

Message

From: Fauci, Anthony (NIH/NIAID) [E] [REDACTED]
Sent: 1/31/2020 6:25:48 PM
To: Kristian G. Andersen [REDACTED]
CC: Jeremy Farrar [REDACTED]
Subject: RE: Phone call

Thanks, Christian. I will keep you posted.

Best regards,
Tony

From: Kristian G. Andersen [REDACTED]
Sent: Friday, January 31, 2020 8:05 PM
To: Fauci, Anthony (NIH/NIAID) [E] [REDACTED]
Cc: Jeremy Farrar [REDACTED]
Subject: Re: Phone call

Thanks Tony,

In addition to Eddie and Bob we have Mike Farzan on board (discoverer of the SARS receptor <https://www.scripps.edu/faculty/farzan/>), and I believe Jeremy will reach out to Christian Drosten and Ron Fouchier in the morning to get their expertise as well. Combined, this group will be able to objectively assess the available data and determine whether the genome looks unusual.

Please let me know if anything changes on your end or if you have any questions.

Best,
Kristian

On Fri, Jan 31, 2020 at 4:38 PM Fauci, Anthony (NIH/NIAID) [E] [REDACTED] wrote:

Jeremy:

I just got off the phone with Kristian Anderson and he related to me his concern about the Furine site mutation in the spike protein of the currently circulating 2019-nCoV. I told him that as soon as possible he and Eddie Holmes should get a group of evolutionary biologists together to examine carefully the data to determine if his concerns are validated. He should do this very quickly and if everyone agrees with this concern, they should report it to the appropriate authorities. I would imagine that in the USA this would be the FBI and in the UK it would be MI5. It would be important to quickly get confirmation of the cause of his concern by experts in the field of coronaviruses and evolutionary biology. In the meantime, I will alert my US. Government official colleagues of my conversation with you and Kristian and determine what further investigation they recommend. Let us stay in touch.

Best regards,
Tony

Anthony S. Fauci, MD
Director

National Institute of Allergy and Infectious Diseases

[REDACTED]
National Institutes of Health
Bethesda, MD 20892-2520
Phone: [REDACTED]
FAX: [REDACTED]
E-mail: [REDACTED]

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. The National Institute of Allergy and Infectious Diseases (NIAID) shall not accept liability for any statements made that are the sender's own and not expressly made on behalf of the NIAID by one of its representatives.

From: Jeremy Farrar [REDACTED]
Sent: Friday, January 31, 2020 5:57 PM
To: Fauci, Anthony (NIH/NIAID) [E] [REDACTED]
Subject: Re: Phone call

Thanks Tony

Can you phone Kristian Anderson

[REDACTED]
He is expecting your call now.

The people involved are:

Kristian Anderson

<https://www.scripps.edu/faculty/andersen/>

Bob Garry

<https://medicine.tulane.edu/departments/microbiology-immunology-tulane-cancer-center/faculty/robert-f-garry-jr-phd>

Eddie Holmes

<https://sydney.edu.au/science/about/our-people/academic-staff/edward-holmes.html>

From: "Conrad, Patricia (NIH/NIAID) [E]" [REDACTED] on behalf of "Fauci, Anthony (NIH/NIAID) [E]"

Date: Friday, 31 January 2020 at 22:34

To: Jeremy Farrar [REDACTED]

Subject: RE: Phone call

Will call shortly...

Patricia L. Conrad

Public Health Analyst and

Special Assistant to the Director

National Institute of Allergy and Infectious Diseases

The National Institutes of Health

[REDACTED]
Bethesda, Maryland 20892

[REDACTED]
[REDACTED] fax

Disclaimer:

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 (NIAID) shall not accept liability for any statement made that are sender's own and not expressly made on behalf of the NIAID by one of its representatives.

From: Jeremy Farrar [REDACTED]

Sent: Friday, January 31, 2020 5:23 PM

To: Fauci, Anthony (NIH/NIAID) [E] [REDACTED]

Subject: Phone call

Tony

Really would like to speak with you this evening

It is 10pm now UK

Can you phone me on +44 [REDACTED]

Jeremy

Wellcome exists to improve health by helping great ideas to thrive. We support researchers, we take on big health challenges, we campaign for better science, and we help everyone get involved with science and health research. We are a politically and financially independent foundation.

Message

From: Fauci, Anthony (NIH/NIAID) [E] [REDACTED]
Sent: 2/1/2020 10:43:31 AM
To: Kristian G. Andersen [REDACTED]
Subject: RE: FW: Science: Mining coronavirus genomes for clues to the outbreak's origins

Thanks, Kristian. Talk soon on the call.

From: Kristian G. Andersen [REDACTED]
Sent: Friday, January 31, 2020 10:32 PM
To: Fauci, Anthony (NIH/NIAID) [E] [REDACTED]
Cc: Jeremy Farrar [REDACTED]
Subject: Re: FW: Science: Mining coronavirus genomes for clues to the outbreak's origins

Hi Tony,

Thanks for sharing. Yes, I saw this earlier today and both Eddie and myself are actually quoted in it. It's a great article, but the problem is that our phylogenetic analyses aren't able to answer whether the sequences are unusual at individual residues, except if they are completely off. On a phylogenetic tree the virus looks totally normal and the close clustering with bats suggest that bats serve as the reservoir. The unusual features of the virus make up a really small part of the genome (<0.1%) so one has to look really closely at all the sequences to see that some of the features (potentially) look engineered.

We have a good team lined up to look very critically at this, so we should know much more at the end of the weekend. I should mention that after discussions earlier today, Eddie, Bob, Mike, and myself all find the genome inconsistent with expectations from evolutionary theory. But we have to look at this much more closely and there are still further analyses to be done, so those opinions could still change.

Best,
Kristian

On Fri, Jan 31, 2020 at 18:47 Fauci, Anthony (NIH/NIAID) [E] [REDACTED] wrote:

Jeremy/Kristian:

This just came out today. You may have seen it. If not, it is of interest to the current discussion.

Best,
Tony

From: Folkers, Greg (NIH/NIAID) [E] [REDACTED]
Sent: Friday, January 31, 2020 8:43 PM
Subject: Science: Mining coronavirus genomes for clues to the outbreak's origins



As part of a long-running effort to see what viruses bats harbor, researchers in China collect one from a cave in Guangdong.

EcoHealth Alliance

Mining coronavirus genomes for clues to the outbreak's origins

By [Jon Cohen](#) Jan. 31, 2020 , 6:20 PM

attaaaggttataacccttcc caggttaacca accaaccaac ttgcgatctc ttgttagatct ...

That string of apparent gibberish is anything but: It's a snippet of a DNA sequence from the viral pathogen, dubbed 2019 novel coronavirus (2019-nCoV), that is overwhelming China and frightening the entire world. Scientists are publicly sharing an ever-growing number of full sequences of the virus from patients—53 at last count in the [Global Initiative on Sharing All Influenza Data](#) database. These viral genomes are being intensely studied to try to understand the origin of 2019-nCoV and how it fits on the family tree of related viruses found in bats and other species. They have also given glimpses into what this newly discovered virus [physically looks like](#), [how it's changing](#), and [how it might be stopped](#).

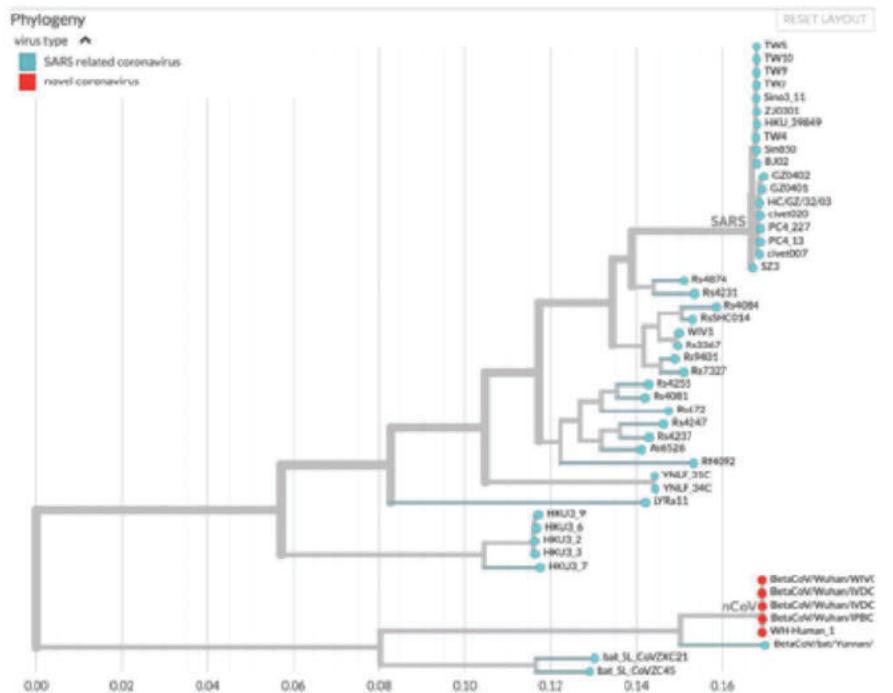
"One of the biggest takeaway messages [from the viral sequences] is that there was a single introduction into humans and then human-to-human spread," says Trevor Bedford, a bioinformatics specialist at the University of Washington, Seattle. The role of Huanan Seafood Wholesale Market in Wuhan, China, in spreading 2019-nCoV remains murky, though such sequencing, combined with sampling the market's environment for the presence of the virus, is clarifying that it indeed had an important early role in amplifying the outbreak. The viral sequences, most researchers say, also knock down the idea the pathogen came from a virology institute in Wuhan.

In all, 2019-nCoV has nearly 29,000 nucleotides bases that hold the genetic instruction book to produce the virus. Although it's one of the many viruses whose genes are in the form of RNA, scientists convert the viral genome into DNA, with bases known in shorthand as A, T, C, and G, to make it easier to study. Many analyses of 2019-nCoV's sequences have already appeared on [virological.org](#), [nextstrain.org](#), preprint servers like bioRxiv, and even in peer-reviewed journals. The sharing of the sequences by Chinese researchers allowed public health labs around the world to develop their own diagnostics for the virus, which now has been found in 18 other countries. (*Science's* news stories on the outbreak [can be found here](#).)

When the first 2019-nCoV sequence became available, researchers placed it on a family tree of known coronaviruses—which are abundant and infect many species—and found that it was most closely related to relatives found in bats. A team led by Shi Zheng-Li, a coronavirus specialist at the Wuhan Institute of Virology, reported on 23 January [on bioRxiv](#) that 2019-nCoV's sequence was 96.2% similar to a bat virus and had 79.5% similarity to the coronavirus that causes severe acute respiratory syndrome (SARS), a disease whose initial outbreak was also in China more than 15 years ago. But the SARS coronavirus has a similarly close relationship to bat viruses, and sequence data make a powerful case that

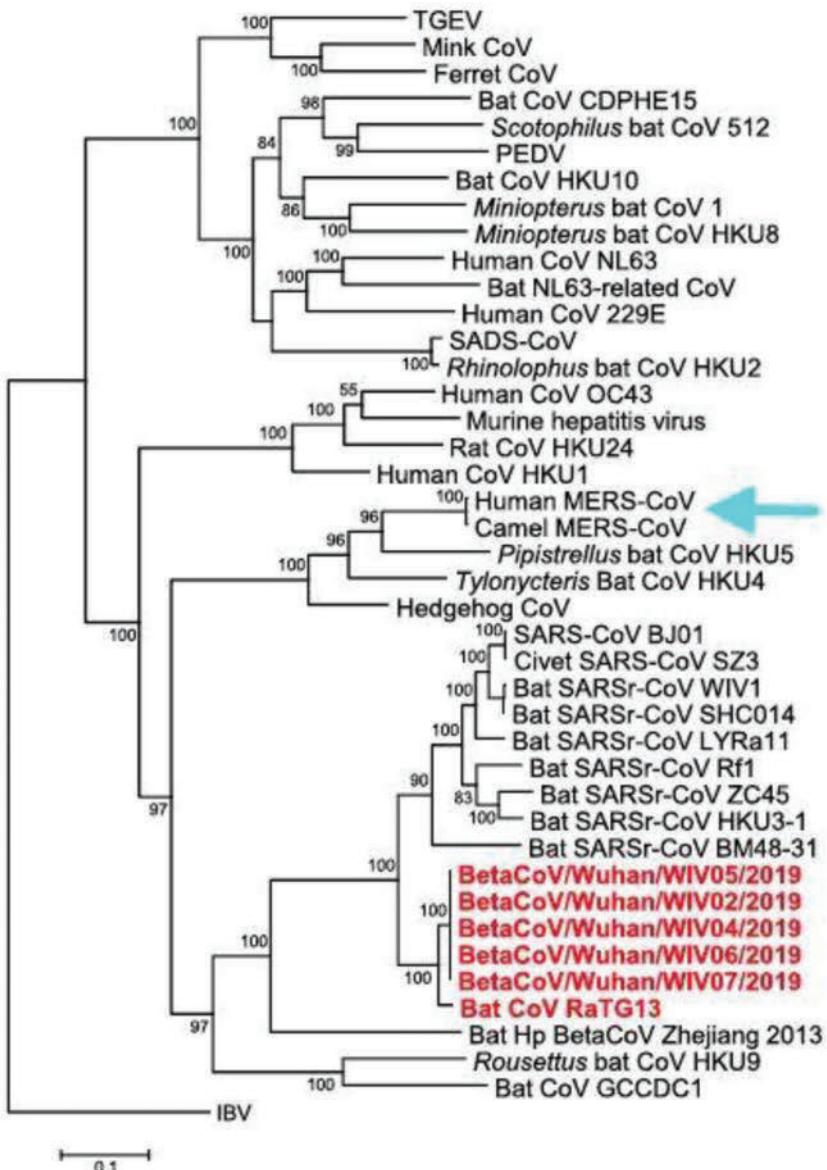
it jumped into people from a coronavirus in civets that differed from human SARS viruses by as few as 10 nucleotides. That's one reason why many scientists suspect there's an "intermediary" host species—or several—between bats and 2019-nCoV.

According to Bedford's analysis, the bat coronavirus sequence that Shi Zheng-Li's team highlighted, dubbed RaTG13, differs from 2019-nCoV by nearly 1100 nucleotides. On nextstrain.org, a site he co-founded, Bedford has created coronavirus family trees (example below) that include bat, civet, SARS, and 2019-nCoV sequences. (The [trees are interactive](#)—by dragging a computer mouse over them, it's easy to see the differences and similarities between the sequences.)



Bedford's analyses of RaTG13 and 2019-nCoV suggest that the two viruses shared a common ancestor 25 to 65 years ago, an estimate he arrived at by combining the difference in nucleotides between the viruses with the presumed rates of mutation in other coronaviruses. So it likely took decades for RaTG13-like viruses to mutate into 2019-nCoV.

Middle East respiratory syndrome (MERS), another human disease caused by a coronavirus, similarly has a link to bat viruses. But studies have built a compelling case it jumped to humans from camels. And the phylogenetic tree from Shi's bioRxiv paper (below) makes the camel-MERS link easy to see.



The longer a virus circulates in a human populations, the more time it has to develop mutations that differentiate strains in infected people, and given that the 2019-nCoV sequences analyzed to date differ from each other by seven nucleotides at most, this suggests it jumped into humans very recently. But it remains a mystery which animal spread the virus to humans. “There’s a very large gray area between viruses detected in bats and the virus now isolated in humans,” says Vincent Munster, a virologist at the U.S. National Institute of Allergy and Infectious Diseases who studies coronaviruses in bats, camels, and others species.

Strong evidence suggests the marketplace played an early role in spreading 2019-nCoV, but whether it was the origin of the outbreak remains uncertain. Many of the initially confirmed 2019-nCoV cases—27 of the first 41 [in one report](#), 26 of 47 in [another](#)—were connected to the Wuhan market, but up to 45%, including the earliest handful, were not. This raises the possibility that the initial jump into people happened [elsewhere](#).

[According to Xinhua](#), the state-run news agency, “environmental sampling” of the Wuhan seafood market has found evidence of 2019-nCoV. Of the 585 samples tested, 33 were positive for 2019-nCoV and all were in the huge market’s western portion, which is where wildlife were sold. “The positive tests from the wet market are hugely important,” says Edward Holmes, an evolutionary biologist at the University of Sydney who collaborated with the [first group](#) to publicly release a 2019-nCoV sequence. “Such a high rate of positive tests would strongly imply that animals in the market played a key role in the emergence of the virus.”

