From: Fauci, Anthony (NIH/NIAID) [E]
Sent: Fri, 24 Jul 2020 10:37:46 +0000

To: Jeremy Farrar

Subject: RE: Made it to UK press

I threw a brick!

From: Jeremy Farrar (b) (6)

Sent: Friday, July 24, 2020 4:47 AM

To: Fauci, Anthony (NIH/NIAID) [E] (b) (6)

Subject: Made it to UK press

https://www.theguardian.com/sport/2020/jul/23/mlb-opening-night-fauci-yankees-nationals

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From: Fauci, Anthony (NIH/NIAID) [E]
Sent: Tue, 21 Jul 2020 16:28:01 +0000

To: Jeremy Farrar

Subject: RE: Hope you are OK

Thanks, Jeremy. I hope that I do not embarrass myself ©

Anthony S. Fauci, MD
Director
National Institute of Allergy and Infectious Diseases
Building 31, Room 7A-03
31 Center Drive, MSC 2520
National Institutes of Health
Bethesda, MD 20892-2520
Phone:
(b) (6)
FAX: (301) 496-4409

E-mail: (b) (6)

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From: Jeremy Farrar (b) (6)

Sent: Tuesday, July 21, 2020 11:28 AM

To: Fauci, Anthony (NIH/NIAID) [E] (b) (6)

Subject: Re: Hope you are OK

Enjoy



OFFICIAL STATEMENT

A STATEMENT FROM THE WASHINGTON NATIONALS REGARDING OPENING DAY

The Washington Nationals are thrilled to announce that Nats super-fan, Dr. Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases, has accepted our invitation to throw out the ceremonial first pitch on Opening Day, Thursday, July 23.

Dr. Fauci has been a true champion for our country during the Covid-19 pandemic and throughout his distinguished career, so it is only fitting that we honor him as we kick off the 2020 season and defend our World Series Championship title.



From: "Fauci, Anthony (NIH/NIAID) [E]" (6) (6)

Date: Thursday, 9 July 2020 at 12:55

To: Jeremy Farrar (b) (6)

Subject: RE: Hope you are OK

Jeremy:

Thank you for your kind and considerate note. I am hanging in there, but it is not easy. Stay well and safe.

Warm regards,

Tony

Anthony S. Fauci, MD
Director
National Institute of Allergy and Infectious Diseases
Building 31, Room 7A-03
31 Center Drive, MSC 2520
National Institutes of Health
Bethesda, MD 20892-2520
Phone:
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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 (b) (6)

Sent: Thursday, July 9, 2020 7:37 AM

To: Fauci, Anthony (NIH/NIAID) [E] (b) (6)

Subject: Hope you are OK

Watching events from a distance - all thoughts with you. Best wishes Jeremy

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From: Jeremy Farrar

Sent: Wed, 13 May 2020 21:25:59 +0000

To: Viner, Russell;Collins, Francis (NIH/OD) [E];Fauci, Anthony (NIH/NIAID) [E]

Cc: Bianchi, Diana (NIH/NICHD) [E];Gibbons, Gary (NIH/NHLBI) [E]

Subject: Re: confidential - update on Paediatric Multisystem Inflammatory Syndrome

(PIMS)

Let us know if we can help

From: "Viner, Russell"

Date: Wednesday, 13 May 2020 at 22:22

To: Francis Collins

(b) (6), Jeremy Farrar

(b) (6), "Fauci,
Anthony (NIH/NIAID) [E]"

(b) (6)

Cc: "Bianchi, Diana (NIH/NICHD) [E]"

(b) (6)

(b) (6), "Gibbons, Gary (NIH/NHLBI) [E]"

Subject: Re: confidential - update on Paediatric Multisystem Inflammatory Syndrome (PIMS)

Dear Francis, Diana and Gary – and Jeremy

Many thanks.

We have a unique opportunity to study this emerging phenomenon and ensure we have all the bases covered in terms of epi, mechanisms and treatment

I represent the Royal College of Paediatrics & Child Health who have had a role in coordinating responses here in the UK.

Colleagues here in the UK have networked extensively with other European countries in terms of sharing data and organising collection of research samples. I understand they have also linked with colleagues in the USA who particularly work on Kawasaki Disease - in Boston and San Diego.

I wonder if an international effort would be possible to pull together data across Europe and the USA – and ensure that we have adequately powered quality studies of epi, mechanisms and treatment. The number of cases will almost certainly preclude adequately powered studies in single countries, potentially even in the USA.

It appears that case numbers are now dropping in the UK/Europe – as the curve appeared to present and peak approximately a month after the covid peak – and I suspect a similar peak and decline will be seen in the USA if the post-infectious hypothesis is correct. Clearly more cases are likely with any secondary covid peaks

A collaboration between NIH and Wellcome could be very powerful in ensuring that this initial cluster from the first peak is well studied and prepare for prospective studies for future cases.

Treatment studies in particular might need to be international. None of the current covid-19 treatment studies would appear entirely appropriate as they stand

We have been planning an expert taskforce to oversee the research and clinical responses here in the UK – and it would make sense for this to be international given the above.

Yours and best

Russell

From: "Collins, Francis (NIH/OD) [E]"		(b) (6)		
Date: Wednesday, 13 May 2020 at	01:52	L 31.07			
To: Russell Viner < r.viner@ucl.ac.u	k>, Jerer	ny Farrar		(b) (6)	"Fauci,
Anthony (NIH/NIAID) [E]"		(b) (6)			
Cc: "Bianchi, Diana (NIH/NICHD) [E]"·		(b) (6)	, "Gibbons, Gary	
(NIH/NHLBI) [E]"	(b) (6)	1 1 1 1	- 3		
Subject: RE: confidential - update (PIMS)	on Paedia	atric Multi	system In	flammatory Syndro	ome

Dear Russell,

Thanks for your note and this additional information. I am looping in Dr. Diana Bianchi (Director, National Institute of Child Health and Human Development) and Dr. Gary Gibbons (Director, National Heart, Lung, and Blood Institute). I have asked them to cochair an urgent NIH team on PMIS. I am sure they will want to connect with you.

Best, Francis

```
From: Viner, Russell (b) (6)

Sent: Tuesday, May 12, 2020 6:12 PM

To: Jeremy Farrar (b) (6) Collins, Francis (NIH/OD) [E]

(b) (6); Fauci, Anthony (NIH/NIAID) [E] (b) (6)

Subject: Re: confidential - update on Paediatric Multisystem Inflammatory Syndrome (PIMS)
```

Thanks Jeremy and hello to Francis and Tony

Colleagues here have been linked in with pediatric id/imm colleagues through Boston but a fully national collaborative approach would be very valuable.

We've started a national (across UK and Ireland) surveillance study using a well-established physician reporting system (British Paediatric Surveillance Unit, BPSU) – started yesterday, with weekly reporting by all paediatricians (95% coverage) in the UK – that will provide initially prevalence data next week/fortnight and then start to provide incidence data. Reported cases will be fed into established research systems to obtain biological specimens etc.

However cross national studies clearly much more useful if can be organised quickly. For epi, biological samples and treatment studies.

Re Rx - there is a recommendation to recruit to the multi-arm all-age Recovery Trial (https://www.recoverytrial.net) for more severe cases of this syndrome; however there is a concern that some of the arms may not be appropriate for this potentially post-covid syndrome – e.g. hydroxychloroquine or azithromycin. The standard treatment So there is the potential for a very rapid development of a pediatric rct – however this would be entirely underpowered in one country – and where a joint UK-USA plus others trial might be very powerful

Re etiology – a powerful prospective case-control design might be very useful in identifying environmental and other risk factors – again a single country study will be difficult to power.

The implications for vaccine development is something we've been discussing with Andy Pollard from the Oxford Vaccine Centre.

Keen to facilitate dialogue between UK and US teams. Let me know how we might do this. Best
Russell

From: Jeremy Farrar (b) (6)

Date: Tuesday, 12 May 2020 at 19:33

To: Russell Viner (b) (6) Francis Collins (b) (6)

"Fauci, Anthony (NIH/NIAID) [E]" (b) (6)

Subject: Re: confidential - update on Paediatric Multisystem Inflammatory

Syndrome (PIMS)

Russell

I shared your note with Francis Collins and Tony Fauci at NIH.

The NIH is looking at this in the USA – can we link you up with the teams in the USA?

Best wishes Jeremy

From: "Viner, Russell" (b) (6)

Date: Tuesday, 12 May 2020 at 13:16

To: "Vallance, Patrick (GO-Science)"

(b) (6), "Whitty,
Chris"

(b) (6) Jeremy Farrar

(b) (6)

Cc: Natasha Neill (b) (6)

Subject: confidential - update on Paediatric Multisystem Inflammatory

Syndrome (PIMS)

Dear Chris and Patrick, cc to Jeremy

I think you are also being updated by NHSE and perhaps also by Callum Semple but just a quick update from RCPCH perspective

We had an update call yesterday, which somewhat raised my level of concern and changed the picture slightly – so thought you should be in the picture. I have of course

real concerns about how we balance this with the issues about public confidence re schools.

Case definition: RCPCH case definition published Friday a week ago, now adopted in the UK and likely by WHO

Numbers – we appear to be close to 60 across the UK. One concern from the call yesterday was that there appears to be some milder forms sitting on paediatric wards – i.e. not fulfilling case definition but essentially children with very high CRP and a symptom or two. Discussions about revision to case definition – on hold for the moment. I am concerned that this will dilute the situation and artificially inflate figures.

Clinical picture: as before. There appear to be potentially 2-3 phenotypes; one with multisystem inflammatory symptoms, one with shock and perhaps one with essentially Kawasaki Disease (KD e.g. coronary artery aneurisms in young children) but refractory to treatment

Larger numbers coming from across the world, where COVID has been an issue. Italy, Spain, USA.

Deaths: 2 known deaths thus far, one London one Bristol. One was a 6 month old with refractory Kawasaki Disease (KD).

Severity - around 50% need PICU. As before

COVID status: I can't give you the exact new numbers, but unchanged i.e. a proportion around 25-30% test negative for virus but some later found to be serology positive (where this is available).

