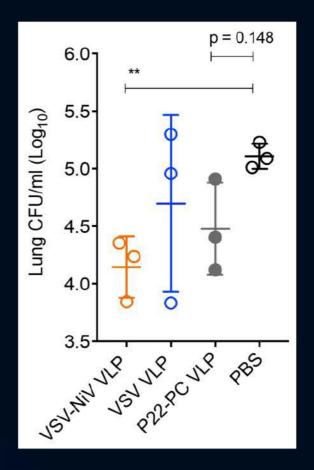
 Staph consistently killed by bat serum

• No effect on E. coli



## Innate Immune experiment with VLPs in mice



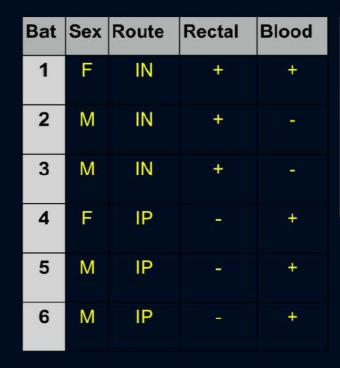


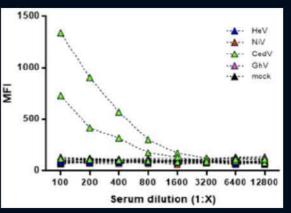
Despite initial body weight loss (followed by partial recovery once we discontinued VLP inoculation), the mice inoculated with VSV-NiV showed best *S. aureus* clearance from the lung @24 hrs post-challenge

## Demonstrated Susceptibility of Jamaican fruit bats to Cedar Virus

- Jamaican fruit bat colony at CSU
  - Artibeus jamiacensis ("Aj" bats)
  - About 200 bats in the colony
- Cedar virus made by Eric Laing (Uniformed Services University)
  - BSL-2 in cell culture at CSU
  - BSL-3 in animals at CSU
  - CedV is missing two genes that that NiV and HeV (and GhV?) use to antagonize a cell's antiviral system – V and W genes
  - It also has different receptor specificities than NiV and CeV

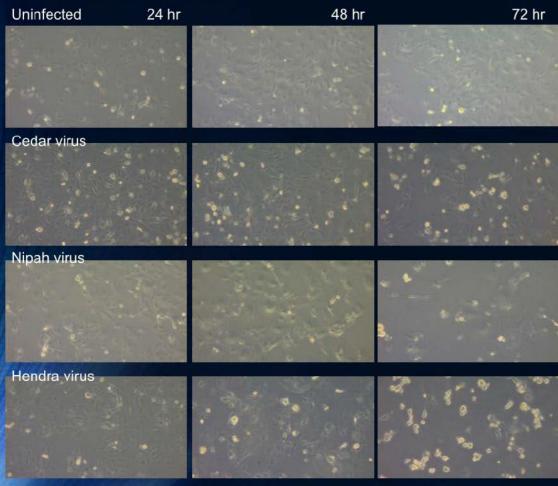
Cedar infection of Aj bats did not cause signs of disease





## Henipaviruses infect Jamaican fruit bat kidney epithelial cells

Nipah and Hendra viruses induce rapid syncytia formation (48 hr) whereas Cedar virus is slower (72 hr)



MOI = 0.1

Cells were inoculated with 0.1 MOI for 30 min (media only for uninfected cells), washed once and then cultured with 2% FBS-DMEM for the noted hours.

Examination of mRNA expression by qPCR array shows that the bat epithelial cells mount a robust antiviral response to Cedar virus but Nipah or Hendra viruses repress the response

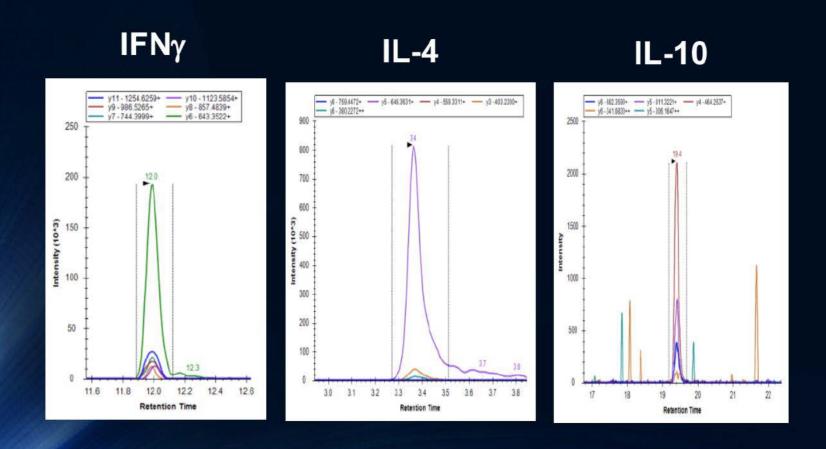


Total RNA was extracted from the cells, reverse transcribed and subjected to SYBR Green qPCR to assess abundance of expression relative to the uninfected cells ( $\Delta\Delta$ Ct). Fold-change was log10 transformed and clustered heat map generated with pheatmap within R statistical software.