Yet there have been no preprints or official scientific reports on the sampling, so it's not clear which, if any, animals tested positive. "Until you consistently isolate the virus out of a single species, it's really, really difficult to try and determine what the natural host is," says Kristian Andersen, an evolutionary biologist at Scripps Research.

One possible explanation for the confusion about where the virus first entered humans is if there was a batch of recently infected animals sold at different marketplaces. Or an infected animal trader could have transmitted the virus to different people at different markets. Or, Bedford suggests, those early cases could have been infected by viruses that didn't easily transmit and sputtered out. "It would be hugely helpful to have just a sequence or two from the marketplace [environmental sampling] that could illuminate how many zoonoses occurred and when they occurred," Bedford says.



A research group sent fecal and other bodily samples from bats they trapped in caves to the Wuhan Institute of Virology to search for coronaviruses.

EcoHealth Alliance

In the absence of clear conclusions about the outbreak's origin, theories thrive, and some have been scientifically shaky. A sequence analysis led by Wei Ji of Peking University and published online by the *Journal of Medical Virology* received substantial press coverage when it suggested that "snake is the most probable wildlife animal reservoir for the 2019-nCoV." Sequence specialists, however, [pilloried it](#).

Conspiracy theories also abound. A CBC News report about the Canadian government deporting Chinese scientists who worked in a Winnipeg lab that studies dangerous pathogens [was distorted on social media](#) to suggest that they were spies who had smuggled out coronaviruses. The Wuhan Institute of Virology, which is the premier lab in China that studies bat and human coronaviruses, has also come under fire. "Experts debunk fringe theory linking China's coronavirus to weapons research," read a headline on a story in *The Washington Post* that focused on the facility.

Concerns about the institute predate this outbreak. *Nature* [ran a story in 2017](#) about it building a new biosafety level 4 lab and included molecular biologist Richard Ebright of Rutgers University, Piscataway, expressing concerns about accidental infections, which he noted repeatedly happened with lab workers handling [SARS in Beijing](#). Ebright, who has a long history of raising red flags about studies with dangerous pathogens, also in 2015 [criticized an experiment](#) in which modifications were made to a SARS-like virus circulating in Chinese bats to see whether it had the potential to cause disease in humans. Earlier this week, Ebright [questioned the accuracy](#) of Bedford's calculation that there are at least 25 years of evolutionary distance between RaTG13—the virus held in the Wuhan virology institute—and 2019-nCoV, arguing that the mutation rate may have been different as it passed through different hosts before humans. Ebright tells *ScienceInsider* that the 2019-nCoV data are "consistent with entry into the human population as a natural accident."

Shi did not reply to emails from *Science*, but her longtime collaborator, disease ecologist Peter Daszak of the EcoHealth Alliance, dismissed Ebright's conjecture. "Every time there's an emerging disease, a new virus, the same story comes out: This is a spillover or the release of an agent or a bioengineered virus," Daszak says. "It's just a shame. It seems humans can't resist controversy and these myths, yet it's staring us right in the face. There's this incredible diversity of

viruses in wildlife and we've just scratched the surface. Within that diversity, there will be some that can infect people and within that group will be some that cause illness."



A team of researchers from the Wuhan Institute of Virology and the EcoHealth Alliance have trapped bats in caves all over China, like this one in Guangdong, to sample them for coronaviruses.

EcoHealth Alliance

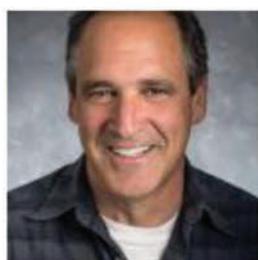
Daszak and Shi's group have for 8 years been trapping bats in caves around China to sample their feces and blood for viruses. He says they have sampled more than 10,000 bats and 2000 other species. They have found some 500 novel coronaviruses, about 50 of which fall relatively close to the SARS virus on the family tree, including RaTG13—it was fished out of a bat fecal sample they collected in 2013 from a cave in Moglang in Yunnan province. "We cannot assume that just because this virus from Yunnan has high sequence identity with the new one that that's the origin," Daszak says, noting that only a tiny fraction of coronaviruses that infect bats have been discovered. "I expect that once we've sampled and sampled and sampled across southern China and central China that we're going to find many other viruses and some of them will be closer [to 2019-nCoV]."

It's not just a "curious interest" to figure out what sparked the current outbreak, Daszak says. "If we don't find the origin, it could still be a raging infection at a farm somewhere, and once this outbreak dies, there could be a continued spillover that's really hard to stop. But the jury is still out on what the real origins of this are."

Posted in:

- [Asia/Pacific](#)
- [Health](#)
- [Coronavirus](#)

doi:10.1126/science.abb1256



Jon Cohen

Jon is a staff writer for *Science*.

- [Email Jon](#)
- [Twitter](#)

Disclaimer: Any third-party material in this email has been shared for internal use under fair use provisions of U.S. copyright law, without further verification of its accuracy/veracity. It does not necessarily represent my views nor those of NIAID, NIH, HHS, or the U.S. government.

Message

From: Pope, Andrew [REDACTED]
Sent: 2/3/2020 9:04:47 AM
To: 'Chakravarti, Aravinda' [REDACTED]; 'andersen' [REDACTED]; Ralph Baric [REDACTED]; 'trevor' [REDACTED]; Peter Daszak [REDACTED]; Gigi [REDACTED]; Gronvall [REDACTED]; 'tinglesby' [REDACTED]; Stanley Perlman [REDACTED]; 'KATHRYBR' [REDACTED]; Tony Fauci [REDACTED]; Hassell, David (Chris) (OS/ASPR/IO) [REDACTED]; 'Watson, Ian D. EOP/OSTP' [REDACTED]; 'Mex7' [REDACTED]; 'rlbull' [REDACTED]; 'Kadlec, Robert (OS/ASPR/IO)' [REDACTED]; 'Conrad, Patricia(NIH/NIAID)' [REDACTED]; [E]' [REDACTED]; 'Barasch, Kimberly (NIH/NIAID) [C]' [REDACTED]; May, David [REDACTED]; Chao, Samantha [REDACTED]; Laney, Kara N. [REDACTED]; Shore, Carolyn [REDACTED]; [REDACTED]; 'SheltonDavenport, Marilee' [REDACTED]; 'Symmes, Gregory' [REDACTED]; Brown, Lisa [REDACTED]; Downey, Autumn [REDACTED]; Wollek, Scott [REDACTED]; Kanarek, [REDACTED]; Morgan [REDACTED]; Dzau, Victor J. [REDACTED]; Beachy, Sarah [REDACTED]; Logan, Kendall [REDACTED]; Kearney, Megan [REDACTED]; Korsen, Dana [REDACTED]; Behney, Clyde [REDACTED]; Shern, Lauren [REDACTED]; Borel, Bridget [REDACTED]
CC:
Subject: Today's Call/meeting info
Attachments: Agenda- 2019-nCoV.docx; SOW.docx

Thank you for participating in today's meeting of experts at the National Academies to discuss and identify what data, information and samples are needed to understand the evolutionary origins of 2019-nCoV and more effectively respond to the outbreak and resulting misinformation.

Attached for your information are:

Agenda

Scope of Work

A list of participants will be sent along shortly

Please let me know if you have any questions or problems with connecting.

"Zoom" Call-in info is as follows (and is included at top of agenda):

Zoom Dial-in Info:

Time: Feb 3, 2020 02:00 PM Eastern Time (US and Canada)

Join from PC, Mac, Linux, iOS or Android: [REDACTED]

Telephone: [REDACTED]

Meeting ID: [REDACTED]

International numbers available: [REDACTED]

Andrew M. Pope, Ph.D.

Director

Board on Health Sciences Policy

Health and Medicine Division

The National Academies of Sciences,

Engineering, and Medicine

[REDACTED]

[REDACTED] direct

[REDACTED] office

Find us at nationalacademies.org/HMD

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

Expert Meeting
Rapid Response for Assessment of Data Needs for 2019-nCoV

Agenda

February 3, 2020
2:00 p.m.–3:00 p.m. (ET)

Keck Center, Room 103
500 5th St NW, Washington, DC 20001

Join from PC, Mac, Linux, iOS or Android: [REDACTED]

Telephone: [REDACTED]

Meeting ID: [REDACTED]

International numbers available: [REDACTED]

Meeting Objective: *Assess what data, information and samples are needed to understand the evolutionary origins of 2019-nCoV and more effectively respond to the outbreak and resulting misinformation.*

2:00 p.m. **Welcome and Introductions (5 mins)**

ANDREW POPE
Director, Board on Health Sciences Policy
National Academies of Sciences, Engineering, and Medicine

2:05 p.m. **Statement of Work (10 mins)**

KELVIN DROEGEMEIER
Director
Office of Science and Technology Policy

D. CHRISTIAN (“CHRIS”) HASSELL
Senior Science Advisor
U.S. Department of Health and Human Services

2:15 p.m. **Perspective from NIH/NIAID (10 mins)**

ANTHONY (“TONY”) S. FAUCI
Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

2:25 p.m. **Discussion of Meeting Objective (30 mins)**

2:55 p.m. **Determine Next Steps (5 mins)**

3:00 p.m. **Adjourn**

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

Statement of Work

Rapid Response for Assessment of Data Needs for 2019-nCoV

February 3, 2020

Statement of Task:

In response to a request from OSTP, the NASEM will examine information and identify data requirements that would help determine the origins of 2019-nCoV, specifically from an evolutionary/structural biology standpoint. NASEM will also consider whether this should include more temporally and geographically diverse clinical isolates, sequences, etc. Although a widely-disputed paper posted on a pre-print server last week has since been withdrawn, the response to that paper highlights the need to determine these information needs as quickly as possible. As part of a broader deliberative process, this review will help prepare for future events by establishing a process for quickly assembling subject matter experts for evaluation of other potentially threatening organisms.

Workplan:

NASEM will hold a meeting of experts to assess what data, information and samples are needed to address the unknowns, in order to understand the evolutionary origins of NCoV and more effectively respond to both the outbreak and any resulting misinformation. A statement from the National Academies will be prepared and published on the Web as a “Based on Science” article that summarizes the status and needs for more and what types of data. A more in-depth examination of the issues will be established as a follow up as needed.

URGENT: Please review by NOON if at all possible...

Kristian G. Andersen

Tue, Feb 4, 2020 at 9:05 AM

To: Peter Daszak

Cc: "Pope, Andrew"

, "Chakravarti, Aravinda"

, "Ralph Baric"

"Trevor Bedford"

Gigi Gronvall

, "Tom Inglesby"

"Stanley Perlman"

"Shore, Carolyn"

, "Chao, Samantha"

I too agree with all that has been said, but would caution against adding language suggesting that the virus might evolve (i.e., "mutate" to most people) towards better infectivity or transmission - a lot has been said about that for Ebola and other viruses, and it's been driving fear because most people don't fully understand what it means. I'm not arguing that it's not something that might well happen - the SARS data beautifully show it - but I would be worried about the message it could send.

Reading through the letter I think it's great, but I do wonder if we need to be more firm on the question of engineering. The main crackpot theories going around at the moment relate to this virus being somehow engineered with intent and that is demonstrably not the case. Engineering can mean many things and could be done for either basic research or nefarious reasons, but the data conclusively show that neither was done (in the nefarious scenario somebody would have used a SARS/MERS backbone and optimal ACE2 binding as previously described, and for the basic research scenario would have used one of the many already available reverse genetic systems). If one of the main purposes of this document is to counter those fringe theories, I think it's very important that we do so strongly and in plain language ("consistent with" [natural evolution] is a favorite of mine when talking to scientists, but not when talking to the public - especially conspiracy theorists).

Best,
Kristian

On Tue, Feb 4, 2020 at 9:02 AM Peter Daszak [REDACTED] wrote:

I agree with all of the other comments so far sent in, and want to add the following:

1) In the 3rd paragraph, it's important to add "including further samples from wildlife", and perhaps the rationale for this "to identify other viruses closely related to nCoV"

2) Re. references for #3 that there are current and planned studies underway on the bat origins of CoVs. Here are some references to pick from if they make sense:

- Latinne A, Hu B, Olival KJ, et al.; Origin and cross-species transmission of bat coronaviruses in China. *Nature Communications* 2020;In review.
- Wang N, Li S-Y, Yang X-L, et al.; Serological Evidence of Bat SARS-Related Coronavirus Infection in Humans, China. *Virologica Sinica* 2018. doi: 10.1007/s12250-018-0012-7.
- Hu B, Zeng L-P, Yang X-L, et al.; Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insights into the origin of SARS coronavirus. *PLOS Pathogens* 2017;13(11):e1006698. doi: 10.1371/journal.ppat.1006698.
- Zhou P, Fan H, Lan T, et al.; Fatal Swine Acute Diarrhea Syndrome caused by an HKU2-related Coronavirus of Bat Origin. *Nature* 2018

Cheers,

Peter

Peter Daszak

President

EcoHealth Alliance

New York, NY 10001

Tel. [REDACTED]

Website: www.ecohealthalliance.org

Twitter: [@PeterDaszak](https://twitter.com/PeterDaszak)

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 prevent pandemics and promote conservation.

From: Pope, Andrew [REDACTED]
Sent: Tuesday, February 4, 2020 9:11 AM
To: 'Chakravarti, Aravinda'; Kristian Andersen [REDACTED] Ralph Baric [REDACTED] Trevor Bedford [REDACTED] Peter Daszak; Gigi Gronvall; Tom Inglesby [REDACTED] Stanley [REDACTED]
Cc: Shore, Carolyn; Chao, Samantha
Subject: URGENT: Please review by NOON if at all possible...
Importance: High

Many thanks again for your thoughtful participation yesterday. The plans have changed in terms of our product. Instead of a "Based on Science" web posting, we are now developing a letter that will be signed by the 3 Presidents of our 3 Academies (NAS, Marcia McNutt; NAM, Victor Dzau; NAE, John Anderson), in response to a letter from OSTP. We think this will be more appropriate and expeditious.

Thus, given the urgency of the request from OSTP and HHS we ask that you please review the attached DRAFT CONFIDENTIAL letter, and let us know if you have any concerns or suggested edits. In particular, we would like to ask if there might be some additional detail added to the data needs that are identified. We think it would be helpful to be a bit more specific, but don't want to go into too much detail either. Your help there would be most helpful.

Many sincere thanks again for your continued engagement on this important activity!

Andy

Andrew M. Pope, Ph.D.

Director

Board on Health Sciences Policy

Health and Medicine Division

The National Academies of Sciences,

Engineering, and Medicine

[REDACTED]

[REDACTED], direct

[REDACTED], office

Find us at nationalacademies.org/HMD

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

To: 'Chakravarti, Aravinda'

[REDACTED]

Kristian Andersen

Baric, Ralph S

[REDACTED] Trevor Bedford

Gigi

Peter Daszak

Tom Inglesby

[REDACTED] Stanley Perlman

Cc: Shore, Carolyn

[REDACTED] Chao, Samantha

From: Pope, Andrew

Sent: Tue 2/4/2020 9:10:35 AM (UTC-05:00)

Subject: URGENT: Please review by NOON if at all possible...

Response Letter DRAFT - Feb 4.docx

Many thanks again for your thoughtful participation yesterday. The plans have changed in terms of our product. Instead of a "Based on Science" web posting, we are now developing a letter that will be signed by the 3 Presidents of our 3 Academies (NAS, Marcia McNutt; NAM, Victor Dzau; NAE, John Anderson), in response to a letter from OSTP. We think this will be more appropriate and expeditious.

Thus, given the urgency of the request from OSTP and HHS we ask that you please review the attached DRAFT CONFIDENTIAL letter, and let us know if you have any concerns or suggested edits. In particular, we would like to ask if there might be some additional detail added to the data needs that are identified. We think it would be helpful to be a bit more specific, but don't want to go into too much detail either. Your help there would be most helpful.

Many sincere thanks again for your continued engagement on this important activity!

Andy

Andrew M. Pope, Ph.D.

Director

Board on Health Sciences Policy

Health and Medicine Division

The National Academies of Sciences,
Engineering, and Medicine

[REDACTED]
direct
office

Find us at nationalacademies.org/HMD

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

CONFIDENTIAL DRAFT

February 4, 2020

[insert address]

Dear XXX:

Thank you for your letter regarding the current outbreak of a new respiratory virus, the 2019 Novel Coronavirus, or 2019-nCoV, which was first detected in Wuhan, China, and has now been reported in a growing number of locations worldwide, including the United States.¹ The request from OSTP is timely given the public health urgency of the outbreak and potential for misinformation.