The particular concerns for me from yesterday were four:

- a. that some apparently very mild cases have been appearing as above potentially inflating the numbers, although these are also increasing for the full syndrome b. that some apparently very well children can suddenly deteriorate this is rare however
- c. some reports, without clear data, that cardiac abnormalities are more common than previously recognised when echoed. Raising concerns about longer term complications. d. Aetiology and risk factors: The higher proportion from BME backgrounds has been described before. A new concern was an apparently high proportion of parents who are healthcare workers. This is very concerning and I emphasised the need to recognise this is supposition, to collect good data and keep confidential for now until we have some actual data. However the potential to worry the public is very high.

Aetiology; remains unclear. Speculation that this is a post-inflammatory condition due to i) phenotype; ii) peaking 2-4 weeks after covid peak; iii) virus testing negative in some

patients. The absence of this syndrome in China/Japan/SK is puzzling, given that KD was described in Japan plus high prevalence there, presumably genetic.

This remains very much a mostly London phenomenon, with 1-2 cases only in Scotland and NI and a larger cluster in Wales. Which raises concerns about recognition. Note the occurrence in teenagers – and likely a syndrome that overlaps with young adults

Research

Brit Paediatric Surveillance Unit (BPSU) study started today. This is routine RCPCH rare disease surveillance methodology but will now run weekly to all paediatricians in the UK.

WHO is starting some surveillance as well – Uk people linked into this Routine recruitment into Diamonds/ISARIC studies of patients notified through BPSU.

However I believe that a more comprehensive research strategy is needed - e.g. encompassing a case-control study to examine risk factors such as ethnicity and parent occupation, deprivation etc. We are working very closely with NHSE and we have suggested that a formal joint Taskforce be formed to oversee the research and clinical responses. We hope Steve Powis will agree to this.

Publicity

An Italian description of 10 cases of a KD-like syndrome will appear in Lancet later today or tomorrow, with a commentary (by me and Liz Whittaker from Imperial – trying to balance the importance of recognising the new syndrome with the public health messages).

The UK experience has been submitted (NEJM).

These will undoubtedly raise public concern. The RCPCH is working hard to ensure that messages are clear and recognise the bigger, public health picture.

I hope this is helpful. Let me know if you wish further information or have advice for us.

Best Russell From: Fauci, Anthony (NIH/NIAID) [E]
Sent: Tue, 12 May 2020 18:49:04 +0000

To: Jeremy Farrar Subject: Re: Take Care

Jeremy:

Thank you for your kind note. Much appreciated.

(b) (6)

Best regards,

Tony

On May 12, 2020, at 12:57 PM, Jeremy Farrar

(b) (6) wrote:

Tony - Hope you are OK, take care, best wishes Jeremy

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From: Jeremy Farrar

Sent: Tue, 12 May 2020 17:42:11 +0000

To: Fauci, Anthony (NIH/NIAID) [E]; Collins, Francis (NIH/OD) [E]

Subject: FW: confidential - update on Paediatric Multisystem Inflammatory Syndrome

(PIMS)

Just to update.

Any news on this from US?

From: Viner, Russell (b) (6)

Sent: 12 May 2020 13:17

To: Vallance, Patrick (GO-Science) (b) (6); Whitty, Chris

(b) (6); Jeremy Farrar (b) (6)

Cc: Natasha Neill (b) (6)

Subject: confidential - update on Paediatric Multisystem Inflammatory Syndrome (PIMS)

Dear Chris and Patrick, cc to Jeremy

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- d. Aetiology and risk factors: The higher proportion from BME backgrounds has been described before. A new concern was an apparently high proportion of parents who are healthcare workers. This is very concerning and I emphasised the need to recognise this is supposition, to collect good data and keep confidential for now until we have some actual data. However the potential to worry the public is very high.

Aetiology; remains unclear. Speculation that this is a post-inflammatory condition due to i) phenotype; ii) peaking 2-4 weeks after covid peak; iii) virus testing negative in some patients. The absence of this syndrome in China/Japan/SK is puzzling, given that KD was described in Japan plus high prevalence there, presumably genetic.

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These will undoubtedly raise public concern. The RCPCH is working hard to ensure that messages are clear and recognise the bigger, public health picture.

I hope this is helpful. Let me know if you wish further information or have advice for us.

Best

Russell

From: Jeremy Farrar

Sent: Tue, 5 May 2020 12:00:28 +0000

To: kickbusch@bluewin.ch;'SMITH, Ian Michael';'Dzau Victor';'Chris.Elias';Fauci,
Anthony (NIH/NIAID) [E];'Fore Henrietta';'Gao Fu';'Gashumba Diane';'Kaag Sigrid';'Suzuki Yasuhiro';'Vega
Morales Jeanette';'Vega Morales Jeanette';'Veronika Skvortsova';'VijayRaghavan Krishnaswamy'

Cc: 'As Sy';'Gro'

Subject: Re: GPMB Board Teleconference; Tuesday 5 May 13.00-14.30 CEST

lan, Gro and As

Apologies - I will have to leave at 1pm UK time.

Best wishes Jeremy

From:	(b) (6)	(b) (6)			
Date: Tuesday, 5 May	2020 at 10:12				
To: "SMITH, Ian Micha	ael''' (b)	(6)>, Victor Dzau		(b) (6) "'Chris.Eli:	as"
	(b) (6), Jeren	ny Farrar		டுடு, 'Fauci An	thony'
(b) (, 'Fore Henrietta'	0	b) (6), 'Gao Fu'	The state of the s	(b) (6),
Diane Gashumba	(ъ) (б),	'Kaag Sigrid'	(b) (6)	'Suzuki Yasuhiro	1
	(b) (6), 'Vega Mo	orales Jeanette'		(b) (6)	, 'Vega
Morales Jeanette	(b) (6)	, 'Veronika Skvo	rtsova'	(t) (6)
'VijayRaghavan Krishn	aswamy'	(b) (6) >			
Cc: 'As Sy'	(b) (6), 'Gro	o' <gro@brundt< td=""><td>land.org></td><td></td><td></td></gro@brundt<>	land.org>		
Subject: AW: GPMB B	oard Teleconference	e; Tuesday 5 Ma	y 13.00-14.30	CEST	

Dear Ian – thank you very much for this. And thank you for the work of the secretariat. I have just two points:

Not each GPMB member has a Sherpa (at least I don't)

I am worried that all background papers are written by institutions from the Global North – I would ask that they are asked to reach out to institutions in the Global South – or we commission complementary papers or commentaries.

I would also like to suggest a background paper that deals with all the important "digital" issues at hand – from cyber security, tracking, fake news, digital passports etc.

All the very best (until this afternoon) Ilona

Von: SMITH, Ian Michael (b) (6) Gesendet: Montag, 4. Mai 2020 13:38 An: 'Dzau Victor' (b) (6) Chris.Elias (b) (6); J.Farrar (b) (6); 'Fauci Anthony' (b) (6); 'Fore Henrietta' (b) (6) >; 'Gashumba Diane' (b) (б); 'Gao Fu' (b) (6) >; 'Kaag Sigrid' (b) (6); Ilona Kickbusch < Kickbusch@bluewin.ch>; 'Suzuki Yasuhiro' 'Vega Morales Jeanette' (b) (6); 'Vega Morales (b) (6): 'Veronika Skvortsova' (b) (6); 'VijayRaghavan Jeanette' (b) (6) Krishnaswamy' (b) (6); Gro (b) (6) Cc: 'As Sy' Betreff: RE: GPMB Board Teleconference; Tuesday 5 May 13.00-14.30 CEST

Dear GPMB co-chairs and members,

Please find attached a short report on the activities of the Board and secretariat for the period 1 January to 30 April 2020. This is provided for information only.

Regards,

lan

```
From: SMITH, Ian Michael
Sent: Friday, May 1, 2020 5:23 PM
                                 (b) (6); 'Elias Chris'
                                                                                   (b) (6) >; 'Farrar Jeremy'
To: 'Dzau Victor'
                        (b) (6); 'Fauci Anthony'
                                                                    (b) (6); 'Fore Henrietta'
                (b) (6); 'Gao Fu'
                                                  (b) (6): 'Gashumba Diane'
                                                                                                 (b) (6) 'Kaag
Sigrid'
                  (b) (6) >; 'Kickbusch Ilona'
                                                                  (b) (6); 'Suzuki Yasuhiro'
                          'Vega Morales Jeanette'
                                                                                 (b) (6); 'Vega Morales
Jeanette'
                              (b) (6); 'Veronika Skvortsova'
                                                                                   (b) (6) 'VijayRaghavan
Krishnaswamy'
                                     (b) (6)
                                  (b) (6); 'Brundtland Gro Harlem'
Cc: 'As Sy'
                                                                                       (b) (6)
Subject: GPMB Board Teleconference; Tuesday 5 May 13.00-14.30 CEST
```

Dear Board members,

In preparation for the Board meeting on Tuesday 5 May from 13.00-14.30 CEST, please find attached the draft annotated outline of the Annual Report.

The sherpa group and secretariat discussed this in their teleconference yesterday. On the Annotated outline of the Annual Report, the Sherpas generally felt that the outline had the right tone and covered the right issues. Some suggestions made included: a stronger focus on equity and solidarity, an analysis of the IHR and how they have performed during the COVID-19 pandemic, examples of good practices from countries with different income levels, a stronger focus on country preparedness and the importance of R&D. There was some divergence of views on whether the report should also examine the COVID-19 response or if the focus should remain entirely on lessons learned for preparedness.

The group also discussed an outline of the Monitoring Framework Interim Report prepared by the secretariat. The Sherpas were asked theirs views on whether the full 7 actions should be addressed in the document or whether 3 priority actions should be selected and which ones. There were widely differing views on priorities and therefore the group suggested that the Report should review progress on the 7 actions but could group the actions in 3 sections: Leadership and solidarity, Financing and R&D.

You will also find copied below the call-in details.

We look forward to the meeting.