Tony Schountz, Colorado State University

## Detection of Aj Cytokines by Mass Spec

Concanavalin A was used to activate spleen cells from an Aj bat 24 hours later, supernatants were collected for MS Scanned for peptides specific to cytokines



## Who helped our work group, and how, in PREEMPT year 1?

- Montana State
  - Evelyn Benson
  - Dan Crowley
  - Caylee Falvo
- RML
  - Neeltje van Doremalen
  - Trent Bushmaker
- Cambridge
  - Elinor Jax
- Colorado State University
  - Juliette Dean

# How our work group's PREEMPT yr 1 output impacts yr 2

- Continuing to make primary Aj bat kidney epithelial cells (7 so far)
- Will test susceptibility to henipaviruses
  - Integrate experiments with Genotype to Phenotype?
- Provides rationale for continuing with bat infection experiments with NiV and HeV

# WHAT excites the Immunology/Bat Experiments work group most in looking forward to PREEMPT year 2!

- Bat infection experiments
  - Susceptibility to NiV, HeV and CedV
  - Effects of dietary protein restriction on susceptibility and shedding

## Work Group(s) we need to work w/more in PREEMPT yr 2 ... and why

- Bat field data
  - Are experimental experimental infection results congruent what happens in the real world?
    - Dietary changes and virus shedding
- Genotype to phenotype
  - Do gene expression profiles of infected Aj cells offer clues as to how bats control infection without disease?
    - Infection of cells with viruses, assess transcriptional profiles

How a successful PREEMPT yr 2 enables Phase 2/yr 3 funding



Add slides as you see fit. They can be blended with the suggested slides above. HOWEVER, please note...

We recommend 10 slides total (15 slides max).

We have only 25 min per work group for 7 work groups. We ask you to plan for 15 min (max) presentation, plus 10 min Q&A.

The Q&A is important, not for providing complete answers but to help seed successful workshop breakout sessions & develop our key deliverable: year 2 (&3) PREEMPT planning.

From: Plowright, Raina

Sent: Tue, 8 Oct 2019 22:47:36 +0000
To: LaTrielle, Sara; Scott Bischke

Cc: (b) (6) (b) (6) Barbara Han; Cara Brook; Emily Gurley; Hamish McCallum; Hector Aguilar-Carreno; (b) (6) (6) (6)

Nita Bharti; Olivier Restif; Peggy Eby; Peter Hudson; Schountz, Tony; Munster, Vincent (NIH/NIAID) [E];
Benson, Evelyn; Tamika Lunn; Baranowski, Kelsee Taylor; Aaron Morris; Amandine Gamble; Gary Palmer;
Manuel Ruiz Aravena; Devin Jones; Madden, Wyatt; Dan Crowley; David William Buchholz; Seifert,
Stephanie (NIH/NIAID) [F];

(b) (6) Caylee Falvo; Kwe Claude, Yinda (NIH/NIAID) [F];
Maureen Kessler;
(b) (6) Alex Washburne; Scott Bischke; McFadzen, Mary; Hodges,

Jennifer

Re: PREEMPT meeting agenda items with pre-meeting work requests from ALL

Subject: attendees

Hi Everyone,

I nominate Amandine, Barbara, and Devin for a prize — as the first people to fill in the google sheets — thanks folks!

One of the most important pieces of information we need is a list of the groups that must meet (see google sheet). Although working groups (as previously defined) have structured meeting times, we also need discussions outside of working groups. I just added these ideas but I know there are more circulating out there!

- Phylodynamic discussion "to define & prioritize analyses/papers and determine contingencies" Kwe, Alex, Amandine are the critical folk and then a few other people would be valuable.
- Discussion to review field sampling frameworks. Anyone who is using field data for their research should have a say in how frequency/distribution/intensity of sampling is altered.

If you fill these in early, we can structure the schedule so groups can meet simultaneously, with as little overlap as possible.

Sara, Scott, Emily and myself met with the students and postdocs via zoom last week. They had excellent suggestions that have improved the structure of the meeting. We also added a couple of things to support their needs, such as the speed science requests where students/postdocs/researchers indicate PIs they need to meet with. We will design a lunch around these meetings (hey students, don't forget to fill this in!).