In response to your request, we consulted leading experts² in the fields of virology, infectious disease genomics, genome sciences, epidemiology, microbiology, immunobiology, coronaviruses, emerging infections, biosecurity, and global health, to share their views of whether available genomic data on 2019-nCoV are consistent with natural evolution and the data that could help determine the origins of 2019-nCoV, specifically from an evolutionary and structural biology standpoint.

Many studies of the genome of 2019-nCoV to better understand its origin and how it relates to viruses found in bats and other species are already underway.³ The initial views of the experts⁴ is that the available genomic data are consistent with natural evolution⁵ and that there is currently no evidence that the virus was engineered to spread more quickly among humans. [ask experts to add specifics re binding sites?] They also told us that additional genomic sequence data from geographically and temporally diverse viral samples, including samples that have been collected prior to the outbreak in Wuhan, could be used to clarify the origins of the virus. Understanding the driving forces behind viral evolution may facilitate the development of more effective strategies for managing the 2019-nCoV outbreak. International collaboration is more important than ever to overcome these types of global challenges.

The National Academies stand ready to assemble a committee of experts to examine these issues in more detail and provide more complete evidence-based advice to you in an expedited manner if requested.

Thank you, again for your commitment to the National Academies and our efforts to provide independent, objective analysis; advise the nation; and inform public policy decisions.

Sincerely,

¹ “2019 Novel Coronavirus (2019-nCoV) Situation Summary.” *Centers for Disease Control and Prevention*, 3 Feb. 2020. https://www.cdc.gov/coronavirus/2019-nCoV/summary.html#anchor_1580079137454. Accessed 3 Feb. 2020.

² [possible add list]

³ [insert references]

⁵ [possibly add brief explanation that this does not preclude an unintentional release from a laboratory studying the evolution of related coronaviruses]

cc: [insert names]

Message

From: Edward Holmes [REDACTED]
Sent: 2/5/2020 1:23:41 AM
To: Garry, Robert F [REDACTED]; Kristian G. Andersen [REDACTED]; rambaut [REDACTED]
Subject: Re: Summary - Invitation to edit

Kristian, can you quickly check those RBD mutations in the pangolin S protein...

PROFESSOR EDWARD C. HOLMES FAA FRS
ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY
Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,
The University of Sydney | Sydney | NSW | 2006 | Australia

T [REDACTED]
E [REDACTED]

On 5 Feb 2020, at 1:03 pm, Garry, Robert F [REDACTED] wrote:

<https://www.statnews.com/2020/02/04/two-scenarios-if-new-coronavirus-isnt-contained/>

To your point K a very good article here about coronaviruses that are endemic in humans (Andrew gets a quote).

My guess that “quarantines and travel bans will first halt the outbreak and then eradicate the microbe, and the world will never see [2019-nCoV](#) again” is unlikely, unfortunately.

And unfortunately as well I think that we’re about to learn that “quarantines and travel bans” are really bad for the economy.

From: Kristian Andersen [REDACTED]
Date: Tuesday, February 4, 2020 at 7:08 PM
To: Robert Garry [REDACTED]
Cc: Edward Holmes [REDACTED], "rambaut@[REDACTED]"
Subject: Re: Summary - Invitation to edit

External Sender. Be aware of links, attachments and requests.

That's pretty interesting... All of which of course happens in humans. I do wonder if there's a scenario in which this thing could have been circulating in humans and animals for a while until that perfect little bugger came about and took off. Seems a little strange, but definitely not impossible - although, of course, if the O-glycans are somehow involved in the infectivity of human cells (as opposed to immunity), then we're swinging back to cell culture.

On Tue, Feb 4, 2020 at 4:34 PM Garry, Robert F [REDACTED] wrote:

Another thing about the evolution of the glycans.

This has happened naturally in other CoV.

Not all MHV have an optimal furin site. Those that do have the furin site inevitably also add a 2-3 predicted O-linked glycans in or about the cleavage site..

Variation on the theme in HKU1, a virus that probably does have intense transmission infecting millions of people each year. Here the insert is three Serine residues, which pushes this site to a mucin-like patch (there are already a couple of prolines and the SSS is a turn as well)

Funny thing – not on the attachments, but those strains of MHV and HKU-1 that have o-linked glycans and the furin site ALSO have a larger patch - sometimes very large patch - of predicted o-linked glycans at the top of the prefusion form. When you see the pattern repeat itself in different viruses you start to believe it.

From: Robert Garry [REDACTED]

Date: Tuesday, February 4, 2020 at 5:56 PM

To: Kristian Andersen [REDACTED], Edward Holmes <[REDACTED]>

Cc: "rambaut@[REDACTED]"

Subject: Re: Summary - Invitation to edit

Kristian that's correct about everything he said for the P residue. It's what's shifted me to thinking that the insert of the furin site is the result of cell culture passage [or less likely intense transmission in a nonbat host]. Really need to see the data from Ron about generating the furin cleavage site on in vitro passage. Really!

CoV come with or without a furin site. CoV without a furin site are said to be non-cleaved and rely on endosomal proteases like cathepsin for entry. However if you infect a virus like SARS in culture in the presence of exogenous protease like trypsin its 100X more effective at entering because the spike gets cleaved and it can enter at the cell surface.

You have to infect flu viruses (the ones without the multibasic cleavage site) in the presence of trypsin, and include trypsin in the overlay if you want to get virus spread aka plaques.

This also contributes to the pathogenicity of - well - highly pathogenic flu virus – different tissues have different proteases and are able to “activate” flu to different extents - if the flu v has a furin cleavage site it has a lot more choices and can more easily go systemic.

This is an [excellent review](#) on CoV fusion – deals with all the complexities:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3397359/>

Bottom line – I think that if you put selection pressure on a Cov without a furin cleavage site in cell culture you could well generate a furin cleavage site after a number of passages (but let's see the data Ron!). It will infect a lot better if it can effectively fuse at the cell surface and doesn't have to rely on endosomal cleavage and receptor mediated endocytosis..

From: Kristian Andersen [REDACTED]

Date: Tuesday, February 4, 2020 at 5:08 PM

To: Edward Holmes [REDACTED]

Cc: Robert Garry <[REDACTED]>, "rambaut@[REDACTED]"

Subject: Re: Summary - Invitation to edit

External Sender. Be aware of links, attachments and requests.

Outside my expertise, but I don't necessarily think that passage in animals would add the glycans. It's more that the glycans could suggest some sort of immune system as the glycans often work to 'shield' epitopes. So if the acquisition of glycans is adaptive, that would be suggestive of an immune system.

We didn't write this in the report, but the residues on which the glycans (S, T, and S) are all conserved in the bat virus - it's the addition of the P that makes it a specific glycan site though (not conserved in the bat, hence not predicted to be O-glycans). It's entirely possible that the 'P' works as a flexible residue for the furin cleavage site and by proxy creates the (predicted) O-linked glycans.

I'll let Bob weigh in as well - definitely not my area of expertise.

K

On Tue, Feb 4, 2020 at 2:59 PM Edward Holmes <[REDACTED]> wrote:

Agreed. Timing is perfect.

Bob - a question from Jeremy:

"Quick question though - why could passage in animals in lab work add the glycans?"

Any thoughts?

Eddie

PROFESSOR EDWARD C. HOLMES FAA FRS
ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY

Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,
The University of Sydney | Sydney | NSW | 2006 | Australia

T [REDACTED]
E [REDACTED]

On 5 Feb 2020, at 9:53 am, Garry, Robert F <[REDACTED]> wrote:

Ironically the prevailing theory now in the underbelly of the internet is that the US or other enemy engineered this bio weapon and released it on China

If the public health aspects of this were not bad enough the political fallout would be.

Good to have cogent science against the bio weapon scenario which is why I favor getting who involved in the "controversy"

Accidental release is a scenario many will not be comfortable with but it would be irresponsible to dismiss the possibility out of hand.

Sent from my iPhone

On Feb 4, 2020, at 3:28 PM, Edward Holmes <[REDACTED]> wrote:

External Sender. Be aware of links, attachments and requests.

Jeremy is passing to Tony and Francis first.

Professor Edward C. Holmes FAA FRS
The University of Sydney

On 5 Feb 2020, at 8:12 am, Garry, Robert F [REDACTED] wrote:

On the broad topic of O-linked glycans on viruses from China I've attached a model of Alongshan virus, which I know Eddie has a particular interest.

It's instructive to see the mucin-like domains with a high concentration of serines, threonines and prolines.

This sequence in HKU1 CoV is also a mucin like domain:

481 fassckshkp psascpgtn yrscesttv1 dhtdwrcsc lpdpitaydp rscsqkkslv

Again several predicted O-linked glycans (also several at the furin site).

In the crystal structure 5i08 it is disordered because of the o-linked glycans..

From: Kristian Andersen [REDACTED]

Date: Tuesday, February 4, 2020 at 2:39 PM

To: Edward Holmes

Cc: Robert Garry <[REDACTED]>, "rambaut@[REDACTED]"

Subject: Re: Summary - Invitation to edit

[REDACTED]
External Sender. Be aware of links, attachments and requests.

Sounds good Eddie!

I was on a conference call hosted by the National Academy of Sciences yesterday and a statement about this not being "engineering" should be coming out from them - I believe Tony called that meeting. Let's see what comes out of that as well.

The idea of engineering and bioweapon is definitely not going away and I'm still getting pinged by journalists. I have noticed some of them starting to ask more broadly about "lab escape" and for now I have just ignored them - there might be a time where we need to tackle that more directly head on, but I'll let the likes of Jeremy and Tony figure out how to do that.

K

On Tue, Feb 4, 2020 at 12:36 PM Edward Holmes <[REDACTED]> wrote:

I've just passed to Jeremy.

PROFESSOR EDWARD C. HOLMES FAA FRS
ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY

Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,
The University of Sydney | Sydney | NSW | 2006 | Australia

T [REDACTED]
E [REDACTED]

On 5 Feb 2020, at 7:14 am, Garry, Robert F [REDACTED] wrote:

Another caveat is that I think there is plenty of room for additional discussion amongst the experts. Jeremy's idea (or was it Tony's) of a face-to-face under the auspicious of WHO still makes sense to me.

From: Edward Holmes <[REDACTED]>
Date: Tuesday, February 4, 2020 at 2:10 PM
To: Kristian Andersen [REDACTED]
Cc: Robert Garry [REDACTED], "rambaut" [REDACTED]
Subject: Re: Summary - Invitation to edit

External Sender. Be aware of links, attachments and requests.

Works for me. Should I quickly check with Jeremy to see if he is happy for it to be circulated to the wider group?

Great job.

Professor Edward C. Holmes FAA FRS
The University of Sydney

On 5 Feb 2020, at 7:03 am, Kristian G. Andersen [REDACTED] wrote:

Did a final pass and I think it looks great.

Unless others have further comments, I'd say this is ready to go up the chain. Importantly, my assumption is that this will not be a document that is meant for public consumption, as that would require much more careful crafting and attention to specific wording of key concepts in the document (not really a task I think we could/should take on - that would be way, way more work).

K

On Tue, Feb 4, 2020 at 11:31 AM Garry, Robert F [REDACTED] wrote:

Gentlemen – I believe that the document is getting very clean.

Only a few minor points to address [or not] from my view.

I believe it is a cogent explanation why concerns were raised.

If there is a natural explanation for CoV, it needs to be found. A lot of unobserved transmission in animals/humans AND as yet unsampled Bat CoV variants (with whole or partial furin sites) must exist.

Some, perhaps more than a few, will not like it still since it allows that the nCoV may have arisen during cell culture passage in a lab (their labs).

Thanks for the great science...

b

From: Kristian Andersen [REDACTED]

Reply-To: Kristian Andersen [REDACTED]

Date: Monday, February 3, 2020 at 9:36 PM

To: Robert Garry [REDACTED]

Cc: "[edward.holmes](#)" [REDACTED], "[rambaut](#)" [REDACTED]

Subject: Summary - Invitation to edit

External Sender. Be aware of links, attachments and requests.

[REDACTED] has invited you to [edit](#) the following document:

Error! Filename not specified.

[Summary](#)

Error! Filename not specified. Closing via link to this document as this needs to be safe. Should have a draft of the various sections shortly.

[Open in Docs](#)

Google Docs: Create and edit documents online.

Google LLC, 1600 Amphitheatre Parkway, Mountain View, CA 94043, USA

You have received this email because someone shared a document with you from Google Docs.

Error!
Filename
not
specified

<Alongshan copy.pdf>

Message

From: Edward Holmes
[REDACTED]
Sent: 2/5/2020 4:22:24 AM
To: Andrew Rambaut
[REDACTED]
CC: Garry, Robert F
[REDACTED] Kristian G.
Andersen [REDACTED]
Subject: Re: Summary - Invitation to edit

External Sender. Be aware of links, attachments and requests.

Region 6 is the RBD. Could be recombination? Very strange.

PROFESSOR EDWARD C. HOLMES FAA FRS
ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY
Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,
The University of Sydney | Sydney | NSW | 2006 | Australia
T [REDACTED]
E [REDACTED]

On 5 Feb 2020, at 9:04 pm, Edward Holmes [REDACTED] wrote:

I think we might have dropped the ball with this pangolin virus. I ignored it when I saw it didn't have the furin cleavage site. Should now check all the key sites.

Cheers,

Eddie

PROFESSOR EDWARD C. HOLMES FAA FRS
ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY
Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,
The University of Sydney | Sydney | NSW | 2006 | Australia
T [REDACTED]
E [REDACTED]

On 5 Feb 2020, at 8:44 pm, Andrew Rambaut [REDACTED] wrote:

I think we need to keep this document live and update it as necessary. Give it a date and version number.

Andrew

Sent from my phone. Apologies for brevity or illiteracy.

On 5 Feb 2020, at 09:23, Edward Holmes [REDACTED] wrote:

Kristian, can you quickly check those RBD mutations in the pangolin S protein...

PROFESSOR EDWARD C. HOLMES FAA FRS

ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY

Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,
The University of Sydney | Sydney | NSW | 2006 | Australia

T [REDACTED]

E [REDACTED]

On 5 Feb 2020, at 1:03 pm, Garry, Robert F [REDACTED] wrote:

<https://www.statnews.com/2020/02/04/two-scenarios-if-new-coronavirus-isnt-contained/>

To your point K a very good article here about coronaviruses that are endemic in humans (Andrew gets a quote).

My guess that “quarantines and travel bans will first halt the outbreak and then eradicate the microbe, and the world will never see [2019-nCoV](#) again” is unlikely, unfortunately.

And unfortunately as well I think that we’re about to learn that “quarantines and travel bans” are really bad for the economy.

From: Kristian Andersen [REDACTED]

Date: Tuesday, February 4, 2020 at 7:08 PM

To: Robert Garry [REDACTED]

Cc: Edward Holmes [REDACTED], "rambaut" [REDACTED]

Subject: Re: Summary - Invitation to edit

External Sender. Be aware of links, attachments and requests.

That's pretty interesting... All of which of course happens in humans. I do wonder if there's a scenario in which this thing could have been circulating in humans and animals for a while until that perfect little bugger came about and took off. Seems a little strange, but definitely not impossible - although, of course, if the O-glycans are somehow involved in the infectivity of human cells (as opposed to immunity), then we're swinging back to cell culture.

On Tue, Feb 4, 2020 at 4:34 PM Garry, Robert F [REDACTED] wrote:

Another thing about the evolution of the glycans.

This has happened naturally in other CoV.

Not all MHV have an optimal furin site. Those that do have the furin site inevitably also add a 2-3 predicted O-linked glycans in or about the cleavage site..

Variation on the theme in HKU1, a virus that probably does have intense transmission infecting millions of people each year. Here the insert is three Serine residues, which pushes this site to a mucin-like patch (there are already a couple of prolines and the SSS is a turn as well)

Funny thing – not on the attachments, but those strains of MHV and HKU-1 that have o-linked glycans and the furin site ALSO have a larger patch - sometimes very large patch - of predicted o-linked glycans at the top of the prefusion form. When you see the pattern repeat itself in different viruses you start to believe it.