Regards,

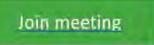
lan

When it's time, join the Webex meeting here.

Meeting number (access code): (b) (6)

Meeting password: (b) (6)

Tuesday, May 5, 2020
1:00 pm | (UTC+02:00) Brussels, Copenhagen, Madrid, Paris | 1 hr 30 mins



Join by phone

Tap to call in from a mobile device (attendees only)

41445750282 SWITZERLAND Toll

+1-415-655-0003 US Toll

Global call-in numbers | Toll-free calling

restrictions

Need help? Go to http://help.webex.com

ay, April 29, 2020 8:18 PM To: 'Dzau Victor' (b) (6); Chris. Elias (b) (6); J.Farrar (b) (6) 'Fore Henrietta' (b) (6); 'Fauci Anthony' (b) (6); 'Gao Fu' (b) (6) 'Gashumba Diane' (b) (6) >; 'Kaag (b) (6); Ilona Kickbusch (b) (6); 'Suzuki Yasuhiro' Sigrid' 'Vega Morales Jeanette' (b) (6); 'Vega Morales Jeanette' (b) (6); 'Veronika Skvortsova' (b) (6); 'VijayRaghavan (b) (6) Krishnaswamy' Cc: 'As Sy' (b) (6); Gro Subject: GPMB Board Teleconference; Tuesday 5 May 13.00-14.30 CEST

Dear Board members, dear colleagues,

Please find attached an annotated agenda for the Board teleconference scheduled for Tuesday 5 May from 13.00-14.30 CEST. In order to make as much time available as possible for discussion on the outline of the 2020 annual report, we have limited the number of topics for discussion.

Remaining documents for the meeting will be sent to you on Friday.

For those who have not yet done so, we would be grateful if you could confirm your participation in teleconference.

Many thanks,

lan

Ian Smith

(b) (6

Desk: +41 22 7913979

Mobile/WhatsApp: (b) (6)

Fauci, Anthony (NIH/NIAID) [E] From: Sent: Thu, 30 Apr 2020 22:35:34 +0000 Jeremy Farrar; Dzau, Victor J.; George GAO To: Cc: Hatchett (b) (6) (b) (6); Hannon, Emma; Conrad, Patricia (NIH/NIAID) [E];Teresa Miller de Vega (b) (6) Rebeka Yasmin -CEPI; (b) (6) (b) (6) (b) (6); McGinnis, J. Michael; Balatbat, Celynne; Mun, Jenny (b) (6); Redfield, Robert R. (CDC/OD) RE: NAS Annual Meeting Session on COVID-19 -- Information regarding your Subject: Saturday April 25 participation Jeremy: Many thanks for the update. Please continue to keep me informed. Best, Tony Anthony S. Fauci, MD Director National Institute of Allergy and Infectious Diseases Building 31, Room 7A-03 31 Center Drive, MSC 2520 National Institutes of Health Bethesda, MD 20892-2520 Phone: (FAX: (301) 496-4409 E-mail: 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	(b) (6)		
Sent: Tuesday, April 28, 2020 1	.0:39 AM		
To: Fauci, Anthony (NIH/NIAID) [E]	(b) (6) Dzau, Victor J.	(b) (6) George
GAO (b) (6) >			
Cc: Richard Hatchett	(b) (6)	(ъ	(6)
Control of the last	(b) (6); Hannon, Emma	(b) (6)	Conrad, Patricia
(NIH/NIAID) [E] <	(b) (6); Teresa Mi	ller de Vega	(b) (6);>
(b) (6); Rebeka Yasmin -	CEPI < Rebeka.yasmin@	cepi.net>; ben.tinker@	@cnn.com;
Amanda.Sealy@cnn.com; Neel	.Khairzada@turner.con	n; Tia.Miller@turner.c	om; hujr@chinacdc.cn;
McGinnis, J. Michael	(b) (6) >; Balatba	t, Celynne	(b) (6); Mun, Jenny
	(b) (6) Redfield, Rob	ert R. (CDC/OD)	(b) (6) _' >
Subject: Re: NAS Annual Meeti participation	ing Session on COVID-1	9 Information regard	ding your Saturday April 25

Quick update

Update in confidence

European network from this morning:

16 Paris, 2 Geneva, few Madrid last 10 days - nothing like this usually seen even with seasonal KD or TSS

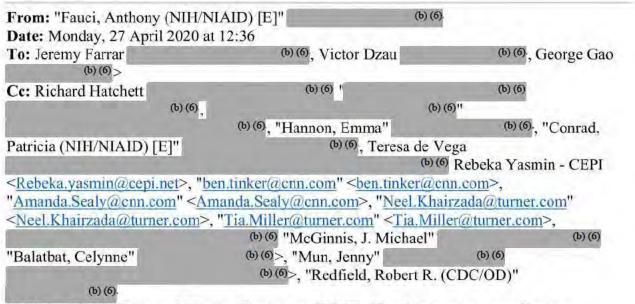
Barcelona have slightly different experience of 6 'Kawasaki' in last 2 weeks - couple now who have large coronary aneurysms, as have one child South London and one in Bristol.

Most UK PICU have 1-2 of these type of cases

Phenotype seems Diarrhoea and abdominal pain, refractory shock then various degrees of heart involvement and inflammation ++ - several have had their normal appendix whipped out Most negative respiratory and stool PCR for anything, some positive resp PCR COVID - GOSH early case has seroconverted, but had immunoglobulin

We are establishing database UK and Europe and trying to define what the clinician features are and agree investigations.

Notably, none in US reported (just D/W Boston childrens who have been running shared international COVID experience web calls) and none in Rome, unsure about rest of Italy yet Does seem BAME preponderance -?? immune related or social phenomenon, in terms of deprivation prevalence and ability to isolate



Subject: RE: NAS Annual Meeting Session on COVID-19 -- Information regarding your Saturday April 25 participation

Jeremy:

Thanks for the heads up. Is there any more detailed description of the precise clinical manifestations? They describe a "multisystem inflammatory state". It is vasculitis or anything more specific? Could be an infectious agent that has nothing to do with SARS-CoV-2 infection even though some children are circumstantially infected with SARS-CoV-2or it could be a post-SARS-CoV-2 inflammatory syndrome, perhaps a Kawasaki syndrome-like disease. Please keep me informed if you hear any further information.

Best regards,

Tony

Anthony S. Fauci, MD
Director
National Institute of Allergy and Infectious Diseases
Building 31, Room 7A-03
31 Center Drive, MSC 2520
National Institutes of Health
Bethesda, MD 20892-2520
Phone:
(b) (6)
FAX: (301) 496-4409
E-mail:
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From: Jeremy Farrar	(b) (6)		
Sent: Monday, April 27, 2020 7:13	AM		
To: Fauci, Anthony (NIH/NIAID) [E]	(b)	(6); Dzau, Victor J.	(b) (6); George
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(b)	(6) Hannon, Emma	(b) (б); Con	rad, Patricia
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Amanda.Sealy@cnn.com; Neel.Kha	airzada@turner.com;	Tia.Miller@turner.com;	(6) (6)
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To be aware of – news over night so a huge amount of uncertainty – important for COVID19 now, and a potential concern for how we view immunity, protection, post-infectious immunopathology.

https://www.hsj.co.uk/acute-care/exclusive-national-alert-as-coronavirus-related-condition-may-be-emerging-in-children/7027496.article

https://t.co/Bj6YHLJ8zi

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Date: Sunday, 26 April 20	020 at 19:52		
To: Victor Dzau	(b) (6), George Gao	(b) (6).	
Cc: Jeremy Farrar < J.Farr	ar@wellcome.ac.uk>, Richard	Hatchett	(b) (6) _,
The second secon	(b) (6)	
		AND DESCRIPTION OF THE PARTY OF	(b) (6) "Hannon,
Emma" (b)	(NIH/N		(b) (6)
Teresa de Vega			(b) (6) Rebeka
Yasmin - CEPI	(b) (6) >, "ben.tinker(@cnn.com" <ben.tir< td=""><td>ker@cnn.com>,</td></ben.tir<>	ker@cnn.com>,
"Amanda.Sealy@cnn.com	" <amanda.sealy@cnn.com>,</amanda.sealy@cnn.com>		
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From: Dzau, Victor J. <<u>VDzau@nas.edu</u>> Sent: Saturday, April 25, 2020 3:59 PM

Saturday April 25 participation

inviting me.

To: George GAO (b) (6) Cc: Fauci, Anthony (NIH/NIAID) [E] (b) (6) (b) (6) (b) (6) (b) (6); (b) (6); Hannon, (b) (6); Conrad, Patricia (NIH/NIAID) [E] (b) (6) Emma (b) (6) ben.tinker@cnn.com; Amanda.Sealy@cnn.com; Neel.Khairzada@turner.com; Tía.Miller@turner.com; hujr@chinacdc.cn; McGinnis, J. Michael (b) (6); Balatbat, Celynne (b) (6) Mun, Jenny (b) (6)

Subject: Re: NAS Annual Meeting Session on COVID-19 -- Information regarding your Saturday April 25 participation

Dear Jeremy, Tony, Sanjay, George, Susan and Richard,

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Hope to see you soon.

Warmest regards,

Victor

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I am waiting for being connected and will use slides which were sent to your office George

发自我的iPhone

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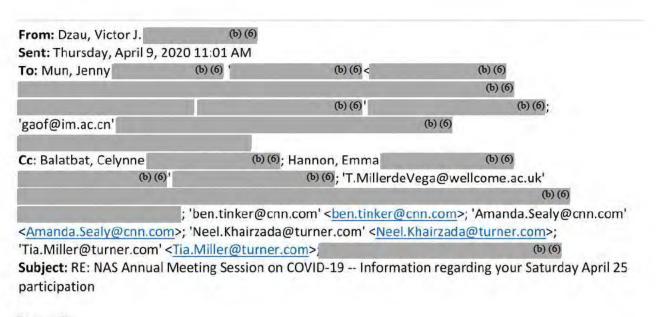
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I would greatly appreciate it if you would respond to this email.