It should take less than 10 minutes to fill in these forms but they will greatly improve the value of our meeting time.

Excited to see you all next week and to see the science that will emerge from our discussions!

Raina

PS the weather forecast looks fantastic (just kidding)

On Oct 4, 2019, at 9:01 AM, LaTrielle, Sara < (b) (6) wrote:

All,

The PREEMPT agenda is ready for your review/feedback- along with a few very **important pieces of feedback we need from each of you- as outlined in Scott's email below.** A big thanks to Scott (and of course Raina!) for working with many team members to understand/extract the needs of the group- it will continue with your feedback/input.

Thanks in advance, Sara/Raina \*\*\*\*\*\*

Hi all,

Scott Bischke ( (b) (6) here, past PREEMPT grant helper and now facilitator for your upcoming PREEMPT meeting. This note deals only with the meeting agenda, process, and output. Sara is handling meeting logistics under separate emails.

The planning group has been working feverishly to complete our PREEMPT meeting agenda (almost there!). Thanks to so many of you for your help to date. We are writing today to request <u>meeting prework from everyone</u>, as follows:

### From all attendees

- Review near-final draft agenda (respond to Raina, Sara, Scott by Wed Oct 9) .--Please
  find attached the current draft meeting agenda. We are working hard to make the meeting a
  success for everyone, and thereby help us achieve our PREEMPT project vision. We think we
  are pretty close. We request you review and provide input as you see fit.
- Provide your top 3 goals for the meeting via Google Docs (by Fri Oct 11).--Click here
  for the link. We'll use this input in our final agenda tuning, plus perhaps create a word cloud or
  similar to help the team visualize its collective goals for the meeting.
- 3. \_\_List the breakout groups that need to meet (by Wed Oct 9).--Click here for the link. This meeting gives us the critical opportunity to sit face-to-face and plan the upcoming year's work. This page allows you to define the individuals or sub-work groups or cross-work groups that are in critical need of meeting (for example, we expect Jamie, Vincent, Hector, and their crews need to design experiments; field team needs to review sampling frameworks, and so on). The group you define here will be essential on Thursday (Sessions 4 and 5), a full day dedicated to PREEMPT year 2 planning. < Note this item is different than the Speed Science request listed under the Postdocs & students label below.>

4. \_\_ Nominate fellow PREEMPT colleagues for year 1 recognition (by Fri Oct 11, respond to Scott only).--The team worked hard in PREEMPT year 1 and Raina and Pete would like to recognize some of that work in a fun PREEMPT Year 1 Retrospective. We invite all attendees to nominate anyone else on the team for recognition of their PREEMPT year 1 work. It can be someone within your work group or from another work group and we aren't capping the number of people to be recognized. Nominations can be for excellent research, incredible dedication, spirit of collaboration ... or equally good we would LOVE to recognize people who may have had an incredibly funny or harrowing or embarrassing moment! The point is that anything goes, just use your imagination. You can send Scott just a name and a sentence or two of description; you'll tell the full story at the Retrospective. We've got some fun swag(!) for those recognized who are present at the meeting.

#### Additionally, from Postdocs and students only

- Complete the proposed publications page on Google docs (by Fri Oct 11).--Click here for the link. This spreadsheet will serve as the starting place for the Postdoc/student Session 3 breakout. (note, Pls are welcome to add their proposed publications if desired)
- Complete the Speed Science matrix (by Wed Oct 9).--Click here for the link. This matrix
  will help the group plan for short (likely 10-15 min) meetings between postdocs/students with
  the PI(s) they need to speak with, both for direct Q&A and to set up future meetings.

#### For the 7 work group leads

 (coming soon) Please note that by early next week we will send out a suggested template to guide you in presenting your group's PREEMPT year 1 results (Session 2).

Best, Scott

PS. For those interested in a bit of local "flavor" see this Sep 26 news item about recent bear attacks in Montana. The location is perhaps 100 miles distant from the B Bar. So while the grizzly caution noted in the agenda is presented with a light-hearted lilt, it is also real.

<2019Oct\_PREEMPT\_AnnualMeeting\_ver191003.docx>

From: Munster, Vincent (NIH/NIAID) [E] Sent: Mon, 7 Oct 2019 08:06:46 -0600

Emily Gurley; Kwe Claude, Yinda (NIH/NIAID) [F] To:

Cc: Ausraful Islam; Dr. Mohammed Ziaur Rahman; Plowright, Raina

Subject: Re: Prelim data Bangladesh

Hi Emily,

We are still trying to work out the best way of extracting the RNA of those samples as they were send in an extraction buffer we typically don't use (and this seems to be the only sample without any back-up). As soon as we know more, we'll let you know. Hopefully, we find some more in the other samples and the new shipment!