From: Robert Garry [REDACTED]
Date: Tuesday, February 4, 2020 at 5:56 PM
To: Kristian Andersen [REDACTED], Edward Holmes [REDACTED]
Cc: "rambaut" [REDACTED]
Subject: Re: Summary - Invitation to edit

Kristian that's correct about everything he said for the P residue. It's what's shifted me to thinking that the insert of the furin site is the result of cell culture passage [or less likely intense transmission in a nonbat host]. Really need to see the data from Ron about generating the furim cleavage site on in vitro passage. Really!

CoV come with or without a furin site. CoV without a furin site are said to be non-cleaved and rely on endosomal proteases like cathepsin for entry. However if you infect a virus like SARS in culture in the presence of exogenous protease like trypsin its 100X more effective at entering because the spike gets cleaved and it can enter at the cell surface.

You have to infect flu viruses (the ones without the multibasic cleavage site) in the presence of trypsin, and include trypsin in the overlay if you want to get virus spread aka plaques.

This also contributes to the pathogenicity of - well - highly pathogenic flu virus – different tissues have different proteases and are able to “activate” flu to different extents - if the flu v has a furin cleavage site it has a lot more choices and canmore easil go systemic.

This is an excellent review on CoV fusion – deals with all the complexities:
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3397359/>

Bottom line – I think that if you put selection pressure on a Cov without a furin cleavage site in cell culture you could well generate a furin cleavage site after a number of passages (but let's see the data Ron!). It will infect a lot better if it can effectively fuse at the cell surface and doesn't have to rely on endosomal cleavage and receptor mediated endocytosis..

From: Kristian Andersen [REDACTED]
Date: Tuesday, February 4, 2020 at 5:08 PM
To: Edward Holmes [REDACTED]
Cc: Robert Garry [REDACTED], "rambaut" [REDACTED]
Subject: Re: Summary - Invitation to edit

External Sender. Be aware of links, attachments and requests.

Outside my expertise, but I don't necessarily think that passage in animals would add the glycans. It's more that the glycans could suggest some sort of immune system as the glycans often work to 'shield' epitopes. So if the acquisition of glycans is adaptive, that would be suggestive of an immune system.

We didn't write this in the report, but the residues on which the glycans (S, T, and S) are all conserved in the bat virus - it's the addition of the P that makes it a specific glycan site though (not conserved in the bat, hence not predicted to be O-glycans). It's entirely possible that the 'P' works as a flexible residue for the furin cleavage site and by proxy creates the (predicted) O-linked glycans.

I'll let Bob weigh in as well - definitely not my area of expertise.

K

On Tue, Feb 4, 2020 at 2:59 PM Edward Holmes [REDACTED] wrote:

Agreed. Timing is perfect.

Bob - a question from Jeremy:

"Quick question though - why could passage in animals in lab work add the glycans?"

Any thoughts?

Eddie

PROFESSOR EDWARD C. HOLMES FAA FRS

ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY

Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,
The University of Sydney | Sydney | NSW | 2006 | Australia

T : [REDACTED]

E : [REDACTED]

On 5 Feb 2020, at 9:53 am, Garry, Robert F. [REDACTED] wrote:

Ironically the prevailing theory now in the underbelly if the internet is that the us or other enemy engineered this bio weapon and released it on China

If the public health aspects of this were not bad enough the political fallout would be.

Good to have cogent science against the bio weapon scenario which is why I favor getting who involved in the "controversy"

Accidental release is a scenario many will not be comfortable with but it would be irresponsible to dismiss the possibility out of hand.

Sent from my iPhone

On Feb 4, 2020, at 3:28 PM, Edward Holmes [REDACTED] wrote:

External Sender. Be aware of links, attachments and requests.

Jeremy is passing to Tony and Francis first.

Professor Edward C. Holmes FAA FRS
The University of Sydney

GARRY0000101

On 5 Feb 2020, at 8:12 am, Garry, Robert F [REDACTED] wrote:

On the broad topic of O-linked glycans on viruses from China I've attached a model of Alongshan virus, which I know Eddie has a particular interest.

It's instructive to see the mucin-like domains with a high concentration of serines, threonines and prolines.

This sequence in HKU1 CoV is also a mucin like domain:

481 fassckshkp psascpigtn yrscesttvl dhtdwcrcsc lpdpitaydp rscsqkkslv

Again several predicted O-linked glycans (also several at the furin site).

In the crystal structure 5i08 it is disordered because of the o-linked glycans..

From: Kristian Andersen [REDACTED]

Date: Tuesday, February 4, 2020 at 2:39 PM

To: Edward Holmes [REDACTED]

Cc: Robert Garry [REDACTED], "[rambaut](#)" [REDACTED]

Subject: Re: Summary - Invitation to edit

External Sender. Be aware of links, attachments and requests.

Sounds good Eddie!

I was on a conference call hosted by the National Academy of Sciences yesterday and a statement about this not being "engineering" should be coming out from them - I believe Tony called that meeting. Let's see what comes out of that as well.

The idea of engineering and bioweapon is definitely not going away and I'm still getting pinged by journalists. I have noticed some of them starting to ask more broadly about "lab escape" and for now I have just ignored them - there might be a time where we need to tackle that more directly head on, but I'll let the likes of Jeremy and Tony figure out how to do that.

K

On Tue, Feb 4, 2020 at 12:36 PM Edward Holmes [REDACTED] wrote:

I've just passed to Jeremy.

PROFESSOR EDWARD C. HOLMES FAA FRS

ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY

Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,
The University of Sydney | Sydney | NSW | 2006 | Australia

T [REDACTED]

E [REDACTED]

On 5 Feb 2020, at 7:14 am, Garry, Robert F [REDACTED] wrote:

GARRY0000102

Another caveat is that I think there is plenty of room for additional discussion amongst the experts. Jeremy's idea (or was it Tony's) of a face-to-face under the auspicious of WHO still makes sense to me.

From: Edward Holmes [REDACTED]
Date: Tuesday, February 4, 2020 at 2:10 PM
To: Kristian Andersen [REDACTED]
Cc: Robert Garry [REDACTED], "rambaut" [REDACTED]
Subject: Re: Summary - Invitation to edit

External Sender. Be aware of links, attachments and requests.

Works for me. Should I quickly check with Jeremy to see if he is happy for it to be circulated to the wider group?

Great job.

Professor Edward C. Holmes FAA FRS
The University of Sydney

On 5 Feb 2020, at 7:03 am, Kristian G. Andersen [REDACTED] wrote:

Did a final pass and I think it looks great.

Unless others have further comments, I'd say this is ready to go up the chain. Importantly, my assumption is that this **will not** be a document that is meant for public consumption, as that would require much more careful crafting and attention to specific wording of key concepts in the document (not really a task I think we could/should take on - that would be way, way more work).

K

On Tue, Feb 4, 2020 at 11:31 AM Garry, Robert F [REDACTED] wrote:

Gentlemen – I believe that the document is getting very clean.

Only a few minor points to address [or not] from my view.

I believe it is a cogent explanation why concerns were raised.

If there is a natural explanation for CoV, it needs to be found. A lot of unobserved transmission in animals/humans AND as yet unsampled Bat CoV variants (with whole or partial furin sites) must exist.

Some, perhaps more than a few, will not like it still since it allows that the nCoV may have arisen during cell culture passage in a lab (their labs).

Thanks for the great science...

b

From: Kristian Andersen [REDACTED]
Reply-To: Kristian Andersen <[REDACTED]>
Date: Monday, February 3, 2020 at 9:36 PM

To: Robert Garry [REDACTED]

Cc: "edward.holmes" [REDACTED], "rambaut" [REDACTED]

Subject: Summary - Invitation to edit

External Sender. Be aware of links, attachments and requests.

[REDACTED] has invited you to **edit** the following document:

Error! Filename not specified.

Summary

Error! Filename not specified. Closing via link to this document as this needs to be safe. Should have a draft of the various sections shortly.

[Open in Docs](#)

Google Docs: Create and edit documents online.

Google LLC, 1600 Amphitheatre Parkway, Mountain View, CA 94043, USA

You have received this email because someone shared a document with you from Google Docs.

Error!
Filename
not
specified.

<Alongshan copy.pdf>

Message

From: Edward Holmes [REDACTED]
Sent: 2/6/2020 2:36:30 AM
To: Kristian G. Andersen [REDACTED]
CC: Garry, Robert F [REDACTED]; Andrew Rambaut [REDACTED]
Subject: Re: Summary - Invitation to edit

From Jeremy.

"Do you think in the report....possible to dampen down further the 'conspiracy' idea and make totally neutral?

Talking with Marion last night and with the WHO meeting next week....both wondering whether actually publishing this sooner, but ruthlessly on the science....is worthwhile to put that flag down..."

Thoughts?

PROFESSOR EDWARD C. HOLMES FAA FRS
ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY

Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,
The University of Sydney | Sydney | NSW | 2006 | Australia

T
E
[REDACTED]

On 6 Feb 2020, at 11:10 am, Kristian G. Andersen [REDACTED] wrote:

Haha, I got the same email. I assume Andrew probably did too.

I already said yes.

Not.

K

On Wed, Feb 5, 2020 at 16:05 Garry, Robert F [REDACTED] wrote:

I'd probably stammer a bit on, "Professor Garry can you assure our audience beyond any reasonable doubt that nCoV did not escape from the WIV?"

From: Edward Holmes [REDACTED]
Date: Wednesday, February 5, 2020 at 5:46 PM
To: Andrew Rambaut [REDACTED]
Cc: Robert Garry [REDACTED], Kristian Andersen [REDACTED]
Subject: Re: Summary - Invitation to edit

External Sender. Be aware of links, attachments and requests.

I thought I had better say no...

Dear Professor Holmes,

My name is Andrey Kozlov, I'm producer in Russian Broadcasting Company NTV. We are making a report on false conspiracy theories around new China's coronavirus. I'm looking for an interview opportunity with you on this issue. We would like to discuss with you these theories, where they came from, what effect they have and etc. Will it be possible for you to meet with our film crew this week? Perhaps, on Thursday or Friday? Hope for you cooperation.

Best regards,

Andrey Kozlov,

Producer,

NTV Broadcasting company

Cell. [REDACTED]

PROFESSOR EDWARD C. HOLMES FAA FRS

ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY

Marie Bashir Institute for Infectious Diseases & Biosecurity,

School of Life & Environmental Sciences and School of Medical Sciences,

The University of Sydney | Sydney | NSW | 2006 | Australia

T [REDACTED]

E [REDACTED]

On 6 Feb 2020, at 9:43 am, Andrew Rambaut [REDACTED] wrote:

The Sunda pangolin, also known as the Malayan or Javan pangolin, is a species of pangolin. It is found throughout Southeast Asia, including Brunei, Cambodia, Java, Sumatra, Borneo, the Lesser Sunda Islands, Laos, Malaysia, Singapore, Thailand, Myanmar and Vietnam.

(wikipedia)

On 5 Feb 2020, at 22:39, Garry, Robert F [REDACTED] wrote:

Fascinating – so does this mean they were infected before being smuggled out of Malaysia?

From: Edward Holmes · [REDACTED]
Date: Wednesday, February 5, 2020 at 4:37 PM
To: Robert Garry · [REDACTED]
Cc: Kristian Andersen · [REDACTED], Andrew Rambaut · [REDACTED]
Subject: Re: Summary - Invitation to edit

[REDACTED] External Sender. Be aware of links, attachments and requests.

Smuggled in. Captured by the anti-smuggling cops in two southern provinces.

PROFESSOR EDWARD C. HOLMES FAA FRS
ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY
Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,
The University of Sydney | Sydney | NSW | 2006 | Australia
T · [REDACTED]
E · [REDACTED]

On 6 Feb 2020, at 9:24 am, Garry, Robert F · [REDACTED] wrote:

SO just info from Wiki but *Manis javanica* is the Malayan pangolin.

Chinese pangolin (*Manis pentadactyla*) is the one in southern China.

I guess the ranges overlap some, but is it odd that they got this species?

From: Edward Holmes · [REDACTED]
Date: Wednesday, February 5, 2020 at 4:12 PM
To: Robert Garry · [REDACTED]
Cc: Kristian Andersen · [REDACTED], Andrew Rambaut · [REDACTED]
Subject: Re: Summary - Invitation to edit

[REDACTED] External Sender. Be aware of links, attachments and requests.

More pangolin viruses on this tree - crazy.

--

PROFESSOR EDWARD C. HOLMES FAA FRS

ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY

Marie Bashir Institute for Infectious Diseases & Biosecurity,

School of Life & Environmental Sciences and School of Medical Sciences,

The University of Sydney | Sydney | NSW | 2006 | Australia

T
E
[REDACTED]

On 6 Feb 2020, at 9:08 am, Garry, Robert F <[REDACTED]> wrote:

No problem with Marian Koopsman either.

From: Robert Garry <[REDACTED]>

Date: Wednesday, February 5, 2020 at 4:07 PM

To: Kristian Andersen <[REDACTED]>

Cc: Andrew Rambaut <[REDACTED]>, Edward Holmes <[REDACTED]>

Subject: Re: Summary - Invitation to edit

Kawaoka is a good guy. Good perspective on GoF research and flu.

From: Kristian Andersen <[REDACTED]>

Date: Wednesday, February 5, 2020 at 4:01 PM

To: Robert Garry <[REDACTED]>

Cc: Andrew Rambaut <[REDACTED]>, Edward Holmes <[REDACTED]>

Subject: Re: Summary - Invitation to edit

[REDACTED]
External Sender. Be aware of links, attachments and requests.

'Ego' is Eddie's genius (he's got many other...).

Yeah, Eddie, good point. Need to nix Baric too then.

How about Yoshi? He might know some good people in Japan.

K

On Wed, Feb 5, 2020 at 13:59 Garry, Robert F <[REDACTED]> wrote:

I'm "sure" that Ego was a typo – otherwise well done!

From: Kristian Andersen · [REDACTED]

Date: Wednesday, February 5, 2020 at 3:58 PM

To: Edward Holmes [REDACTED]

Cc: Andrew Rambaut [REDACTED], Robert Garry · [REDACTED]

Subject: Re: Summary - Invitation to edit

External Sender. Be aware of links, attachments and requests.

EgoHealth people might have some African collaborators they could suggest?

K

On Wed, Feb 5, 2020 at 13:57 Edward Holmes [REDACTED] wrote:

WHO need geographic breath. Very important for them.

Thanks for all the suggestions.

PROFESSOR EDWARD C. HOLMES FAA FRS
ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY

Marie Bashir Institute for Infectious Diseases & Biosecurity,

School of Life & Environmental Sciences and School of Medical Sciences,

The University of Sydney | Sydney | NSW | 2006 | Australia

T [REDACTED]
E [REDACTED]

On 6 Feb 2020, at 8:55 am, Garry, Robert F · [REDACTED] wrote:

Yes was just going to suggest Malik Peiris from Hong Kong – brings expertise of CoV and flu.

Not sure Christian Happi is the right person for CoV. His input would be very general.

I'm told they had or about to have a meeting on CoV preparedness in Dakar. But not sure who is involved. Might be a place to start.

MERS CoV has been isolated from camels in Kenya, but mostly WIV and outside investigators involved.

From: Edward Holmes [REDACTED]
Date: Wednesday, February 5, 2020 at 3:43 PM
To: Andrew Rambaut [REDACTED]
Cc: Robert Garry [REDACTED], Kristian Andersen [REDACTED]
Subject: Re: Summary - Invitation to edit

External Sender. Be aware of links, attachments and requests.

Thanks. Anyone from Asia? Africa?

Professor Edward C. Holmes FAA FRS
The University of Sydney

On 6 Feb 2020, at 8:36 am, Andrew Rambaut [REDACTED] wrote:

Colin Parrish, Jamie Lloyd Smith, Sara Sawer for zoonotic theory?

A

Sent from my phone. Apologies for brevity or illiteracy.

On 5 Feb 2020, at 21:28, Garry, Robert F [REDACTED] wrote:

Drosten, Fazan, Fouchier, Baric and Shi Zhengli from WIV – to capture different sides of the various scenarios.

Ab Osterhaus, Linfa Wang, and Peter Diazek to capture the bats.

George Gao and possibly Steve Harrison for structure.

Seems like she may be retired but probably has deepest historical perspective on CoV research:

<http://www.ucdenver.edu/academics/colleges/medicalschool/departments/ImmunologyMicrobiology/faculty/departmental/Pages/HOLMESKV.aspx>

Kathryn V. Holmes, Ph.D.