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Victor

PS, Celynne Balatbat, my special assistant, will be sending you additional information about the session logistics shortly.



Dear all,

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Best, Victor

From: Mun,	Jenny		
Sent: Wedne	esday, April 8, 2020 10:56 AM		
To:	(b) (6)	(b) (6) ;
	(b) (6) ;	(b)) (6)
Cc: Dzau, Vic	tor J.; Balatbat, Celynne; Mun, Jen	nny ; Hannon, Emma ;	(b) (6);
		(b) (6) ; 'ber	n.tinker@cnn.com';
'Amanda.Sea	aly@cnn.com'; 'Neel.Khairzada@tu	rner.com'; 'Tia.Miller@turner.com	į.
Subject: NAS participation	for a series of the series of the series of the series of the	0-19 Information regarding your S	aturday April 25

Dear Speakers:

I am the logistical contact for the COVID-19 session that will be held as part of the Annual Meeting (online) program on Saturday, April 25 at 2:00 pm EDT. Thank you for agreeing to participate in this session. To help you with your planning, I have provided additional details below.

Please note that the session will be live webcast and the general public will also be able to watch the session. Video from the session will also be uploaded on the NAS YouTube channel (https://www.youtube.com/user/theNASciences) after the meeting. We will need to obtain signed speaker release forms for your participation in this session. I have attached the speaker release form for your review and submission. Please return the signed speaker release form by Monday, April 13.

Session speakers are asked to connect 30 minutes prior to the session start time (by Saturday, April 25 at 1:30 pm EDT) to allow the technical staff to check connections and prepare for the session. Details on how to connect will be sent before the meeting.

We will list you in our promotional materials as noted below. If this is incorrect, please let me know.

Anthony S. Fauci, Director, National Institute of Allergy and Infectious Diseases

Jeremy Farrar, Director, Wellcome Trust
George F. Gao, Director-General, Chinese Center for Disease Control & Prevention
Sanjay Gupta, Chief Medical Correspondent, CNN
Richard J. Hatchett, CEO, Coalition for Epidemic Preparedness Innovations
Susan R. Weiss, Professor of Microbiology, Perelman School of Medicine, University of Pennsylvania

Since many of us have moved to remote work environments, you may already be proficient with Zoom and other online meeting/collaboration applications. I am attaching a 'speaker guidelines' file in case you have any questions on how best to prepare for and stage your remote talk. We have technical staff available to help you become familiar with Zoom and its settings — such as "sharing your screen" (if you have slide presentations that need to be shown during your talk). We can arrange for a training session this week or next week. If you would like to schedule a session, please let me know as soon as possible.

Dr. Dzau's office will be in touch regarding the agenda for this session. If you have any other questions, please let me know.

Regards, Jenny

Jenny Mun Membership Director National Academy of Sciences

(b) (6

From: Fauci, Anthony (NIH/NIAID) [E] Sent: Mon, 27 Apr 2020 12:33:44 +0000

To: Jeremy Farrar

RE: NAS Annual Meeting Session on COVID-19 -- Information regarding your Subject:

Saturday April 25 participation

Thanks, Jeremy. I saw the report in the Post from Saturday. These children had mostly respiratory disease and diarrhea. I will check with the docs at DC Children's Hospital about the presence of "multisystem inflammatory state". This could just be the advanced stage of their disease compatible with advanced SARS-COV-2

Best, Tony

E-mail:

Anthony S. Fauci, MD Director National Institute of Allergy and Infectious Diseases Building 31, Room 7A-03 31 Center Drive, MSC 2520 National Institutes of Health Bethesda, MD 20892-2520 Phone: FAX: (301) 496-4409 (b) (6)

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From: Jeremy Farrar	(b) (6)		
Sent: Monday, April 27, 2020 7:38 AM			
To: Fauci, Anthony (NIH/NIAID) [E]	0	(b) (6); Dzau, Victor J.	(b) (6); George
GAO (b) (6)			
Cc: Richard Hatchett	(b) (6)	(b) (6);	
(b) (6)	Hannon, Emma	(b) (6); Con	rad, Patricia
(NIH/NIAID) [E]	b) (6); Teresa Mi	ller de Vega	(b) (6);
(b) (6) Rebeka Yasmin - CEPI		(b) (6); ben.tinker@cnr	n.com;
Amanda.Sealy@cnn.com; Neel.Khairza	da@turner.con	n; Tia.Miller@turner.com;	(b) (6);
McGinnis, J. Michael	(b) (6)	(b) (6)	6) (6); Mun, Jenny
(b) (6)	; Redfield, Rob	ert R. (CDC/OD) <	(b) (6)
Subject: Re: NAS Annual Meeting Sessi participation	ion on COVID-1	9 Information regarding	your Saturday April 25

Thanks Tony - have asked for that and will share as soon as I can.

I believe there have been reports in the Washington Post.

https://www.washingtonpost.com/local/new-dc-hospital-numbers-suggest-kids-do-face-some-risk-of-coronavirus-hospitalization/2020/04/25/5e78c268-86fe-11ea-878a-86477a724bdb story.html

From: "Fauci, Anthony (NII-	H/NIAID) [E]" (6) ((6).
Date: Monday, 27 April 2020	0 at 12:36	7
To: Jeremy Farrar (b) (6)	(b) (6), Victor Dzau	(b) (6) George Gao
Cc: Richard Hatchett	(6) (6)	(b) (6)
(b) (6	5),	b) (6)"
	(b) (6), "Hannon, Emma"	(b) (6)-, "Conrad,
Patricia (NIH/NIAID) [E]"	(b) (6), Teresa de	
		(6) Rebeka Yasmin - CEPI
(b) (6)>,	"ben.tinker@cnn.com" <ben.tinker@< td=""><td>cnn.com>,</td></ben.tinker@<>	cnn.com>,
	Amanda.Sealy@cnn.com>, "Neel.Kl	
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	(b) (6) >, "McGinnis, J. Michael"	(b) (6)
(b) (6)	(b) (6), "Mun, Jenny"	(6) (6)
"haja.bally@cepi.net"	(b) (6), "Redfield, Robert R	. (CDC/OD)"
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Jeremy:

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https://t.co/Bj6YHLJ8zi

participation

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From: "Fauci, Anthony (NIH/NIAID) [E]"
                                                              (b) (6).
Date: Sunday, 26 April 2020 at 19:52
                               (b) (6). George Gao
                                                               (b) (6)
To: Victor Dzau
                                          (b) (6) Richard Hatchett
                                                                                        (b) (6)
Cc: Jeremy Farrar
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                                     (b) (6) "McGinnis, J. Michael"
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(b) (6) (b) (6) , "Mun, Jenny" (b) (6) , (b) (6)

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Sent: Saturday, April	25, 2020 3:59	PM			
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Cc: Fauci, Anthony (N	IIH/NIAID) [E]		(6) (6); ј	(b) (6)	
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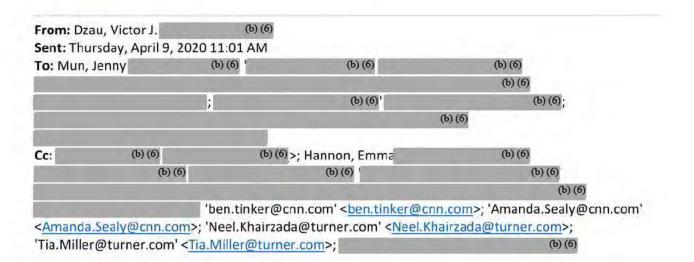
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Best, Victor

From: Mun, Jenny

Sent: Wednesday, April 8, 2020 10:56 AM

To: (b) (6); (b) (6)

(6	0(6);	(b) (6)
Cc: Dzau, Victor J.;	(b) (6); Mun, Jenny; Hannon, Emma;	(b) (6)
National Contract of the Contr		(b) (6); 'ben.tinker@cnn.com'
'Amanda.Sealy@cnn.com	'; 'Neel.Khairzada@turner.com'; 'Tia.Miller@	oturner.com'
CALL MACA LAA		The state of the state of the

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Dear Speakers:

I am the logistical contact for the COVID-19 session that will be held as part of the Annual Meeting (online) program on Saturday, April 25 at 2:00 pm EDT. Thank you for agreeing to participate in this session. To help you with your planning, I have provided additional details below.

Please note that the session will be live webcast and the general public will also be able to watch the session. Video from the session will also be uploaded on the NAS YouTube channel (https://www.youtube.com/user/theNASciences) after the meeting. We will need to obtain signed speaker release forms for your participation in this session. I have attached the speaker release form for your review and submission. Please return the signed speaker release form by Monday, April 13.

Session speakers are asked to connect 30 minutes prior to the session start time (by Saturday, April 25 at 1:30 pm EDT) to allow the technical staff to check connections and prepare for the session. Details on how to connect will be sent before the meeting.

We will list you in our promotional materials as noted below. If this is incorrect, please let me know.

Anthony S. Fauci, Director, National Institute of Allergy and Infectious Diseases
Jeremy Farrar, Director, Wellcome Trust
George F. Gao, Director-General, Chinese Center for Disease Control & Prevention
Sanjay Gupta, Chief Medical Correspondent, CNN
Richard J. Hatchett, CEO, Coalition for Epidemic Preparedness Innovations
Susan R. Weiss, Professor of Microbiology, Perelman School of Medicine, University of Pennsylvania

Since many of us have moved to remote work environments, you may already be proficient with Zoom and other online meeting/collaboration applications. I am attaching a 'speaker guidelines' file in case you have any questions on how best to prepare for and stage your remote talk. We have technical staff available to help you become familiar with Zoom and its settings — such as "sharing your screen" (if you have slide presentations that need to be shown during your talk). We can arrange for a training session this week or next week. If you would like to schedule a session, please let me know as soon as possible.

Dr. Dzau's office will be in touch regarding the agenda for this session. If you have any other questions, please let me know.