Cheers,

Vincent Munster, PhD Chief, Virus Ecology Section Laboratory of Virology **Rocky Mountain Laboratories** NIAID/NIH

(b) (6) From: Emily Gurley < Date: Monday, October 7, 2019 at 7:47 AM (b)(6)To: "Kwe Claude, Yinda (NIH/NIAID) [F]" < (b) (6) < (b) (6) Ausraful Islam Cc: ' (b) (6) "Dr. Mohammed Ziaur Rahman" < (b)(6)"Plowright, Raina" <

Subject: RE: Prelim data Bangladesh

Kwe,

Both of these samples are from nearby human spillover sites.

Any luck on getting more sequence from those historic samples we sent with paramyxos in them? Would be really interesting to compare these to the others we found, during previous outbreak investigations.

Best. **Emily** 

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From: Kwe Claude, Yinda (NIH/NIAID) [F] <
                                                                  (b) (6)
Sent: Wednesday, October 2, 2019 5:57 PM
To: Emily Gurley <
                                  (b) (6) Munster, Vincent (NIH/NIAID) [E] <
                                      (b) (6) Plowright, Raina <
                                                                                           (b) (6) Jamie
Ausraful Islam <
Lloyd-Smith <
                                 (b) (6) Hector Aguilar-Carreno <
                                                                                 (b) (6) Olivier Restif
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< (b) (6) Alison Peel < (b) (6) Cara Brook < (b) (6)

Cc: Schulz, Jonathan (NIH/NIAID) [F] < (b) (6) Bushmaker, Trenton (NIH/NIAID) [E] <

Subject: Re: Prelim data Bangladesh

Hey Emily,

Here are the paramyxo positive samples:

BoxName	SampleType	Species	AnimalID	YearMonth	Tree-Code
BGD-007	Urine swab/Urine in VTM-	Pteropus medius/ Pteropus	NBS-1137	2019	
BGD-007	Urine swab/Urine in VTM- A	giganteus Pteropus medius/	NBS-1149	2019	E12
		Pteropus giganteus			A1

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Kwe

From: Emily Gurley < (b) (6)

Date: Wednesday, October 2, 2019 at 3:31 PM

To: "Munster, Vincent (NIH/NIAID) [E]" < (b) (6) Ausraful Islam

(b) (6) "Plowright, Raina" < (b) (6) Jamie Lloyd-Smith < (b) (6) Hector Aguilar-Carreno < (b) (6) Olivier Restif

< (b) (6) Alison Peel < (b) (6) Cara Brook < (b) (6) Cc: "Kwe Claude, Yinda (NIH/NIAID) [F]" < (b) (6) "Schulz, Jonathan"

(NIH/NIAID) [F]" < (b) (6) "Bushmaker, Trenton (NIH/NIAID) [E]"

(b) (6)

Subject: RE: Prelim data Bangladesh

So exciting, Vincent! Thanks to you and the whole team.

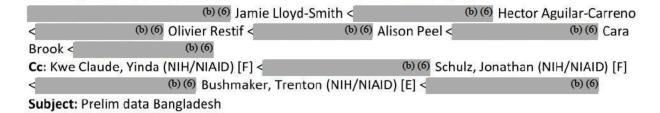
Can you tell us which samples these hits came from?

**Emily** 

From: Munster, Vincent (NIH/NIAID) [E] < (b) (6)

Sent: Wednesday, October 2, 2019 2:08 PM

To: Ausraful Islam (b) (6) Emily Gurley < (b) (6) Plowright, Raina



Hi everyone,

Here is some of the prelim data generated by Kwe and team from the Bangladesh samples (~500 samples screened with the Tong et al assay). So far no henipaviruses, but two sequences (in red) which cluster with an unclassified bat paramyxo lineage which includes bats from Australia and Kenya. We are working to see whether we can get the F and G sequences from these two positives to feed into the genotype-phenotype analyses (even though they are not henipa's). We have around 2-3 plates (96 samples per plate) for analyses, so we should be done with this soon.

We will be running Jordan and Congolese samples soon as well to maximize output (and to alleviate that the Australian samples are under a stringent MTA which prevents us from looking for unidentified paramyxo viruses)

In addition, we are batch sequencing F and G sequences of the Hendra viruses detected in the Australian samples, and will continue with trying to full genome sequencing using the VirCap-seq method. As soon as we have a batch of F and Gs of Hendra, we'll send the sequences to Hector for further phenotypic analyses.