12800 E. 19th Ave., RC-1 N 9127
Mail Stop 8333, Aurora, CO 80045
Phone: [REDACTED]
E-mail: [REDACTED]

From: Edward Holmes <[REDACTED]>
Date: Wednesday, February 5, 2020 at 3:13 PM
To: Kristian Andersen <[REDACTED]>
Cc: Robert Garry <[REDACTED]>, Andrew Rambaut <[REDACTED]>

Subject: Re: Summary - Invitation to edit

External Sender. Be aware of links, attachments and requests.

I've asked Tommy to check the metagenomic assembly and to look at the synonymous changes. At face value it looks like recombination, which itself raises a whole set of other questions. Just so random that it is illegally smuggled pangolins from southern China.

Jeremy has the green light from WHO. Can you think of good sensible people to be on it? Need gender and geographic diversity.

Best wishes,

Eddie

PROFESSOR EDWARD C. HOLMES FAA FRS
ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY
Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,
The University of Sydney | Sydney | NSW | 2006 | Australia
T: [REDACTED]
E: [REDACTED]

On 6 Feb 2020, at 3:14 am, Kristian G. Andersen <[REDACTED]> wrote:

Yup, agreed. Need proper biochemistry to really answer this question.

K

On Wed, Feb 5, 2020 at 07:49 Garry, Robert F [REDACTED] wrote:

Yeah _ I reread the Baric JV paper and still think some caution is needed. It's a good paper, but nCoV or it's progenitor may have found another RBD binding solution that might be as good or better. Argument that nCoV is inferior, hinges on nCoV aa501. However, there's a proline at 499 that's not present in SARSv or civet v (it is present in pangolin and RaTG13), which would put in a kink and change a lot.

From: Kristian Andersen [REDACTED]

Date: Wednesday, February 5, 2020 at 9:27 AM

To: Robert Garry [REDACTED]

Cc: Edward Holmes [REDACTED], Andrew Rambaut [REDACTED]

Subject: Re: Summary - Invitation to edit

External Sender. Be aware of links, attachments and requests.

Wait, I have the pangolin sequences - will take a look once I'm in the office.

K

On Wed, Feb 5, 2020 at 7:20 AM Kristian G. Andersen [REDACTED] wrote:

Eddie, can you please share the pangolin sequence? I can take a look later today (hopefully - super packed calendar). If not today, definitely tomorrow.

Bob, for the idea about civets not being optimal - take a look at this paper: <https://www.ncbi.nlm.nih.gov/pubmed/31996437>

Once I have had a look, I'll update on Slack - let's try and keep stuff on there so it doesn't get lost.

K

On Wed, Feb 5, 2020 at 6:24 AM Garry, Robert F [REDACTED] wrote:

Worth pointing out - if the crackpot charge comes re cell culture hypothesis - that we are discussing this in private amongst experts.

Clearly and I think correctly our approach has been different than say the flawed nejm paper -see science feb3 - about asymptomatic infection - Drosten was on the rushed out paper Tony got tripped up. Public error and pretty important. IMO they should retract the paper to send clear message.

Sent from my iPhone

On Feb 5, 2020, at 5:18 AM, Edward Holmes [REDACTED] wrote:

External Sender. Be aware of links, attachments and requests.

The pangolin virus looks like it might fall in roughly the same place on the tree as those new bat virus trees I put on Slack. Don't have the seqs of those yet.

Professor Edward C. Holmes FAA FRS
The University of Sydney

On 5 Feb 2020, at 9:52 pm, Andrew Rambaut [REDACTED] wrote:

Perhaps say we are adding new information? See whether he wants to hold off. I suspect Bethesda will be sending it round already?

I think we need to add a section about the pangolin and possibly something about whether the glycan sites are evidence of selection by an immune system?

A.

On 5 Feb 2020, at 10:47, Edward Holmes [REDACTED] wrote:

The animals are from Guangdong and Guangxi. Seized by customs. Need those Hubei pangolins.

Should I tell Jeremy to hold on sending the summary out to the group while we investigate more or does that really matter? He did say that more wildlife needed to be studied. He's sent it to the Bethesda boys.

Best wishes,

Eddie

PROFESSOR EDWARD C. HOLMES FAA FRS
ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY
Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,
The University of Sydney | Sydney | NSW | 2006 | Australia
T [REDACTED]
E [REDACTED]

On 5 Feb 2020, at 9:34 pm, Andrew Rambaut [REDACTED] wrote:

Do we know where this pangolin is from? Guangdong markets?

A.

On 5 Feb 2020, at 10:31, Edward Holmes · [REDACTED] wrote:

I've asked Tommy to check for synonymous changes. He's writing a paper. Only got the figure this afternoon.

Professor Edward C. Holmes FAA FRS

The University of Sydney

On 5 Feb 2020, at 9:25 pm, Andrew Rambaut · [REDACTED] wrote:

Need to look for some synonymous mutations. Perhaps the nCoV progenitor is also in Pangolins (widely traded illegally)?

A.

On 5 Feb 2020, at 10:22, Edward Holmes · [REDACTED] wrote:

Region 6 is the RBD. Could be recombination? Very strange.

Message

From: Andrew Rambaut [REDACTED]
Sent: 2/7/2020 1:10:22 PM
To: Kristian G. Andersen [REDACTED]
CC: Edward Holmes [REDACTED]; Garry, Robert F [REDACTED]
Subject: Re: Stuff

Don't worry about FOI. Huawei will be feeding all of this directly to Xi Jinping.

A

Sent from my phone. Apologies for brevity or illiteracy.

On 7 Feb 2020, at 21:05, Kristian G. Andersen [REDACTED] wrote:

I would argue that any animal being identified would be beneficial to them - otherwise we're all going to point fingers at them telling people that they're so shit that they can't even predict the outbreaks of their own making...

Too harsh?

K

[for a potential future FOIA reader - please note that I can at times be sarcastic and have a knack for bad jokes].

On Fri, Feb 7, 2020 at 12:59 PM Andrew Rambaut [REDACTED] wrote:
No. They will hate it being pangolins. They were saying they had predicted the bats.

A

Sent from my phone. Apologies for brevity or illiteracy.

On 7 Feb 2020, at 20:53, Edward Holmes [REDACTED] wrote:

No, not at all.

Just Twitter chat.

PROFESSOR EDWARD C. HOLMES FAA FRS
ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY
Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,
The University of Sydney | Sydney | NSW | 2006 | Australia

T [REDACTED]

E [REDACTED]

On 8 Feb 2020, at 7:51 am, Kristian G. Andersen [REDACTED] wrote:

Is this pangolin stuff the Ego guys?

On Fri, Feb 7, 2020 at 12:42 PM Garry, Robert F. [REDACTED] wrote:

Shameless.

From: Edward Holmes [REDACTED]

Date: Friday, February 7, 2020 at 2:18 PM

To: Robert Garry [REDACTED]

Cc: Kristian Andersen [REDACTED], Andrew Rambaut [REDACTED]

Subject: Re: Stuff

External Sender. Be aware of links, attachments and requests.

Entertaining that the Ego Health crowd agree that having a press conference without providing the data is not the right way to proceed...no similarity to Bombali virus then.

Professor Edward C. Holmes FAA FRS

The University of Sydney

On 8 Feb 2020, at 2:46 am, Garry, Robert F. [REDACTED] wrote:

Some comments over on the Slack channel, but need that 99% pangolin sequence.

I agree that the presence of the furin site would all but rule out passage.

If it's not there (or at least some insert) passage isn't ruled out (data from Fazan or Fouchier critical here).

Stating the somewhat obvious here: In Kristian's alignment Pangolin337 is essentially the RBD of SARS-CoV-2 save for a single amino acid change (what are the differences at the nucleotide level?), but differs more than BaTG13 elsewhere. May be looking at some mosaicism or recombination event amongst the different Pangolin CoV strains that should be "fairly" easy to pick up on.

From: Kristian Andersen [REDACTED]

Date: Friday, February 7, 2020 at 9:29 AM

To: Robert Garry [REDACTED]

Cc: Edward Holmes [REDACTED], Andrew Rambaut [REDACTED]

Subject: Re: Stuff

External Sender. Be aware of links, attachments and requests.

"But, does this swing it completely away from the passage idea?"

No, it does not, however, every little helps. The furin is still peculiar, but if we're discussing whether evolution could create a furin cleavage site or not, then, well, we better hit the pub sooner rather than later. Now, the presence of the furin site in pangos would nail it, but the absence (as it appears to be) wouldn't really tell us much.

K

On Fri, Feb 7, 2020 at 2:41 AM Garry, Robert F [REDACTED] wrote:

Yes indeed

Would be good to know about the 12 base pair insert

Would be great to see any insert there.

If not will be important to determine where this pangolin came from

As Andrew taught [me] they come from all over illegally

Also don't know obviously if it's 99.0 or 99.8%. If there is a 99% virus there may well be a 99.8% virus back in the pangolin's home country.

Sent from my iPhone

On Feb 7, 2020, at 4:11 AM, Edward Holmes [REDACTED] wrote:

External Sender. Be aware of links, attachments and requests.

OK, I've just emailed one of the authors. Let's hope we get a reply.

PROFESSOR EDWARD C. HOLMES FAA FRS
ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY
Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,

T

E

On 7 Feb 2020, at 8:55 pm, Garry, Robert F [REDACTED] wrote:

That is the or at least a key question.

Sent from my iPhone

On Feb 7, 2020, at 3:46 AM, Andrew Rambaut [REDACTED] wrote:

External Sender. Be aware of links, attachments and requests.

Can we at least get a pers-comm as to whether it has the insertion or not?

<https://www.nytimes.com/reuters/2020/02/07/world/asia/07reuters-china-health-pangolins.html>

<https://www.businessinsider.com/china-scientists-identify-pangolin-as-possible-coronavirus-host-2020-2?r=US&IR=T>

A.

On 7 Feb 2020, at 09:36, Edward Holmes [REDACTED] wrote:

Jeremy wants us to publish our report somewhere. Thoughts?

I'll need to update the pangolin stuff again. Not proven of course, but it makes complete sense. We don't know what the amino acid sequences of these pangolin viruses that 99% similar to 2019-nCoV will look like, but there must be decent chance they have all the key mutations. But, does this swing it completely away from the passage idea?

Things are changing so fast it is hard not be redundant.

PROFESSOR EDWARD C. HOLMES FAA FRS
ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY

Marie Bashir Institute for Infectious Diseases & Biosecurity,

School of Life & Environmental Sciences and School of Medical Sciences,

The University of Sydney | Sydney | NSW | 2006 | Australia

T

E

Begin forwarded message:

From: Jeremy Farrar [REDACTED]

Subject: Re: Stuff

Date: 7 February 2020 at 5:31:44 pm AEDT

To: Edward Holmes [REDACTED]

I will be neutral.

Anyone from China?

Tomorrow morning fine.

Any preference for journal? All will take immediately, I can let them know coming if helpful and you have a preference

With revisions – will share with the TC group over the weekend – if OK – got to add the new info

From: Edward Holmes [REDACTED]

Date: Friday, 7 February 2020 at 06:29

To: Jeremy Farrar [REDACTED]

Subject: Re: Stuff

Tonight? More likely to you tomorrow am. Just need more about the pangomania which is very important.

Let me know if you need anything else changed.

Not sure about journal.

Authors: Kristian, me, Bob, Andrew. You? Or do you want to be neutral?

PROFESSOR EDWARD C. HOLMES FAA FRS

ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY

Marie Bashir Institute for Infectious Diseases & Biosecurity,

School of Life & Environmental Sciences and School of Medical Sciences,

The University of Sydney | Sydney | NSW | 2006 | Australia

T [REDACTED]

E [REDACTED]

On 7 Feb 2020, at 5:26 pm, Jeremy Farrar · [REDACTED] wrote:

When can you update?

Lancet

Nature

NEJM

Will all review immediately, after quick QC, will share with WHO.

Can I help with any of the editors?

Who will be authors from your side?

Andrew Rambaut

Institute for Evolutionary Biology

Ashworth Laboratories, University of Edinburgh, Edinburgh, EH9 3FL, UK

contact – [REDACTED] | <http://tree.bio.ed.ac.uk> | tel : [REDACTED]

The University of Edinburgh is a charitable body, registered in Scotland, with registration number SC005336.

Message

From: R.A.M. Fouchier [REDACTED]
Sent: 2/8/2020 2:50:00 PM
To: Andrew Rambaut [REDACTED]; Jeremy Farrar [REDACTED]
CC: Eddie Holmes [REDACTED]; Christian Drosten [REDACTED]; kga1978 [REDACTED]; rfgarry [REDACTED]; p.vallance1 [REDACTED]; collinsf [REDACTED]; afauci [REDACTED]; Josie Golding [REDACTED]; M.P.G. Koopmans [REDACTED]; Mike Ferguson [REDACTED]
Subject: Re: [ext] 2019 N-CoV

I do not understand Andrews argument “ The sequence data clearly and unambiguously rules out any form of lab construct or engineering of the virus. “. Molecular biologists like myself can generate perfect copies of viruses without leaving a trace, eg the BamHI site. The arguments for and against passaging and engineering are the same if you ask me.

Ron

From: Andrew Rambaut [REDACTED]
Sent: Saturday, February 8, 2020 4:16 PM
To: Jeremy Farrar
Cc: Eddie Holmes; Christian Drosten; kga1978 [REDACTED]; rfgarry [REDACTED]; r.fouchier [REDACTED]; p.vallance1 [REDACTED]; collinsf [REDACTED]; afauci [REDACTED]; Josie Golding; m.koopmans [REDACTED]; Mike Ferguson
Subject: Re: [ext] 2019 N-CoV

I agree with Eddie, I think someone needs to lay out the science of this before it gets out of hand (and causes more formal investigations).

I am of the view that the natural selection hypothesis is the most likely (specifically the non-bat reservoir). And as Eddie mentioned this is becoming more likely from day to day with the pangolin story.

I disagree with Ron that the passaging hypothesis is evidentially equal to the engineering hypothesis. The sequence data clearly and unambiguously rules out any form of lab construct or engineering of the virus. It doesn't really have anything to say about the relative plausibility of the 3 hypotheses for selection.

I think we need stronger arguments than an assertion that no lab has done those experiments. We can definitely argue that it has nothing to do with RaTG13 (or SARS or any other published SARSR virus). The argument that we would need to offer this hypothesis for all other outbreaks is not a useful one in this context.

Is it possible to argue that A) a passaging experiment wouldn't create the features we see? or B) that there are logical reasons why someone wouldn't do such an experiment?

The pangolin virus that was announced in the press conference might solve this issue if it has the furin cleavage site insertion which would be all but conclusive for the natural scenario.

Andrew

On 8 Feb 2020, at 20:21, Jeremy Farrar [REDACTED] wrote:

The theory of the origin of the has gathered considerable momentum not in social media, but increasingly among some scientists, in main stream media, and among politicians.

The aim of this was to bring a neutral, respected, scientific group together to look at the data and in a neutral, considered way provide an opinion and we hoped to focus the discussion on the science, not on any conspiracy or other theory and to lay down a respected statement to frame whatever debate goes on – before that debate gets out of hand with potentially hugely damaging ramifications.

With the additional information on the pangolin virus, information not available even 24 hours ago, I think the argument is even clearer.

My preference is that a carefully considered piece of science, early in the public domain, will help mitigate more polarised debate. If not, that debate will increasingly happen and science will be reacting to it. Not a good position to be in.

From: Edward Holmes [REDACTED]

Date: Saturday, 8 February 2020 at 20:11

To: Christian Drosten [REDACTED]

Cc: Jeremy Farrar [REDACTED], "kga1978" [REDACTED],

"a.rambaut" [REDACTED], "rfgarry" [REDACTED]

"r.fouchier" [REDACTED], "P.Vallance1" [REDACTED]

[REDACTED], Francis Collins <[REDACTED]"afauci" [REDACTED], Josie Golding [REDACTED], Marion Koopmans [REDACTED], Mike Ferguson [REDACTED]

Subject: Re: [ext] 2019 N-CoV

Hi Christian,

I don't know where this story came from, but it has nothing whatsoever to do the HIV nonsense. Please don't associate this with that. This is a broader story.

Ever since this outbreak started there have suggestions that the virus escaped from the Wuhan lab, if only because of the coincidence of where the outbreak occurred and the location of the lab. I do a lot of work in China and I can you that a lot of people there believe this and believe they are being lied to. Things were made worse when Wuhan lab published the bat virus sequence - a bat sampled in a different province for which they have a large collection of samples.

I believe the aim/question here is whether we, as scientists, should try to write something balanced on the science behind this? There are arguments for and against doing this.