Regards, Jenny

Jenny Mun Membership Director National Academy of Sciences (b) (6)

From: Jeremy Farrar

Sent: Fri, 24 Apr 2020 16:55:47 +0000

To: SMITH, Ian Michael; 'Dzau Victor'; Chris. Elias; Fauci, Anthony (NIH/NIAID)

[E]; 'Fore Henrietta'; 'Gao Fu'; 'Gashumba Diane'; 'Kaag Sigrid'; Ilona Kickbusch; 'Suzuki Yasuhiro'; 'Vega Morales Jeanette'; 'Vega Morales Jeanette'; 'Veronika Skvortsova'; 'VijayRaghavan Krishnaswamy'

Cc: 'As Sy';Gro

Subject: Re: Statement from the GPMB Co-chairs on the Access to COVID-19 Tools

Accelerator

Thank you

From: "SMITH, Ian M	ichael"	(b) (6)			
Date: Friday, 24 April	2020 at 16:08	100			
To: Victor Dzau	(b) (6)	"Chris.Elias"		(b) (6);>, Je	remy
Farrar	(b) (6)	'Fauci Anthor	ny'	டு டு, 'Fore Henr	ietta'
			(b) (6) Diane Gashu	mba	(b) (6)
'Kaag Sigrid'	(b) (6), Ilona	Kickbusch		6) (6), 'Suzuki Yasuh	iro'
	(b) (6) 'V∈	ega Morales J	eanette'	(b)	6, 'Vega
Morales Jeanette		டுடு'Vero	nika Skvortsova'		(b) (6),
'VijayRaghavan Krishi	naswamy'		(b) (6)		
Cc: 'As Sy'	(b) (6., Gro	(b) (6)		
Subject: Statement for	om the GPMB	Co-chairs on	the Access to CO	VID-19 Tools Acceler	ator

Dear Board members,

Today, WHO and many partners launched the Access to COVID-19 Tools (ACT) Accelerator, a global collaboration mechanism to accelerate development, production and deployment of safe and effective technologies to prevent, diagnose and treat COVID-19. The GPMB co-Chairs have issued the attached statement welcoming the initiative.

We encourage you to circulate the attached statement through your channels and networks.

With kind regards,

lan

Ian Smith

(b) (6)

Desk: +41 22 7913979

Mobile/WhatsApp: (b) (6)

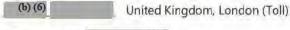
From: Teresa Miller de Vega on behalf of "Jeremy Farrar" (6) (6)

Sent: Wed, 22 Apr 2020 13:38:32 +0000

To: Collins, Francis (NIH/OD) [E]; Fauci, Anthony (NIH/NIAID) [E]; Dzau, Victor J.

Subject: CALL: T. Fauci, F. Collins, V. Dzau & J. Farrar

Join Microsoft Teams Meeting



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(b) (6) VTC Conference ID: (b) (6)

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From: Fauci, Anthony (NIH/NIAID) [E]
Sent: Wed, 8 Apr 2020 13:19:09 +0000

To: Jeremy Farrar Subject: RE: COVID

Jeremy:

Many thanks for your kind note. Much appreciated. Running on fumes, but still running. Hope to chat with you soon to catch up.

Warm regards,

Tony

Anthony S. Fauci, MD
Director
National Institute of Allergy and Infectious Diseases
Building 31, Room 7A-03
31 Center Drive, MSC 2520
National Institutes of Health
Bethesda, MD 20892-2520
Phone: (6) (6)
FAX: (301) 496-4409

E-mail: (b) (6)

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behalf of the NIAID by one of its representatives.

From: Jeremy Farrar (b) (6)

Sent: Tuesday, April 7, 2020 5:14 PM

To: Fauci, Anthony (NIH/NIAID) [E] (b) (6)

Subject: COVID

Tony

Hope you are OK

Thank you, again, for your remarkable leadership – best wishes Jeremy

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Fauci, Anthony (NIH/NIAID) [E] From: Sent: Thu, 26 Mar 2020 02:26:41 +0000

Jeremy Farrar To: RE: COVID19 Subject:

OK. Let us talk over the weekend.

From: Jeremy Farrar (b) (6)

Sent: Wednesday, March 25, 2020 4:32 PM

To: Fauci, Anthony (NIH/NIAID) [E] (b) (6)

Subject: Re: COVID19

Sorry Tony....

Cannot tonight I am afraid.

Weekends marginally few things on - if better for you!

My number is:

(b)(6)

Jeremy

From: "Fauci, Anthony (NIH/NIAID) [E]" (b) (6)

Date: Wednesday, 25 March 2020 at 13:15 (b) (6) To: Jeremy Farrar

Subject: RE: COVID19

Will call before 9:00 AM EST. I cannot find your cell phone number. Please send it to me by e-mail

Anthony S. Fauci, MD

Director

National Institute of Allergy and Infectious Diseases

Building 31, Room 7A-03 31 Center Drive, MSC 2520 National Institutes of Health Bethesda, MD 20892-2520 Phone: (30

FAX: (301) 496-4409

E-mail:

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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 (b) (6) Sent: Wednesday, March 25, 2020 8:23 AM

To: Fauci, Anthony (NIH/NIAID) [E] (b) (6)

Subject: COVID19

Tony

Good to hear you on these WHO calls.

And your leadership in USA!

If you have time for a 5 min update let me know – very best wishes Jeremy

Physically Distanced, socially connected

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.

Sent: Fri, 13 Mar 2020 21:27:36 +0000

To: Fauci, Anthony (NIH/NIAID) [E]; Victor Dzau

Subject: Washington

Tony

A privilege to know you and to observe and learn from your leadership, particularly over the last few weeks in the media and elsewhere.

I may be in Washington on Wednesday and Thursday next week, with a few meetings, seeing Victor etc – assuming still possible to fly UK-USA.

You are 24/7 I know, but if you had anytime, always great to see you.

Best wishes 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.

From: Sent:	Jeremy Farrar Fri, 6 Mar 2020 14:33:45 +0000		
Sent: To:	and the second s	is;'Esveld, Marja';'Gro Brundtla	and'.'As
Sy';'Dzau, Victor J.'		i, Anthony (NIH/NIAID) [E];'For	
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	van Krishnaswamy';'Skvortsova Vero		, vega iviolate
Cc:	'SCHWARTLANDER, Bernhard F.';'		X'.'Tore
Godal';'Godal, Tore'		/AN, Michael J.';'Kanarek,	0.7 1.51.5
Morgan'		tricia (NIH/NIAID)	
[E]		டு (6) (6); Sheila Austria	;William
	Vega; Marston, Hilary (NIH/NIAID) [E		10000000
7			
k.	(b)	(6) 'Zacharie Gahungu'; 'DSO'; 'C	GEV';'Gonggrijp
Mette'			(b) (6); (b) (6)
	Toomas Palu';Edwa	ard Whiting;Alice Jamieson	
Subject:	Re: URGENT - GPMB COVID-19 FU	JNDING NOTE	
	and the second second		
Agree, very positive a	nd appreciated		
7.4			
From:	A control of	(b) (6)	
Date: Friday, 6 Mar	ch 2020 at 14:13		
Chever's Westing at American			
To: Alex Harris		(b) (6)	
	, 'Gro Brundtland'	(b) (б) (b) (б) 'As Sy'	
			(ъ) (б
	, 'Gro Brundtland'	(b) (6) 'As Sy'	
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To: Alex Harris	, 'Gro Brundtland' (b)(6), Victor Dzau Farrar (b)(6), 'Fore Henrietta'	(ხ) (6) 'As Sy' (ხ) (6) , 'Gao Fu'	Anthony Fauc
To: Alex Harris	, 'Gro Brundtland' (b)(6), Victor Dzau Farrar (b)(6), 'Fore Henrietta' (b)(6), 'R'	ക്ര (As Sy' കര്, ',	Anthony Fauc (b) (6) (b) (6)
To : Alex Harris (Diane Gashumba	, 'Gro Brundtland' (b)(6), Victor Dzau Farrar (b)(6), 'Fore Henrietta' (b)(6), 'R'	(b) (6) 'As Sy' (b) (6), ', (b) (6)>, 'Gao Fu' (b) (6) 'Suzuki Yasuhiro'	Anthony Fau (b) (6) (b) (6)
To: Alex Harris (Diane Gashumba Morales Jeanette	, 'Gro Brundtland' (b) ⑥, Victor Dzau Farrar b) ⑥, 'Fore Henrietta' (b) ⑥, 'R' , '	(త్) (As Sy' (త్) (త్), ', (త్) (త్), 'Gao Fu' (త్) (త్)'Suzuki Yasuhiro' avan Krishnaswamy'	Anthony Fau (b) (6) (b) (6)
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To: Alex Harris (Diane Gashumba Morales Jeanette	, 'Gro Brundtland' (b)(6), Victor Dzau Farrar (b)(6), 'Fore Henrietta' (b)(6), 'R' , ' (b)(6)'VijayRagh (b)(6), 'Skvortsova Veronika'	(b) (6) 'As Sy' (b) (6), 'Gao Fu' (b) (6) 'Suzuki Yasuhiro' avan Krishnaswamy' (b) (6) (b) (6), 'Pate Muhamed'	Anthony Faud (b) (6) (b) (6) (b) (6)>, 'Veg
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To: Alex Harris (Diane Gashumba Morales Jeanette' Cc: Bernhard Schwa (b) (6)	, 'Gro Brundtland' (b) (6) , Victor Dzau Farrar (b) (6) , 'Fore Henrietta' (b) (6) , 'R' , ' (b) (6) 'VijayRagh (b) (6) , 'Skvortsova Veronika' ortländer (b) (6) , 'Amelie RIOUX' , '''Godal, Tore''	(b) (6) 'As Sy' (b) (6) , 'Gao Fu' (b) (6) 'Suzuki Yasuhiro' avan Krishnaswamy' (b) (6) (b) (6) 'Pate Muhamed' (b) (6) 'Tore Goda (b) (6) "'Kanare	Anthony Faud (b) (6) (b) (6) (b) (6)>, 'Veg (l) (b) (6) (c) (d) (d)
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'Zacharie Gahungu'	(b) (6), 'DSO'	®®, 'GEV'
(b) (6) "'Gonggr	ijp, Mette'"	(ь) (б)
		, Alice
Jamieson	(b) (6)	
Subject: AW: URGENT - GPM	B COVID-19 FUNDING NOTE	