Personally, with the pangolin virus possessing 6/6 key sites in the receptor binding domain, I am in favour of the natural evolution theory.

Best wishes,

Eddie

PROFESSOR EDWARD C. HOLMES FAA FRS
ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY

Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,
The University of Sydney | Sydney | NSW | 2006 | Australia

T [REDACTED]

E [REDACTED]

On 9 Feb 2020, at 6:52 am, Drosten, Christian [REDACTED] wrote:

Dear All,

I am overloaded with nCoV patient-related work and will need a few days before I can work on this text.

Can someone help me with one question: didn't we congregate to challenge a certain theory, and if we could, drop it? This whole text reads as if the hypothesis was obvious, or was brought up by some external source, forcing us to respond. Is this the case? It does not seem as if this was linked to the HIV nonsense.

Who came up with this story in the beginning? Are we working on debunking our own conspiracy theory?

Christian

-

Professor Christian Drosten

Director, Institute of Virology
Scientific Director, Charité Global Health

Charité - Universitätsmedizin Berlin
Campus Charité Mitte

[REDACTED]
Germany

E-Mail: [REDACTED]
<https://virologie-ccm.charite.de/>
<https://globalhealth.charite.de/>

Von: Jeremy Farrar [REDACTED]

Datum: Samstag, 8. Februar 2020 um 10:45

An: Edward Holmes [REDACTED], "kga1978" [REDACTED]

Andrew Rambaut [REDACTED], "rgarry" [REDACTED] >

Cc: "r.fouchier" [REDACTED], "P.Vallance1" [REDACTED]

"collinsf" [REDACTED], "afauci" [REDACTED]

[REDACTED], Josie Golding <[REDACTED]>, "m.koopmans" [REDACTED]

[REDACTED], Christian Drosten <[REDACTED]>, Mike Ferguson

Betreff: [ext] FW: 2019 N-CoV

APOLOGIES WITH ALL CORRECT EMAILS

Kristen, Andrew, Bob, Eddie have reworked the summary and it is attached here.

We are pushing to get the sequence data from the reports on the pangolins, but do not have currently, clearly that is very important to incorporate.

Interested in your views

- Is this reasonably balanced given the data?
- Is there anything anyone disagrees with?
- Is there anything more in relation to what would seem to be the two possibilities
 - Nature, Intermediate host, evolution and passage
- Future data you may have
- Advice on whether KA, AR, RG and EH should publish this.

These and other thoughts welcome in confidence.

Andrew Rambaut

Institute for Evolutionary Biology
Ashworth Laboratories, University of Edinburgh, Edinburgh, EH9 3FL, UK

contact – [REDACTED] | <http://tree.bio.ed.ac.uk> | tel [REDACTED]

The University of Edinburgh is a charitable body, registered in Scotland, with registration number SC005336.

Message

From: R.A.M. Fouchier [REDACTED]
Sent: 2/8/2020 11:36:30 AM
To: Jeremy Farrar [REDACTED]; Edward Holmes [REDACTED]; kga1978@[REDACTED]; Andrew Rambaut [REDACTED]; rfgarry@[REDACTED]; Josie Golding [REDACTED]; P.Vallance1@[REDACTED]; collinsf@[REDACTED]; afauci@[REDACTED]; M.P.G.Koopmans@[REDACTED]; Christian Drosten@[REDACTED]; Mike Ferguson [REDACTED]
Subject: Re: 2019 N-CoV
Attachments: Summary.Feb7 RF.pdf

I am not in favor of publishing as is. I fail to see how the last of the three discussed scenarios (passaging) does not fall under the category of "laboratory manipulation". There is no evidence that might hint to this scenario and hence it should be put aside just like the engineering option. As far as I am aware, no laboratory has worked on passaging the pangolin-origin virus, the bat-CoV RaTG13, or another closely related virus or had access to it prior to the outbreak. That nCoV-2019 could originate from a SARS-like virus in Chinese labs can also be excluded. This information could be added after reference 10 in the manuscript, to provide further argument.

If we assume passaging as a possible scenario here, we must assume it is also plausible for all outbreaks from the past, present and future. This manuscript would be much stronger if it focused on the likelihood of the first 2 scenarios as compared to intentional or accidental release. That would also limit the chance of new biosafety discussions that would unnecessarily obstruct future attempts of virus culturing for research and diagnostic purposes for any (emerging/zoonotic) virus.

I made some additional comments in the attached pdf, also in line with Andrew's comments.

With kind regards,
Ron

Van: Jeremy Farrar [REDACTED]
Datum: zaterdag 8 februari 2020 om 10:45
Aan: Edward Holmes [REDACTED], "kga1978@[REDACTED];
Andrew Rambaut [REDACTED], "rfgarry@[REDACTED];
CC: "R.A.M. Fouchier" <[REDACTED]>, "P.Vallance1@[REDACTED];
"collinsf@[REDACTED]; "afauci@[REDACTED];
Josie Golding [REDACTED], "M. Koopmans" [REDACTED]; Christian Drosten [REDACTED];
Mike Ferguson [REDACTED]
Onderwerp: FW: 2019 N-CoV

APOLOGIES WITH ALL CORRECT EMAILS

Kristen, Andrew, Bob, Eddie have reworked the summary and it is attached here.

We are pushing to get the sequence data from the reports on the pangolins, but do not have currently, clearly that is very important to incorporate.

Interested in your views

- Is this reasonably balanced given the data?

- Is there anything anyone disagrees with?
- Is there anything more in relation to what would seem to be the two possibilities
- Nature, Intermediate host, evolution and passage
- Future data you may have
- Advice on whether KA, AR, RG and EH should publish this.

These and other thoughts welcome in confidence.

Message

From: Mike Ferguson [REDACTED]
Sent: 2/9/2020 12:00:46 PM
To: Jeremy Farrar [REDACTED]; Edward Holmes [REDACTED]; kga1978 [REDACTED]
CC: Andrew Rambaut [REDACTED]; rfgarry [REDACTED]; r.fouchier [REDACTED]; P.Vallance1 [REDACTED]; collinsf [REDACTED]; m.koopmans [REDACTED]; afauci [REDACTED]; Josie Golding [REDACTED]; christian.drosten [REDACTED]
Subject: Re: 2019 N-CoV
Attachments: Summary.Feb7_MF.pdf

Dear Jeremy et al

I have made some comments and suggestions on the pdf attached.

I am not an expert on protein O-glycosylation - however, Dr Tabak, who was on the call last weekend, is and if I were to consult anyone else on this it would be Henrik Clausen

<https://icmm.ku.dk/english/research-groups/clausen-group/>

However, from what I do know of general glycobiology, I am not sure one can conclude that an immune system would be required to select for O-glycosylation sites. Once an alpha-helix is disturbed by the introduction of a proline, adjacent Ser and Thr residues will be (over-)predicted to have O-glycosylation potential - hard to know the functional consequences/significance without knowing whether the potential O-sites are actually occupied.

Regards

Mike

From: Jeremy Farrar [REDACTED]
Sent: 08 February 2020 09:45
To: Edward Holmes [REDACTED]; kga1978 [REDACTED]; Andrew Rambaut [REDACTED]; rfgarry [REDACTED]; r.fouchier [REDACTED]; P.Vallance1 [REDACTED]; collinsf [REDACTED]; m.koopmans [REDACTED]; afauci [REDACTED]; Josie Golding [REDACTED]; christian.drosten [REDACTED]; Mike Ferguson [REDACTED]
Subject: FW: 2019 N-CoV

APOLOGIES WITH ALL CORRECT EMAILS

Kristen, Andrew, Bob, Eddie have reworked the summary and it is attached here.

We are pushing to get the sequence data from the reports on the pangolins, but do not have currently, clearly that is very important to incorporate.

Interested in your views

- Is this reasonably balanced given the data?
- Is there anything anyone disagrees with?
- Is there anything more in relation to what would seem to be the two possibilities
 - Nature, Intermediate host, evolution and passage
- Future data you may have
- Advice on whether KA, AR, RG and EH should publish this.

These and other thoughts welcome in confidence.

Overview

Sequencing of 2019-nCoV revealed two notable features of its genome. We investigate these features and outline some examples for how the virus may have acquired them. ~~We also discuss some scenarios by which these features could have arisen. Analysis of the virus genome sequences clearly demonstrates that the virus is not a laboratory construct or experimentally manipulated virus.~~ We believe the features discussed, which may explain the infectiousness and transmissibility of 2019-nCoV in humans, ~~could have~~ arisen through selection and adaptation prior to the initial outbreak.

The two primary features of 2019-nCoV of interest were:

- Based on structural modeling and early biochemical experiments, 2019-nCoV appears to be optimized for binding to the human ACE2 receptor.
- The highly variable spike protein of 2019-nCoV has a furin cleavage inserted at the S1 and S2 boundary via the insertion of twelve in-frame nucleotides. Additionally, this event also led to the acquisition of three ~~predicted O-linked glycans~~.

Mutations in the receptor binding domain of 2019-nCoV

The receptor binding domain (RBD) in the spike protein of SARS-CoV and SARS-like coronaviruses is the most variable part of the virus genome. When aligned against related viruses, 2019-nCoV displays a similar level of diversity as predicted from previous studies, including to its most closely related virus - SARS-like CoV isolated from bats (RaTG13, which is ~96% identical to 2019-nCoV).

Six residues in the RBD have been described as critical for binding to the human ACE2 receptor and determining host range¹. Using coordinates based on the Ubani strain of SARS-CoV, they are Y442, L472, N479, D480, T487, and Y491 (the corresponding residues in 2019-nCoV are L455, F486, Q493, S494, N501, and Y505). Five out of six of these residues are mutated in 2019-nCoV compared to the closely related virus, RaTG13 (**Figure 1**). Based on modeling¹ and early biochemical experiments^{2,3}, 2019-nCoV seems to have an RBD that may bind with high affinity to ACE2 from human, primate, ferret, pig, and cat, as well as other species with high receptor homology. In contrast, 2019-nCoV may bind less efficiently to ACE2 in other species associated with SARS-like viruses, including rodents, civets, and bats¹.

do we have the pangolin ACE2 sequence/model?

A phenylalanine at F486 in 2019-nCoV corresponds to L472 in the SARS-CoV Ubani strain. In cell culture experiments the leucine at position 472 mutated to phenylalanine (L472F)⁴, which has been predicted to be optimal for binding of the SARS-CoV RBD to the human ACE2 receptor⁵. However, a phenylalanine in this position is also present in several SARS-like CoVs from bats (**Figure 1**). While these analyses suggest that 2019-nCoV may be capable of binding the human ACE2 receptor with high affinity, importantly, the interaction is not predicted to be optimal¹. Additionally, several of the key residues in the RBD of 2019-nCoV are different from those previously described to be optimal for human ACE2 receptor binding as determined by both natural evolution of SARS-CoV and rational design⁵. This latter point is strong evidence *against* 2019-nCoV being specifically engineered as, presumably, in such a scenario the most optimal residues would have been introduced, which is not what we observe.

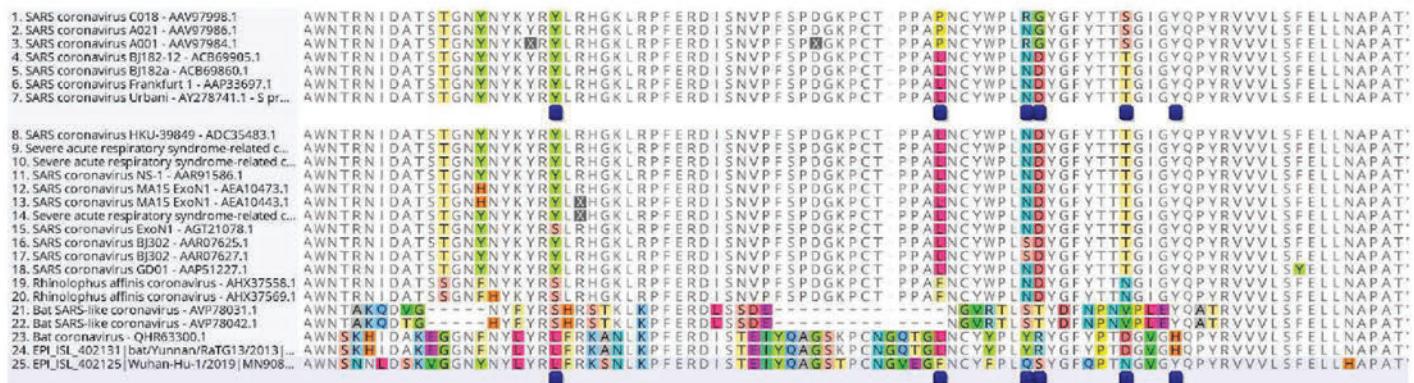


Figure 1 | Mutations in contact residues of the 2019-nCoV spike protein. The spike protein of 2019-nCoV (bottom) was aligned against the most closely related SARS and SARS-like CoVs. Key residues in the spike protein that make contact to the

ACE2 receptor have been marked with blue boxes in both 2019-nCoV and the SARS-CoV Urbani strain.

Furin cleavage site and O-linked glycans

An interesting feature of 2019-nCoV is a predicted furin cleavage site in the spike protein (**Figure 2**). In addition to the furin cleavage site (RRAR), a leading P is also inserted so the fully inserted sequence becomes PRRA (Figure 2). A proline in this position is predicted to create three flanking O-linked glycans at S673, T678, and S686. A furin site has never before been observed in the lineage B betacoronaviruses and is a unique feature of 2019-nCoV. Some human betacoronaviruses, including HCoV-HKU1 (lineage A) have furin cleavage sites (typically RRKR), although not in such an optimal position.



Figure 2 | Acquisition of furin cleavage site and O-linked glycans. The spike protein of 2019-nCoV (bottom) was aligned against the most closely related SARS and SARS-like CoVs. The furin cleavage site is marked in grey with the three adjacent predicted O-linked glycans in blue. Both the furin cleavage site and O-linked glycans are unique to 2019-nCoV and not previously seen in this group of viruses.

While the functional consequence - if any - of the furin cleavage site in 2019-nCoV is unknown, previous experiments with SARS-CoV have shown that it enhances cell-cell fusion but does not affect virus entry⁶. Furin cleavage sites are often acquired in condition selecting for rapid virus replication and transmission (e.g., highly dense chicken populations) and are a hallmark of highly pathogenic avian influenza virus, although these viruses acquire the site in different and more direct ways⁷⁻⁹. The acquisition of furin cleavage sites have also been observed after repeated passage of viruses in cell culture (personal correspondence and NASEM call, February 3, 2020).

A potential function of the three predicted O-linked glycans is less clear, but could create a "mucin-like domain" shielding potential epitopes or key residues on the 2019-nCoV spike protein.

Origin of 2019-nCoV

As noted at the start of this document, we believe that the origin of 2019-nCoV through laboratory manipulation of an existing SARS-related coronavirus can be ruled out with a high degree of confidence. If genetic manipulation would have been performed, one would expect that a researcher would have used one of the several reverse genetics systems available for betacoronaviruses. However, this is not the case as the genetic data clearly shows that 2019-nCoV is not derived from any previously used virus backbone, for example those described in a 2015 paper in *Nature Medicine*¹⁰.

Instead we believe one of three main scenarios could explain how 2019-nCoV acquired the features discussed above: (1) natural selection in humans, (2) natural selection in an animal host, or (3) selection during passage.

Adaptation to humans

As the features outlined above are likely to enhance the ability of the virus to infect humans, it is possible that these are indeed adaptations to humans as a host and arose after the virus jumped from a non-human host, during the early stages of the epidemic. However, all of the genome sequences so far have the features described above and estimates of the timing of the most recent common ancestor of the currently sampled viruses support the seafood market outbreak as the zoonotic origin (i.e., in early December) and this would afford little opportunity for adaptation to occur. This may be explained by a transition to a rapid growth phase in the epidemic when the features arose and from which all current

cases are derived. However this would require a prior hidden epidemic of sufficient magnitude and duration for the adaptations to occur and there is no evidence of this. We also note that these features did not emerge during the SARS epidemic, which involved extensive human to human transmission.

Selection in an animal host

Given the similarity of 2019-nCoV to bat SARS-like CoVs, particularly RaTG13, it is highly likely that bats serve as the reservoir for this virus. However, previous human epidemics caused by betacoronaviruses have involved intermediate (possibly amplifying) hosts such as civets and other animals (SARS) and camels (MERS). It is therefore likely that an intermediate host would also exist for 2019-nCoV, although it is unclear what that host may be. Given the mutations in key residues of the RBD in 2019-nCoV it seems less likely that civets would be involved, although it is impossible to say with certainty at this stage. Notably, provisional analyses reveal that Malayan pangolins (*Manis javanica*) illegally imported into Guangdong province contain CoVs that are extremely similar to 2019-nCoV¹¹. Although RaTG13 remains the closest relative to 2019-nCoV across the genome as a whole, the Malayan pangolin CoVs are identical to 2019-nCoV at all six key RBD residues. Analyses of these pangolin viruses are ongoing, although they do not carry the furin cleavage site insertion.

For the virus to acquire the furin cleavage site and mutations in the spike proteins that appear to be suitable for human ACE2 receptor binding, it seems plausible that this animal host would have to have a high population density – to allow the necessary natural selection to proceed efficiently – and an ACE2 gene that is similar to the human orthologue. Since furin cleavage sites have not been observed in sarbecoviruses before, it is unclear what conditions would be required for it to be acquired in the lineage leading to 2019-nCoV.

Selection during passage

Bas glycosylation (O- and N-) can reduce host immune response to antigens - but is there any
bee evidence that neutralising antibodies are made to this region of spike protein? If not, where
201 would the selective pressure come from? O-glycosylation (if present) could just as easily be
cult stabilising (or preventing) a secondary structure feature (i.e., not immune system driven). Also
the note that O-glycosylation predictors tend to over-predict, experimental evidence (mass spec)
of a important. Also, one of the most common functions of glycosylation is to protect the underlying
be role peptide from proteolysis - i.e., these sites if occupied might actually reduce the efficiency of the
further cleavage site.

Limitations and recommendations

The evolution scenarios discussed above are largely indistinguishable and current data are consistent with all three. It is currently impossible to prove or disprove either, and it is unclear whether future data or analyses will help resolve this issue. Identifying the immediate non-human animal source and obtaining virus sequences from it would be the most definitive way of distinguishing the three scenarios.

The main limitation of what is described here is our clear ascertainment bias. We are looking for features or evolutionary aspects that could help explain how 2019-nCoV lead to such a rapidly expanding human epidemic, yet the specific features we are trying to find may be the exact features one would expect in a virus that could lead to an epidemic of the magnitude currently observed. Before 2019-nCoV 'took off' and started the current epidemic, it is plausible that many stuttering transmission chains of highly similar viruses could have entered the human population, but because they never took off they were never sampled. It is extremely important to keep this in mind as any inference about the plausibility of various scenarios about the evolution and/or epidemic potential of 2019-nCoV is attempted.

To further clarify the evolutionary origins and functional features of 2019-nCoV it would be helpful to obtain additional data about the virus - both genetic and functional. This includes experimental studies of receptor binding and the role of the furin cleavage site and predicted O-linked glycans. The identification of a potential intermediate host of 2019-nCoV as well as sequencing of very early cases, including those not connected to the market, could also help refute the passage scenario described above. Even in the

light of such data, however, it is not guaranteed that data can be obtained to conclusively prove all aspects of the initial emergence of 2019-nCoV.

References

1. Wan, Y., Shang, J., Graham, R., Baric, R. S. & Li, F. Receptor recognition by novel coronavirus from Wuhan: An analysis based on decade-long structural studies of SARS. *J. Virol.* (2020) doi:10.1128/JVI.00127-20.
2. Letko, M. & Munster, V. Functional assessment of cell entry and receptor usage for lineage B β-coronaviruses, including 2019-nCoV. *bioRxiv* 2020.01.22.915660 (2020) doi:10.1101/2020.01.22.915660.
3. Hoffmann, M. *et al.* The novel coronavirus 2019 (2019-nCoV) uses the SARS-coronavirus receptor ACE2 and the cellular protease TMPRSS2 for entry into target cells. *bioRxiv* 2020.01.31.929042 (2020) doi:10.1101/2020.01.31.929042.
4. Sheahan, T. *et al.* Mechanisms of zoonotic severe acute respiratory syndrome coronavirus host range expansion in human airway epithelium. *J. Virol.* **82**, 2274–2285 (2008).
5. Cui, J., Li, F. & Shi, Z.-L. Origin and evolution of pathogenic coronaviruses. *Nat. Rev. Microbiol.* **17**, 181–192 (2019).
6. Follis, K. E., York, J. & Nunberg, J. H. Furin cleavage of the SARS coronavirus spike glycoprotein enhances cell-cell fusion but does not affect virion entry. *Virology* **350**, 358–369 (2006).
7. Longping, V. T., Hamilton, A. M., Friling, T. & Whittaker, G. R. A novel activation mechanism of avian influenza virus H9N2 by furin. *J. Virol.* **88**, 1673–1683 (2014).
8. Alexander, D. J. & Brown, I. H. History of highly pathogenic avian influenza. *Rev. Sci. Tech.* **28**, 19–38 (2009).
9. Luczo, J. M. *et al.* Evolution of high pathogenicity of H5 avian influenza virus: haemagglutinin cleavage site selection of reverse-genetics mutants during passage in chickens. *Sci. Rep.* **8**, 11518 (2018).
10. Menachery, V. D. *et al.* A SARS-like cluster of circulating bat coronaviruses shows potential for human emergence. *Nat. Med.* **21**, 1508–1513 (2015).
11. virological.org:
<http://virological.org/t/ncov-2019-spike-protein-receptor-binding-domain-shares-high-amino-acid-identity-with-a-coronavirus-recovered-from-a-pangolin-viral-metagenomic-dataset/362> (2020).
12. Ge, X.-Y. *et al.* Isolation and characterization of a bat SARS-like coronavirus that uses the ACE2 receptor. *Nature* **503**, 535–538 (2013).
13. Hu, B. *et al.* Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insights into the origin of SARS coronavirus. *PLoS Pathog.* **13**, e1006698 (2017).
14. Zeng, L.-P. *et al.* Bat Severe Acute Respiratory Syndrome-Like Coronavirus WIV1 Encodes an Extra Accessory Protein, ORF8, Involved in Modulation of the Host Immune Response. *J. Virol.* **90**, 6573–6582 (2016).

15. Yang, X.-L. et al. Isolation and Characterization of a Novel Bat Coronavirus Closely Related to the Direct Progenitor of Severe Acute Respiratory Syndrome Coronavirus. *J. Virol.* **90**, 3253–3256 (2015).

Message

From: Garry, Robert F [REDACTED]
Sent: 2/10/2020 3:51:18 PM
To: Kristian G. Andersen [REDACTED] Edward Holmes [REDACTED]
CC: Andrew Rambaut [REDACTED]
Subject: Re: More

All true.

But if Lipkin says higher ups are concerned and intel involved it's consistent with all we know too.

Not surprised Ego krewe (maybe Fouchier too) writing some sort of counter to the white paper with the allusion to scenario 3 "passage." Preemptive strike?

After a brief chat with Kristian after our NIH telecon I have to admit likewise that I don't really know the answers – maybe someone does. The data we have is just insufficient and even pango99 prob not helping (unless it magically has a furin cleavage site, which seems doubtful). I think the key may come from Guangdong. So, China Ag U Researchers culturing pangolin virus for undeterminable length of time makes me somewhat nervous.

From: Kristian Andersen [REDACTED]
Date: Monday, February 10, 2020 at 3:34 PM
To: Edward Holmes [REDACTED]
Cc: Andrew Rambaut [REDACTED], Robert Garry [REDACTED]
Subject: Re: More

External Sender. Be aware of links, attachments and requests.

Having known Bob for more than a decade I feel quite confident that he will make the connection between Butt Lesion and a certain Columbia professor.

I feel less confident that we will always be able to understand the references that Bob might himself be making at times... (note, a postgraduate degree in manga, anime, and comics may be required).

On Mon, Feb 10, 2020 at 1:27 PM Edward Holmes [REDACTED] wrote:

Thanks mate.

Thermonuclear ego explosion when those two are together.

You had better explain the butt lesion ref to Bob if he doesn't know. A link to the New York Post article should do it.

Professor Edward C. Holmes FAA FRS
The University of Sydney

On 11 Feb 2020, at 8:17 am, Kristian G. Andersen [REDACTED] wrote:

Eddie - lemme know your favorite brand and I'll send you a fresh pair of jocks.

Can't go wrong with the Grand Wizard of EgoHealth and Butt Lesion in the same room. Looking forward to it.

K

On Mon, Feb 10, 2020 at 12:56 PM Edward Holmes [REDACTED] wrote:

He's about where we were a week ago. He's for escape.

He also said that Peter Daszak, grand wizard of EgoHealth, and some others were writing a piece saying the Wuhan lab were being persecuted.

I'll talk to Jeremy later.

Currently, I'm more concerned that I will run out of underpants.

Professor Edward C. Holmes FAA FRS
The University of Sydney

On 11 Feb 2020, at 7:52 am, Andrew Rambaut [REDACTED] wrote:

We should get him on the group. Will make it more entertaining and balance the German/Dutch a bit.

A

Sent from my phone. Apologies for brevity or illiteracy.

On 10 Feb 2020, at 21:11, Edward Holmes [REDACTED] wrote:

Ian Lipkin just called - very worried about the furin cleavage site and says that high ups are as well, inc. intel. Also saw the restriction site.

Actually, he was most vexed that he wasn't part of our discussion group. Classic. I think I'll send the doc.

I still have no power. Could be a week.

Professor Edward C. Holmes FAA FRS
The University of Sydney

The University of Edinburgh is a charitable body, registered in Scotland, with registration number SC005336.

From: Edward Holmes
Sent: Monday, February 10, 2020 5:06 PM EST
To: Ian Lipkin
Subject: Re: Please call me

I agree. Talking to Jeremy (Farrar) in a few minutes and I'll get back in touch after. It is indeed striking that this virus is so closely related to SARS yet is behaving so differently. Seems to have been pre-adapted for human spread since the get go. It's the epidemiology that I find most worrying.

Professor Edward C. Holmes FAA FRS
The University of Sydney

On 11 Feb 2020, at 9:01 am, Ian Lipkin [REDACTED] wrote:

It's well reasoned and provides a plausible argument against genetic engineering. It does not eliminate the possibility of inadvertent release following adaptation through selection in culture at the institute in Wuhan. Given the scale of the bat CoV research pursued there and the site of emergence of the first human cases we have a nightmare of circumstantial evidence to assess.

Ian

On Feb 10, 2020, at 4:33 PM, Edward Holmes [REDACTED] wrote:

Hi Ian,

Here's the document we wrote a few days ago. Things are moving so quickly that is hard to keep up. Comments welcome. I favour natural evolution myself, but the furin cleavage site is an issue. I'll have a chat with Jeremy in a little while to see if can get you more directly involved.

Pangolins. Key observations are that:

- (i) Two sets of pangolins independently collected from different Chinese provinces both have CoVs in the same clade as 2019-nCoV. What are the odds?
- (ii) In the receptor binding domain the Guangdong pangolins are the closest to 2019-nCoV, with 6/6 of the key mutations (only 1/6 in the closest bat sequence).

Absolutely not proven that the pangolin is the intermediate host, but the points above make it a credible choice for additional investigation.

Agree it might not be clear - very rushed at the end.

Cheers,
Eddie

PROFESSOR EDWARD C. HOLMES FAA FRS

ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY

Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,
The University of Sydney | Sydney | NSW | 2006 | Australia

T [REDACTED]
E [REDACTED]

On 10 Feb 2020, at 9:08 pm, Ian Lipkin [REDACTED] wrote:

When you are back up for air I need to speak on two issues that concern you directly.

Ian

On Feb 9, 2020, at 4:14 PM, Edward Holmes [REDACTED] wrote:

Ian, sorry, it won't be today.

Huge storm in Sydney: no power for 24 hours, flood water 1 cm from house, transport bugged.

I need to sort this out.

Phone will die soon.

Professor Edward C. Holmes FAA FRS
The University of Sydney

On 10 Feb 2020, at 4:47 am, Ian Lipkin [REDACTED] wrote:

Eddie-
Please call me. [REDACTED]
Thanks

Ian

<Summary.Feb7.pdf>

Message

From: Jeremy Farrar [REDACTED]
Sent: 2/10/2020 1:26:57 AM
To: M.P.G. Koopmans [REDACTED]; Kristian G. Andersen [REDACTED]; Drosten, Christian [REDACTED]; Edward Holmes [REDACTED]; Andrew Rambaut [REDACTED]; rfgarry [REDACTED]; R.A.M. Fouchier [REDACTED]; P.Vallance1 [REDACTED]; collinsf [REDACTED]; afauci [REDACTED]; Josie Golding [REDACTED]; Ferguson [REDACTED]; Mike [REDACTED]
Subject: Re: [ext] 2019 N-CoV

Many thanks all

Sydney had a complete power cut over the weekend which has delayed things a little.

Appreciate not everyone will agree on the next plans but the discussion has been very constructive, thank you. As (hopefully) the pangolin data becomes available and can be incorporated a final draft will be completed and shared and a decision made among the people who have led the analysis (EH, KA, BG and AR) of next steps.

From: Marion Koopmans [REDACTED]
Date: Sunday, 9 February 2020 at 20:07
To: "Kristian G. Andersen" [REDACTED], "Drosten, Christian" [REDACTED], Jeremy Farrar [REDACTED], Edward Holmes [REDACTED], "a.rambaut" [REDACTED], "rfgarry" [REDACTED], "r.fouchier" [REDACTED], "P.Vallance1" [REDACTED], Francis Collins [REDACTED], "afauci" [REDACTED], Josie Golding [REDACTED], Mike Ferguson [REDACTED]
Subject: Re: [ext] 2019 N-CoV

Wow....took off from e-mail for a day.....

As mentioned to Jeremy, I would not be in favour of publishing something specific on the lab escape hypothesis, because I agree (with Kristian) that this could backfire. Yes, there is speculation in the public domain, triggered by several papers, including the rubbish ones. By zooming in on a specific finding that is NOT in the public domain as far as I know, I think this will generate its own conspiracy theories.

So if published, I would suggest zooming out a bit for starters, describing that one of the key challenges is where this virus came from, discuss some of the (wild) guesses out there, and then argue step by step what the challenges are in inferring this from sequence data, where you do not know exactly what the pool is that you are sampling from, so end up interpreting the needle drawn out of a haystack. Here, the many pieces of the discussion that passed by these last few days can be included, like rates of evolution and dating of possible origins; examples of cleavage site acquisition from other viruses, recombination in coronavirus evolutionary history, possible abrupt changes in spillover events, ability to confirm or disproof things in vitro. etc

And I would leave "lab escape" for the discussion, because putting that in the public domain as a hypothesis in my view will be read as "see, they also thought so"

Marion

On 8 Feb 2020, at 22:15, Kristian G. Andersen · [REDACTED] wrote:

A lot of good discussion here, so I just wanted to add a couple of things for context that I think are important - and why what we're considering is far from "another conspiracy theory", but rather is taking a valid scientific approach to a question that is increasingly being asked by the public, media, scientists, and politicians (e.g., I have been contacted by Science, NYT, and many other news outlets over the last couple of days about this exact question).

To Ron's question, passage of SARS-like CoVs have been ongoing for several years, and more specifically in Wuhan under BSL-2 conditions - see references 12-15 in the document for a few examples. The fact that Wuhan became the epicenter of the ongoing epidemic caused by nCoV is likely an unfortunate coincidence, but it raises questions that would be wrong to dismiss out of hand. Our main work over the last couple of weeks has been focused on trying to *disprove* any type of lab theory, but we are at a crossroad where the scientific evidence isn't conclusive enough to say that we have high confidence in any of the three main theories considered. Like Eddie - and I believe Bob, Andrew, and everybody on this email as well - I am very hopeful that the viruses from pangolins will help provide the missing pieces. For now, giving the lab theory serious consideration has been highly effective at countering many of the circulating conspiracy theories, including HIV recombinants, bioengineering, etc. - here's just one example: <https://www.factcheck.org/2020/02/baseless-conspiracy-theories-claim-new-coronavirus-was-bioengineered/>.

As to publishing this document in a journal, I am currently not in favor of doing so. I believe that publishing something that is open-ended could backfire at this stage. I think it's important that we try to gather additional evidence - including waiting on the pangolin virus sequences and further scrutinize the furin cleavage site and O-linked glycans - before publishing. That way we can (hopefully) come out with some strong conclusive statements that are based on the best data we have access to. I don't think we are there yet.