Wonderful news Ilona

Von: Alex Harris		(b) (6)				
Gesendet: Freitag	, 6. März 2020 11:56					
An: Esveld, Marja		(b) (6); Gro Bru	undtland	_	(b) (6); A	As Sy
4	(b) (6) >; Dzau, Victor	J.	(b) (6)			(b) (6) Jeremy
Farrar	(b) (6); Anth	nony Fauci		(b) (6); For	e Henriett	a
(b) (6	;>; Gao Fu	(b) (6); Ga	shumba Dian	e	0	6) (6); R
(b) (6);	Ilona Kickbusch		டு டு Suzuki Y	asuhiro	(b) (6)	
		(b) (б);	Vega Morales	Jeanette		(b) (6)
VijayRaghavan Kri	shnaswamy	(b) (6)	Skvortsova V	eronika		(ъ) (б)
Cc: SCHWARTLAN	DER, Bernhard F.		(b) (6); Pate	Muhame	d	
	(b) (6); Amelie RIOU	X	(b) (6);	Tore Goda	d and	(b) (6);
Godal, Tore	AND THE PERSON NAMED IN		(b) (6)	; RYAN, M	lichael J.	-
(b) (d)	Nanarek, Morgan				100	(b) (6)
	0) (6);			(b) (6)	
	(b) (б) 'Sh	eila Austria'			(p) (6; William Hal
	(b) (6)>; Teresa Mille	er de Vega			(b) (6); ¹N	larston Hilary
<	(6) (6);	2000			(b) (6)	
	d	Zacharie Gahui	ngu		(ы) (б); DSO
(b) (6)	l>; GEV	(b) (6); Gonggrij	p, Mette			(b) (6)
						(b) (6)
		Toomas Palu		(b) (6)	Edward W	hiting
	(b) (6) Alice Jan	nieson		(b) (6)		
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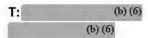
Betreff: RE: URGENT - GPMB COVID-19 FUNDING NOTE

Dear Marja,

This is very good news and we greatly appreciate Minister Kaag's flexibility and support on this. With very best wishes,

Alex

Alex Harris
Head of Global Policy & Advocacy
Wellcome



From: Esveld, Maria (b)(6)Sent: 06 March 2020 10:34 To: Alex Harris (b) (6) >; Gro Brundtland (b) (6); As SV (b) (6); Jeremy (b) (6) >; Dzau, Victor J. (b) (6) >; Anthony Fauci (b) (6) >; Fore Henrietta Farrar (b) (6); Gao Fu (b) (6) >; Gashumba Diane < (b) (6) R (b) (6); Ilona Kickbusch (b) (6) >; Suzuki Yasuhiro < (b) (6); Vega Morales Jeanette (b) (6) VijayRaghavan Krishnaswamy (b) (6); Skvortsova Veronika (b) (6) > Cc: SCHWARTLANDER, Bernhard F. (b) (6) Pate Muhamed (b) (6) Amelie RIOUX (b) (6); Tore Godal (b) (6) (b) (6); RYAN, Michael J. Godal, Tore (b) (6); Kanarek, Morgan (b) (6) (b) (6) 'Sheila Austria' (b) (6) >; William Hall (b) (6); 'Marston Hilary' (b) (6) Teresa Miller de Vega (b) (6) (b) (6); JPavlin@nas.edu; oaabdi@unicef.org; (b) (6) ; Zacharie Gahungu (b) (6) >; DSO (b) (6); GEV (b) (6) Gonggrijp, Mette (b) (6) Toomas Palu (b) (6) >; Edward Whiting (b) (6); Alice Jamieson (b) (6) Subject: RE: URGENT - GPMB COVID-19 FUNDING NOTE

Dear all, sorry to bother you again but after careful considerations internally, I am happy to confirm that our Minister is willing to sign the letter.

Although we remain concerned that a specific appeal for Covid response may jeopardize investments in other urgent and worldwide health threats, we do (ofcourse) see the point in raising awareness that more investments to address the current epidemic are needed. As long as we emphasize the importance of a health systems approach (ie non-vertical) to preparedness, and the importance to free up 'fresh' money for Covid R&D (preferably by strengthening generic R&D infrastructure for epidemic diseases etc), we can support the appeal.

Kind regards, Marja

From: Esveld, Marja

Sent: vrijdag 6 maart 2020 09:23

To: 'Alex Harris		(b) (6) Gro Bru	ındtland	(b) (6); As	Sy Sy
	(b) (6) >; Dzau, Vict	or	(b) (6);		(b) (6); Jeremy
Farrar	(b) (6); A	nthony Fauci	(b) (6)	; Fore Henriet	ta
17.5	(b) (6); Gao Fu	(b) (6); (Gashumba Diane		(b) (6); R
(b) (6)	>; Ilona Kickbusch		(b) (6) >; Suzuki Yasuh	iro < (b) (6)	
de la companya de la		(b) (6	; Vega Morales Jear	nette <	(b) (6)
VijayRaghavan	Krishnaswamy	(b)	6 Skvortsova Veron	ika	(b) (6) >
Cc: SCHWARTL	ANDER, Bernhard F.		(b) (6); Pate Muh	named	
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Godal, Tore	A STATE OF THE PARTY OF THE PAR		(b) (6) RYA	AN, Michael J.	
(I	6) (6); Kanarek, Morgan	0.00			(b) (6)
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	(b)(6);	Sheila Austria'		(b)	(6); William Hall
	(b) (6); Teresa M	iller de Vega		(b) (6); 'I	Marston Hilary'
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					(b) (6)
		Toomas Palu		(b) (6) Edward W	/hiting
ALC: NO THE REAL PROPERTY.	(b) (6) >; Alice J	amieson		(b) (6)	

Subject: RE: URGENT - GPMB COVID-19 FUNDING NOTE

Dear Alex and others,

Although it has not been possible yet to discuss the letter and note with our Minister, I would like to give you a 'heads up' that it is very unlikely that our Minister is willing to co-sign the letter. We are not in favor of disease specific appeals, knowing that resources for health worldwide are scarce. We certainly see the need for investments in R&D and other important – underserved – areas related to the current outbreak, but we are not convinced that this specific 'appeal' is the right way forward, as it may provoke competition with other major health issues such as HIV, TB and malaria. We see the multilateral system as the main vehicle for support to any emergency, and would prefer to support this work as 'unearmarked' as possible.

I will keep you updated, but as long as we do not have a clear signal that points into another direction, I would like to ask you to not to refer to Minister Kaag in the proposed letter.

Kind regards,

Marja

From: Alex Harris (b) (6)

Sent: donderdag 5 maart 2020 15:29

To: Gro Brundtland (b) (6) As Sy (b) (6); Dzau, Victor J. (b) (6); Jeremy Farrar (b) (6);

Anthony Fauci (b) (6) >; Fore Henrietta (b) (6) Gao Fu

b) (6) >;
(b) (6)
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on Hilary'
Esveld,
rijp, Mette
(b) (illian

Subject: URGENT - GPMB COVID-19 FUNDING NOTE

Importance: High

Dear Board Members,

Thank you for your input on the call yesterday regarding the COVID-19 funding request that the GPMB will be making to multilateral financing institutions and G7/G20 nations.

In this regard I attach:

- An updated letter
- An updated background note revising the ask to \$8bn as a result of removing the \$3.5bn we
 had previously included for strengthening country preparedness, given the World Bank
 announcement
- · A table setting out the key stakeholders we will be writing to and following up with

In the interests of speed, the letters will be sent from Jeremy (as the GPMB's Covid-19 spokesperson and on behalf of the Co-Chairs and the Board) as soon as possible. Please let us have any important feedback by the end of today.

We would also be grateful if you could please put your name against any stakeholders on the <u>list below</u> (and return to me) where you are well-placed to help arrange a follow up meeting through your contacts (I am aware that some of you have already begun to reach out, which is great). Together with Amelie we look forward to coordinating our joint outreach efforts.

With many thanks,

Alex

Alex Harris Head of Global Policy & Advocacy Wellcome

T:	(b) (6)
	(b) (6)

G7 leaders and Sherpas

Country	Rep	Sherpa (amendments welcome)	GPMB lead(s)
Canada	Justin Trudeau, Prime Minister	(b)	(6)
France	Emmanuel Macron, President		
Germany	Angela Merkel, Chancellor		Jeremy Farrar
Italy	Giuseppe Conte, Prime Minister		1
Japan	Shinzō Abe, Prime Minister		
United Kingdom	Boris Johnson, Prime Minister		Jeremy Farrar
United States	Donald Trump, President		Victor Dzau
Participants		-	
European Union	Charles Michel, President of the European Council		
European Union	Ursula von der Leyen, President of the European Commission		Victor Dzau Jeremy Farrar

International financial institutions

Institution	Leadership	Sherpa/equivalent or suggested contacts	GPMB lead
World Bank Group	WBG President, David Malpass	(b) (6)	Victor Dzau
IMF	MD, Kristalina Georgieva		As Sy
Asian Development Bank	President, Masatsugu Asakawa		
Inter-American Development Bank	President, Luis Alberto Moreno		
African Development	President,		

Bank	Akinwumi Adesina	(ь) (б)
European Bank for Reconstruction and Development	President, Sir Sumantra "Suma" Chakrabarti	
Asian Infrastructure Investment Bank	President Jin Liqun	Jeremy Farrar
Islamic Development Bank	President, Bandar Hajjar	

To: 'Amelie RIOUX'		(b) (6); Dzau,	Victor J.	(b) (6)	
	(b) (6); Je	remy Farrar		(b) (6); Anthor	ny Fauci
(b)	(6); Fore Henrie	etta	(b) (6); Gao Fu		(b) (6) >; Gashumba
Diane		(b) (б); Ilona k	Kickbusch	(b)	(6)>; Suzuki Yasuhiro
	(b) (6);		(b) (6) Vega	Morales Jeane	tte
(b) (6)	>; VijayRaghav	an Krishnaswam	ıy	(b) (6); Skv	ortsova Veronika
(b) (6)>				
Cc: Gro Brundtland		(b) (6) >; As Sy	a factor of	(b) (6) >; Elhadj	SY
(b) (6)>;	Tore Godal	(b) (6) >	; Godal, Tore <t< td=""><td>ore.Godal@fhi.</td><td>.no>;</td></t<>	ore.Godal@fhi.	.no>;
	(b) (6); S	CHWARTLANDE	R, Bernhard F.		(b) (6)>; RYAN,
Michael J.	(b) (6) >; Pate I	Muhamed	(b	(6); Kanarek, N	Morgan (b) (б)
175		en -			'Sheila
Austria'		(b) (б)>; Will	iam Hall		(b) (6) Teresa Miller
de Vega		(b) (6) 'Marsto	on Hilary'	(t	0) (6)>;
(b) (6) _V ;					(b) (6)



Subject: RE: GPMB: COVID-19 FUNDING NOTE

Dear Board Members,

Ahead of the GPMB Board call on Wednesday, I'm pleased to attach a note (on behalf of Jeremy Farrar, Victor Dzau and a small working group) setting out the urgent need for new funding for the global COVID-19 response.

You will have seen the strong announcement today from the World Bank of up to \$12bn to support country response, which we warmly welcome. We are asking for your feedback on the call and consideration for the GPMB to launch an 'ask' this week regarding needs not likely to be covered by the World Bank announcement – this would target the leaders and policy makers of other financing institutions and G7/G20 nations. The note will clearly need to be updated in light of the World Bank's commitment.

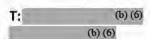
The aim of the note is to encourage an immediate and full response to the needs of the world, recognising that many countries are not well prepared and could be left behind. The \$11bn we are seeking will likely not be sufficient for all the needs over the next 12-18 months, but is based on reasonable estimates of what we know now and most urgently require funds for.

We look forward to the discussion.

With best wishes,

Alex

Alex Harris
Head of Global Policy & Advocacy
Wellcome



Help save paper! Do you really need to print this email?

Dit bericht kan informatie bevatten die niet voor u is bestemd. Indien u niet de geadresseerde bent of dit bericht abusievelijk aan u is toegezonden, wordt u verzocht dat aan de afzender te melden en het bericht te verwijderen. De Staat aanvaardt geen aansprakelijkheid voor schade, van welke aard ook, die verband houdt met risico's verbonden aan het elektronisch verzenden van berichten.

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Sent: Sun, 1 Mar 2020 14:37:48 +0000 **To:** Fauci, Anthony (NIH/NIAID) [E]

Subject: Phone call

Sorry just not possible Saturday.

I can phone you any time after 2pm EST if you have 10 mins!

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.

Sent: Wed, 26 Feb 2020 13:04:13 +0000

To: Barasch, Kimberly (NIH/NIAID) [C]; Teresa Miller de Vega; Fauci, Anthony

(NIH/NIAID) [E]

Subject: Re: Can I give you a ring today

Thanks Kim!

From: "Barasch, Kimberly (NIH/NIAID) [C]" (b) (6)

Date: Wednesday, 26 February 2020 at 13:03

To: Teresa de Vega (b) (6)

Cc: Jeremy Farrar (b) (6)

Subject: RE: Can I give you a ring today

Hi Teresa,

17:30 UK / 13:30 DC time on Thursday, 27 February will work well.

Thank you,

Kim

Kim Barasch [c]

Office of the Director

National Institute of Allergy & Infectious Diseases

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

From: Teresa Miller de Vega (6) (6)

Sent: Wednesday, February 26, 2020 7:59 AM

To: Barasch, Kimberly (NIH/NIAID) [C] (b) (6)

Cc: Jeremy Farrar (b) (6)

Subject: RE: Can I give you a ring today

Hi Kim,

Jeremy will be able to call Tony after 17:30 UK / 13:30 DC time.

I hope this works.

Thank you,

Teresa

From: Jeremy Farrar (b) (6)

Sent: 26 February 2020 12:55

To: Fauci, Anthony (NIH/NIAID) [E]	(b) (6); Teresa Miller de Vega
(b) (6) Cc: Conrad, Patricia (NIH/NIAID) [E] <c< th=""><th>(b) (6); Barasch, Kimberly (NIH/NIAID) [C]</th></c<>	(b) (6); Barasch, Kimberly (NIH/NIAID) [C]
(b) (6) Subject: Re: Can I give you a ring today	
Thanks Tony	
From: "Fauci, Anthony (NIH/NIAID) [E]]" (b) (6) >
Date: Wednesday, 26 February 2020 a	
To: Jeremy Farrar	(b) (6) >
Cc: "Conrad, Patricia (NIH/NIAID) [E]"	
(NIH/NIAID) [C]"	(b) (6)
Subject: RE: Can give you a ring toda	У
Thursday would be better. Any	time between 11:00 AM and 4:00 PM DC time.
	and Kim will pull me out of any meeting I am
	and this will pair the out of any meeting fair
in.	
Anthony S. Fauci, MD	
Director	Diameter Diameter
National Institute of Allergy and Infection Building 31, Room 7A-03	ous Diseases
31 Center Drive, MSC 2520	
National Institutes of Health	
Bethesda, MD 20892-2520	
Phone: ((b) (6) FAX: (301) 496-4409	
E-mail: (b) (6)	
information. It should not be used by a have received this e-mail in error pleas other storage devices. The National In-	of its attachments is confidential and may contain sensitive anyone who is not the original intended recipient. If you see inform the sender and delete it from your mailbox or any stitute of Allergy and Infectious Diseases (NIAID) shall not e that are the sender's own and not expressly made on sentatives.
From: Jeremy Farrar	(6) (6)
Sent: Wednesday, February 26, 2020 7:47	
To: Fauci, Anthony (NIH/NIAID) [E]	(b) (6)
Subject: Re: Can I give you a ring today	
I can much later at night (anytime up to n	nidnight UK time) here Tony if that helpsor Thursday also ok
if that is better for you?	
From: "Fauci, Anthony (NIH/NIAID) [E	(b) (6)

Date: Wednesday, 26 February 2020 at 12:45

	(b) (6)
Subject: RE: Can give you a	ng today
일반이 되면 어떻게 되었다. 이 아이를 하게 되었다.	the middle of a Congressional Hearing with Secretary Any possibility for 1:00 PM DC time?
Anthony S. Fauci, MD	
Director	
National Institute of Allergy a	Infectious Diseases
Building 31, Room 7A-03 31 Center Drive, MSC 2520	
National Institutes of Health	
Bethesda, MD 20892-2520 Phone: (b) (6)	
FAX: (301) 496-4409	
E-mail: (b) (6)	
information. It should not be have received this e-mail in e other storage devices. The N	nd any of its attachments is confidential and may contain sensitions by anyone who is not the original intended recipient. If you or please inform the sender and delete it from your mailbox or artional Institute of Allergy and Infectious Diseases (NIAID) shall not
accept liability for any statem behalf of the NIAID by one of	nts made that are the sender's own and not expressly made on representatives.
behalf of the NIAID by one of	(b) (6)
From: Jeremy Farrar Sent: Wednesday, February 26, To: Fauci, Anthony (NIH/NIAID)	(b) (6) 020 7:40 AM (b) (6)
From: Jeremy Farrar Sent: Wednesday, February 26, To: Fauci, Anthony (NIH/NIAID) Cc: Conrad, Patricia (NIH/NIAID)	(b) (6) 020 7:40 AM (b) (6)
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From: Jeremy Farrar Sent: Wednesday, February 26, To: Fauci, Anthony (NIH/NIAID) Cc: Conrad, Patricia (NIH/NIAID) (b) (6) Subject: Re: Can I give you a rin Thanks Tony as alwaysdoes s	(b) (6) 020 7:40 AM (c) (6) (d) (e) (f) (e) (f) (f) (f) (g) (f) (g)
From: "Fauci, Anthony (NIH/ Date: Wednesday, Anthony (NIH/ Date: Wednesday, February 26, To: Fauci, Anthony (NIH/NIAID) (b) (6) Subject: Re: Can I give you a rin Thanks Tony as alwaysdoes so	(b) (6) 020 7:40 AM (c) (b) (6) E (b) (6) >; Barasch, Kimberly (NIH/NIAID) [C] today mething like 9pm UK time (4pm EST) work for you? AID) [E]" (b) (6) (2020 at 12:39
From: "Fauci, Anthony (NIH/ Date: Wednesday, Anthony (NIH/ Tom: Research (NIH/NIAID) Co: Conrad, Patricia (NIH/NIAID) (b) (6) Subject: Re: Can I give you a rin Thanks Tony as alwaysdoes of	(b) (6) 020 7:40 AM (c) (b) (6) (d) (e) (f) (f) (h) (h) (h) (h) (h) (h) (h) (h) (h) (h
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From: "Fauci, Anthony (NIH/ Date: Wednesday, Anthony (NIH/ Tom: Research (NIH/NIAID) Co: Conrad, Patricia (NIH/NIAID) (b) (6) Subject: Re: Can I give you a rin Thanks Tony as alwaysdoes of	(b) (6) 020 7:40 AM (c) (b) (6) (d) (e) (e) (f) (f) (f) (f) (f) (f) (f) (f) (f) (f

Of course. I will be in and out of meetings, but call my office at

My staff will find me. If that does not work use my cell phone at

(b) (6)

(b) (6)

Anthony S. Fauci, MD
Director
National Institute of Allergy and Infectious Diseases
Building 31, Room 7A-03
31 Center Drive, MSC 2520
National Institutes of Health
Bethesda, MD 20892-2520
Phone:
(b) (6)
FAX: (301) 496-4409

E-mail: (b) (6) v

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From: Jeremy Farrar (b) (6)
Sent: Wednesday, February 26, 2020 7:36 AM

To: Fauci, Anthony (NIH/NIAID) [E] (b) (6)

Subject: Can | give you a ring today

Tony - Can I give you a ring anytime this evening UK time - can be late and fit in with you. 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.