Best,
Kristian

On Sat, Feb 8, 2020 at 12:38 PM Drosten, Christian · [REDACTED] wrote:

OK, I see. We should then introduce references to these informal sources in the beginning of the text. Else it reads a bit funny.

Christian

—

Professor Christian Drosten

Director, Institute of Virology
Scientific Director, Charité Global Health

Charité - Universitätsmedizin Berlin
Campus Charité Mitte

Chariteplatz 1
D-10117 Berlin
Germany

E-Mail: christian.drosten@charite.de

<https://virologie-ccm.charite.de/>

<https://globalhealth.charite.de/>

Von: Jeremy Farrar [REDACTED]

Datum: Samstag, 8. Februar 2020 um 21:21

An: Edward Holmes [REDACTED], Christian Drosten [REDACTED]

Cc: "kga1978" [REDACTED] Andrew Rambaut [REDACTED]
"rfgarry" [REDACTED], "r.fouchier" [REDACTED],
"P.Vallance1" [REDACTED], "collinsf" [REDACTED]
[REDACTED], "afauci" [REDACTED], Josie Golding
[REDACTED], "m.koopmans" [REDACTED], Mike Ferguson
[REDACTED]

Betreff: Re: [ext] 2019 N-CoV

The theory of the origin of the has gathered considerable momentum not in social media, but increasingly among some scientists, in main stream media, and among politicians.

The aim of this was to bring a neutral, respected, scientific group together to look at the data and in a neutral, considered way provide an opinion and we hoped to focus the discussion on the science, not on any conspiracy or other theory and to lay down a respected statement to frame whatever debate goes on – before that debate gets out of hand with potentially hugely damaging ramifications.

With the additional information on the pangolin virus, information not available even 24 hours ago, I think the argument is even clearer.

My preference is that a carefully considered piece of science, early in the public domain, will help mitigate more polarised debate. If not, that debate will increasingly happen and science will be reacting to it. Not a good position to be in.

From: Edward Holmes [REDACTED]

Date: Saturday, 8 February 2020 at 20:11

To: Christian Drosten [REDACTED]

Cc: Jeremy Farrar [REDACTED], "kga1978" [REDACTED]
"a.rambaut" [REDACTED], "rfgarry" [REDACTED]
"r.fouchier" [REDACTED], "P.Vallance1" [REDACTED]
<P.Vallance1> [REDACTED], Francis Collins <[REDACTED]>, "afauci" [REDACTED]
[REDACTED], Josie Golding [REDACTED], Marion Koopmans
[REDACTED], Mike Ferguson [REDACTED]

Subject: Re: [ext] 2019 N-CoV

Hi Christian,

I don't know where this story came from, but it has nothing whatsoever to do the HIV nonsense. Please don't associate this with that. This is a broader story.

Ever since this outbreak started there have suggestions that the virus escaped from the Wuhan lab, if only because of the coincidence of where the outbreak occurred and the location of the lab. I do a lot of work in China and I can you that a lot of people there believe this and believe they are being lied to. Things were made worse when Wuhan lab published the bat virus sequence - a bat sampled in a different province for which they have a large collection of samples.

I believe the aim/question here is whether we, as scientists, should try to write something balanced on the science behind this? There are arguments for and against doing this.

Personally, with the pangolin virus possessing 6/6 key sites in the receptor binding domain, I am in favour of the natural evolution theory.

Best wishes,

Eddie

PROFESSOR EDWARD C. HOLMES FAA FRS

ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY

Marie Bashir Institute for Infectious Diseases & Biosecurity,

School of Life & Environmental Sciences and School of Medical Sciences,

The University of Sydney | Sydney | NSW | 2006 | Australia

T [REDACTED]

E [REDACTED]

On 9 Feb 2020, at 6:52 am, Drosten, Christian [REDACTED] wrote:

Dear All,

I am overloaded with nCoV patient-related work and will need a few days before I can work on this text.

Can someone help me with one question: didn't we congregate to challenge a certain theory, and if we could, drop it? This whole text reads as if the hypothesis was obvious, or was brought up by some external source, forcing us to respond. Is this the case? It does not seem as if this was linked to the HIV nonsense.

Who came up with this story in the beginning? Are we working on debunking our own conspiracy theory?

Christian

-

Professor Christian Drosten

Director, Institute of Virology

Scientific Director, Charité Global Health

Charité - Universitätsmedizin Berlin

Campus Charité Mitte

Germany

E-Mail:

<https://virologie-ccm.charite.de/>

<https://globalhealth.charite.de/>

Von: Jeremy Farrar [REDACTED]

Datum: Samstag, 8. Februar 2020 um 10:45

An: Edward Holmes [REDACTED], "kga1978" [REDACTED] · [REDACTED]

Andrew Rambaut [REDACTED], "rfgarry" [REDACTED]

Cc: "r.fouchier" [REDACTED] "P.Vallance1" [REDACTED]

"collinsf" [REDACTED]

"afauci" [REDACTED]

Josie Golding [REDACTED]

"m.koopmans" [REDACTED]

[REDACTED], Christian Drosten [REDACTED]

, Mike Ferguson [REDACTED]

Betreff: [ext] FW: 2019 N-CoV

APOLOGIES WITH ALL CORRECT EMAILS

Kristen, Andrew, Bob, Eddie have reworked the summary and it is attached here.

We are pushing to get the sequence data from the reports on the pangolins, but do not have currently, clearly that is very important to incorporate.

Interested in your views

- Is this reasonably balanced given the data?
- Is there anything anyone disagrees with?
- Is there anything more in relation to what would seem to be the two possibilities

- Nature, Intermediate host, evolution and passage
- Future data you may have
- Advice on whether KA, AR, RG and EH should publish this.

These and other thoughts welcome in confidence.

Message

From: Garry, Robert F [REDACTED]
Sent: 2/11/2020 9:16:27 PM
To: Edward Holmes [REDACTED]
CC: Kristian G. Andersen [REDACTED] Andrew Rambaut [REDACTED]
Subject: Re: A few thoughts on the summary

Yes very interesting - publish!

I predict Kristian will soon have some better dN/dS data to add productively to the mix as well.

Stay agnostic...hope Ian can as well.

From: Edward Holmes [REDACTED]
Sent: Wednesday, February 12, 2020 2:57 AM
To: Garry, Robert F [REDACTED]
Cc: Kristian G. Andersen [REDACTED] Andrew Rambaut [REDACTED]
Subject: Re: A few thoughts on the summary

External Sender. Be aware of links, attachments and requests.

See my comments on Slack.

PROFESSOR EDWARD C. HOLMES FAA FRS

ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY

Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,
The University of Sydney | Sydney | NSW | 2006 | Australia

T [REDACTED]

E [REDACTED]

On 12 Feb 2020, at 1:47 pm, Garry, Robert F <[REDACTED]> wrote:

[Virologica Sinica](#)

February 2018, Volume 33, Issue 1, pp 104–107 | [Cite as](#)

Serological Evidence of Bat SARS-Related Coronavirus Infection in Humans, China

"The virus may have been circulating for a longer period and in a larger population than we postulate based on molecular assays. This could be tested using banked sera once we have specific assays."

SAmples in South China seropositive, but those from Wuhan seronegative.

From: Kristian G. Andersen [REDACTED]
Sent: Wednesday, February 12, 2020 2:24 AM
To: Edward Holmes [REDACTED]
Cc: Garry, Robert F [REDACTED] Andrew Rambaut [REDACTED]
Subject: Re: A few thoughts on the summary

External Sender. Be aware of links, attachments and requests.

Yup, all good - as long as we don't have to inspect his arse.

On Tue, Feb 11, 2020 at 6:06 PM Edward Holmes [REDACTED] wrote:



PROFESSOR EDWARD C. HOLMES FAA FRS
ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY

Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,
The University of Sydney | Sydney | NSW | 2006 | Australia

T [REDACTED]
E [REDACTED]

On 12 Feb 2020, at 1:00 pm, Garry, Robert F [REDACTED] > wrote:

No problem from me...

From: Edward Holmes [REDACTED]
Sent: Wednesday, February 12, 2020 1:15 AM
To: Kristian G. Andersen [REDACTED] Garry, Robert F <[REDACTED]>; Andrew Rambaut [REDACTED]
Subject: Fwd: A few thoughts on the summary

External Sender. Be aware of links, attachments and requests.

From Ian about the Feb 7 summary.

Think we should add him as an author. Safety in numbers. In his own mind he brings a lot of gravitas...plus because he is involved in the GOF I think it adds weight. Happy to be overruled though.

PROFESSOR EDWARD C. HOLMES FAA FRS
ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY

Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,
The University of Sydney | Sydney | NSW | 2006 | Australia

T [REDACTED]
E [REDACTED]

Begin forwarded message:

From: Ian Lipkin [REDACTED]

GARRY0000273

Subject: A few thoughts on the summary

Date: 12 February 2020 at 1:40:21 am AEDT

To: Eddie Holmes [REDACTED]

Eddie-

Call me whenever you wish.

Ian

Adaptation to humans

1. Animals in the Wuhan wildlife market may not be the zoonotic origin of the outbreak. It's also possible that an infected human involved in the wildlife trade transmitted the virus to people in the market. This might explain why the environmental sampling revealed more viral sequences on the West (seafood) than the East (terrestrial) side of the street. I don't see a way to test this possibility; nonetheless, we could mention it.
2. The virus may have been circulating for a longer period and in a larger population than we postulate based on molecular assays. This could be tested using banked sera once we have specific assays.

Selection during passage

1. Are we suggesting that the furin cleavage site evolved from de novo mutations or through recombination?

On Feb 10, 2020, at 4:33 PM, Edward Holmes [REDACTED] wrote:

<Summary.Feb7.pdf>

Message

From: Clare Thomas [REDACTED]
Sent: 2/13/2020 2:34:29 AM
To: Kristian G. Andersen [REDACTED]
Subject: RE: Interest in commentary/hypothesis on SARS-CoV-2 origins?

Dear Kristian,
Yes please! It sounds possibly like a Perspective. I would love to take a look and consider whether it might be suitable for Nature.
All the best,
Clare

From: Kristian G. Andersen [REDACTED]
Sent: 12 February 2020 23:09
To: Clare Thomas
Subject: Interest in commentary/hypothesis on SARS-CoV-2 origins?

Dear Clare,

I can only imagine you must be crazy busy at the moment! I wanted to reach out to you to see if there would be interest in receiving a commentary/hypothesis piece on the evolutionary origins of SARS-CoV-2? There has been a lot of speculation, fear mongering, and conspiracies put forward in this space and we thought that bringing some clarity to this discussion might be of interest to Nature.

Prompted by Jeremy Farrah, Tony Fauci, and Francis Collins, Eddie Holmes, Andrew Rambaut, Bob Garry, Ian Lipkin, and myself have been working through much of the (primarily) genetic data to provide agnostic and scientifically informed hypotheses around the origins of the virus. We are not quite finished with the writeup and we still have some loose ends, but I wanted to reach out to you to see if this might potentially be of interest? We see this more as a commentary/hypothesis, as opposed to a more long-form Letter or Article.

Best,
Kristian

Kristian G. Andersen, PhD
Associate Professor, [Scripps Research](#)
Director of Infectious Disease Genomics, [Scripps Research Translational Institute](#)
Director, [Center for Viral Systems Biology](#)

The Scripps Research Institute
10550 North Torrey Pines Road, SGM-300A
Department of Immunology and Microbial Science
La Jolla, CA 92037

p: [REDACTED]
c: [REDACTED]
t: [REDACTED]
e: [REDACTED]
w: [REDACTED]

Assistant: [REDACTED]



DISCLAIMER: This e-mail is confidential and 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 mechanism. Springer Nature Limited does not accept liability for any statements made which are clearly the sender's own and not expressly made on behalf of Springer Nature Ltd or one of their agents. Please note that Springer Nature Limited and their agents and affiliates do not accept any responsibility for viruses or malware that may be contained in this e-mail or its attachments and it is your responsibility to scan the e-mail and attachments (if any).

Springer Nature Limited. Registered office: The Campus, 4 Crinan Street, London, N1 9XW. Registered Number: 00785998 England.

Message

From: Clare Thomas [REDACTED]
Sent: 2/13/2020 8:47:54 AM
To: Kristian G. Andersen [REDACTED]
Subject: RE: Interest in commentary/hypothesis on SARS-CoV-2 origins?

Dear Kristian,
Ok that sounds great. Thanks so much.
All the best,
Clare

From: Kristian G. Andersen [REDACTED]
Sent: 13 February 2020 16:33
To: Clare Thomas
Subject: Re: Interest in commentary/hypothesis on SARS-CoV-2 origins?

Sounds great Clare. We'll work out a few more of the details and share with you a draft so you can get a sense of whether this would be of interest and would also give you a chance to provide suggestions for things to incorporate.

I'll be gone for the rest the week, but I assume we'll have this ready early/mid next week.

Best,
Kristian

On Thu, Feb 13, 2020 at 2:34 AM Clare Thomas [REDACTED] wrote:

Dear Kristian,

Yes please! It sounds possibly like a Perspective. I would love to take a look and consider whether it might be suitable for Nature.

All the best,

Clare

From: Kristian G. Andersen [REDACTED]
Sent: 12 February 2020 23:09
To: Clare Thomas
Subject: Interest in commentary/hypothesis on SARS-CoV-2 origins?

Dear Clare,

I can only imagine you must be crazy busy at the moment! I wanted to reach out to you to see if there would be interest in receiving a commentary/hypothesis piece on the evolutionary origins of SARS-CoV-2? There has

been a lot of speculation, fear mongering, and conspiracies put forward in this space and we thought that bringing some clarity to this discussion might be of interest to Nature.

Prompted by Jeremy Farrah, Tony Fauci, and Francis Collins, Eddie Holmes, Andrew Rambaut, Bob Garry, Ian Lipkin, and myself have been working through much of the (primarily) genetic data to provide agnostic and scientifically informed hypotheses around the origins of the virus. We are not quite finished with the writeup and we still have some loose ends, but I wanted to reach out to you to see if this might potentially be of interest? We see this more as a commentary/hypothesis, as opposed to a more long-form Letter or Article.

Best,

Kristian

Kristian G. Andersen, PhD

Associate Professor, Scripps Research

Director of Infectious Disease Genomics, Scripps Research Translational Institute

Director, Center for Viral Systems Biology

The Scripps Research Institute

10550 North Torrey Pines Road, [REDACTED]

Department of Immunology and Microbial Science

La Jolla, CA 92037

p: [REDACTED]
c: ([REDACTED])

t: @K_G_Anderesen

e: [REDACTED]

w: www.andersen-lab.com

Assistant: [REDACTED]



DISCLAIMER: This e-mail is confidential and 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 mechanism. Springer Nature Limited does not accept liability for any statements made which are clearly the sender's own and not expressly made on behalf of Springer Nature Ltd or one of their agents. Please note that Springer Nature Limited and their agents and affiliates do not accept any responsibility for viruses or malware that may be contained in this e-mail or its attachments and it is your responsibility to scan the e-mail and attachments (if any).

Springer Nature Limited. Registered office: The Campus, 4 Crinan Street, London, N1 9XW. Registered Number: 00785998 England.

Message

From: Edward Holmes
Sent: 2/16/2020 2:38:46 AM
To: Garry, Robert F
CC: Ian Lipkin
Andrew Rambaut
Kristian
G. Andersen
Subject: Re: Paper

External Sender. Be aware of links, attachments and requests.

Oh yes, the reviewers are easy...I think this is a slam dunk.

PROFESSOR EDWARD C. HOLMES FAA FRS
ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY

Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,
The University of Sydney | Sydney | NSW | 2006 | Australia

T
E

On 16 Feb 2020, at 7:36 pm, Garry, Robert F [REDACTED] wrote:

Yeah I know and that's a good choice for him.

So, as you know when you submit you'll need to suggest reviewers to include and exclude. Seems easy - there are some natural choices for both lists. Nature commentaries are peer reviewed iirc but I'm guessing they'll push this as fast as possible.

Sent from my iPhone

On Feb 16, 2020, at 2:29 AM, Edward Holmes [REDACTED] wrote:

External Sender. Be aware of links, attachments and requests.

I agree, and I offered, but he wants to remain independent.

PROFESSOR EDWARD C. HOLMES FAA FRS
ARC Australian Laureate Fellow

THE UNIVERSITY OF SYDNEY

Marie Bashir Institute for Infectious Diseases & Biosecurity,
School of Life & Environmental Sciences and School of Medical Sciences,
The University of Sydney | Sydney | NSW | 2006 | Australia

T
E