Sent: Mon, 10 Feb 2020 09:26:57 +0000

To: M.P.G. Koopmans; Kristian G. Andersen; Drosten, Christian; Edward

Holmes; Andrew Rambaut (6) (6); R.A.M. Fouchier; (6) (6); Collins,

Francis (NIH/OD) [E]; Fauci, Anthony (NIH/NIAID) [E]; Josie Golding; Mike Ferguson

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 (b) (6) Date: Sunday, 9 February 2020 at 20:07 To: "Kristian G. Andersen" (b) (6), "Drosten, Christian" (b) (6), Edward Holmes (b) (6), Jeremy Farrar (b) (6), "a.rambaut@ed.ac.uk" (b) (6) (b) (6) (b) (6) (b) (6) , Francis Collins (b) (6) (b) (6), Mike Ferguson (b) (6) >, Josie Golding

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

(b) (6) > 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

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

Von: Jeremy Farrai	(b) (6)			
Datum: Samstag, 8	3. Februar 2020 um 21:21			
An: Edward Holme	s	(b) (6) >, Christian Drosten		
and the second	(b) (6) >			
Cc:		(b) (6) Andrew Rambaut		(b) (6)
		(b) (6)		
			(b) (6)	
	(b) (6), Josie Golding	(b) (6) _,		
		(b) (6) Mike Ferguson		
Street Street	(b) (6)			

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	(b) (6)		
Date: Saturday, 8 February 2020 at			
To: Christian Drosten	(b) (6)		
Cc: Jeremy Farrar	(b) (6)		(b) (6)
(b) (6)	Tennata Callina	(b) (6)	(b) (6)
(0)(0), 1	Francis Collins	4707.000	# N ##
A contract of the contract of	, Josie Goldi	ing	(b) (6),
Marion Koopmans	(b) (6) Mike F	erguson	
(b) (6)			

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 (b) (6)

E (b) (6)

On 9 Feb 2020, at 6:52 am, Drosten, Christian	(b) (6) 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

Chariteplatz 1 D-10117 Berlin Germany

E-Mall	(b) (6)
	1

Von: Jeremy Farrar	(b) (6)	
Datum: Samstag, 8. Februar 20	020 um 10:45	
An: Edward Holmes	(b) (6)	(b) (6)
, Andre	ew Rambaut	(6) (6)
Cc:		(b) (6)
		(6) (6)
	Josie Golding	(b) (6)
	>, CI	nristian Drosten

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.

From: Fauci, Anthony (NIH/NIAID) [E] Sent: Sat, 8 Feb 2020 17:36:34 +0000 Jeremy Farrar; Vallance, Patrick (GO-Science); Edward To: (b) (6) Holmes (b) (6); Andrew Cc: (b) (6)(1;Collins, Francis (NIH/OD) [E];Josie Golding: (b) (6); Mike Ferguson; Government Chief Scientific Adviser (GO-Science) Subject: RE: 2019 N-CoV

Would serial passage in an animal in the laboratory give the same result as prolonged adaptation in animals in the wild? Or is there something fundamentally different in what happens when you serially passage versus natural animal adaption? This is not my specific area of expertise and so I do not know.

From: Jeremy Farrar Sent: Saturday, February 8, 2020 10:13 AM To: Vallance, Patrick (GO-Science) (b) (6) Edward Holmes (b) (6) (b) (6); Andrew Rambaut (b)(6)(b) (6) Cc: (b) (6); Collins, Francis (NIH/OD) [E] (b) (6); Fauci, Anthony (NIH/NIAID) [E] (b) (6) Josie Golding (b) (6); (b) (6) Ferguson (b) (6) Government Chief Scientific Adviser (GO-Science)

Subject: Re: 2019 N-CoV

Bob - Andrew shared your thoughts on the glycans:

"I'd say the existence of the glycans is pretty strong evidence of evolution in the presence of an immune system. I don't think it is random chance since the glycans appear in other betacoronaviruses that "evolve" a furin site, eg MHV and HKU1. MHV and HKU1 also simultaneously evolve a variable and sometimes large patch of O-linked glycans at the top of the prefusion (virion) form of the spike. Seems pretty clear this is immune based selection all around to me.

Yes serial passage in animals would do the same thing. There are a couple passage of H5N1 in chicken papers - the furin site appears in steps."

From: "Vallance, Patrick (GO-	Science)"	(b) (6)		
Date: Saturday, 8 February 2020 at 12:03				
To: Jeremy Farrar	(b) (6), Edward Holmes			
	(b) (6)		(b) (6)	
0	200			(b) (6)
Cc: "	(b) (6) >, F	rancis Collins	3	

(b) (6), Josie Golding
(b) (6), Marion Koopmans
(b) (6)
(b) (6)
(b) (6)
(b) (6)
(d) Mike Ferguson
(e) (6) (GO-Science)"

<<u>GCSA@go-science.gov.uk</u>> Subject: RE: 2019 N-CoV

Jeremy

Thanks for sharing, and thanks to those involved for a really important piece of work. I think this looks pretty balanced and is useful. I do think it would be helpful to make sure that the sequence data from the pangolins is included and to indicate what that might mean in terms of a potential prolonged period of adaptation in animals. The glycan point is important and could be given further weight against an passage origin.

Once complete I think it would be helpful to publish this

Best wishes

Patrick

From: Jeremy Farrar < (b) (6)

Sent: 08 February 2020 09:46

To: Edward Holmes (b) (6) (b) (6); Andrew Rambaut

(b) (6)

Cc: (c); Vallance, Patrick (GO-Science) (b) (6)

(b) (6); Josie Golding (b) (6)

(b) (6); Mike Ferguson

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
 - o 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.

Sent: Fri, 7 Feb 2020 18:54:20 +0000

To: Collins, Francis (NIH/OD) [E]; Fauci, Anthony (NIH/NIAID) [E]

Cc: Tabak, Lawrence (NIH/OD) [E]

Subject: Re: Revised draft

I do not think so yet but ... chasing!

From: Francis Collins (b) (6)

Date: Friday, 7 February 2020 at 12:17

To: Jeremy Farrar (b) (6) >, "Fauci, Anthony (NIH/NIAID) [E]"

(b) (6)

Cc: "Tabak, Lawrence (NIH/OD) [E]" (b) (6)

Subject: RE: Revised draft

Has the actual sequence of the pangolin coronavirus isolate been released? That will be VERY interesting. Does it have the furin cleavage site?

Francis

From: Jeremy Farrar (b) (6)

Sent: Friday, February 7, 2020 1:21 AM

To: Collins, Francis (NIH/OD) [E] (b) (6); Fauci, Anthony (NIH/NIAID) [E]

(b) (6)

Subject: Re: Revised draft

Plus two updates

- Reports coming out overnight that Chinese group have pangolin viruses that are 99% similar. This would be a crucially important finding and if true could be the 'missing link' and explain a natural evolutionary link
- I have asked the Human Cell Atlas people to look at expression of the n-CoV in the nose/throat/respiratory tract/deep lunch tissue and if affected by age, smoking, pollution, gender, other.

Sent: Fri, 7 Feb 2020 15:05:56 +0000

To: Victor Dzau; Fauci, Anthony (NIH/NIAID) [E]; Vallance, Patrick (GO-Science)

Subject: Phone call

Victor

Let me know if a call on this would help, with either Tony, Patrick or I

https://abcnews.go.com/Politics/white-house-asks-scientists-investigate-origins-coronavirus/story?id=68807304

Tony (Francis), Patrick, myself and a close knit group have been looking at this for the last 10 days and might have some information to share which might help.

Best wishes 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.

Sent: Fri, 7 Feb 2020 06:09:31 +0000

To: Collins, Francis (NIH/OD) [E]; Fauci, Anthony (NIH/NIAID) [E]

Subject: Revised draft

Attachments: Summary.Feb7.pdf

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.

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 around the furin cleavage site.

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.

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.

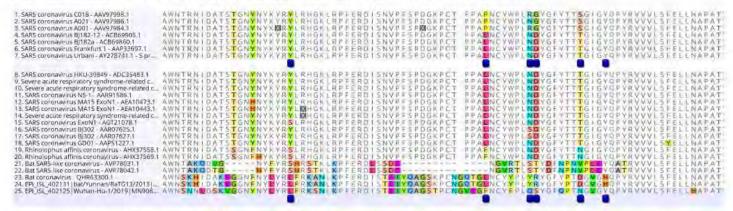


Figure 1 | Mutations in contact residues of the 2019-nCoV spike protein. The spike protein of 2019-nCoV (bottom) was aligned against the most closely related SARS and SARS-like CoVs. Key residues in the spike protein that make contact to the

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 (<u>RRAR</u>), 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.

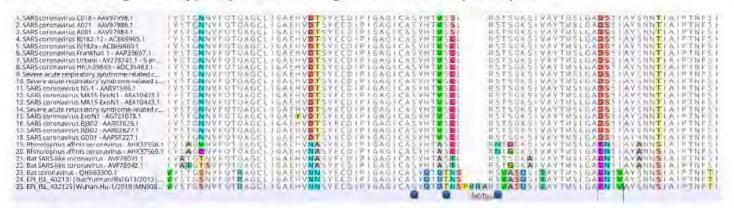


Figure 2 | Acquisition of furin cleavage site and O-linked glycans. The spike protein of 2019-nCoV (bottom) was aligned against the most closely related SARS and SARS-like CoVs. The furin cleavage site is marked in grey with the three adjacent predicted O-linked glycans in blue. Both the furin cleavage 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

Basic research involving passage of bat SARS-like coronaviruses in cell culture and/or animal models have been ongoing in BSL-2 for many years across the world, including in Wuhan (e.g., 12-15). It is possible that 2019-nCoV could have acquired the RBD mutations and furin cleavage site as part of passage in cell culture, which have been observed in previous studies with e.g., SARS-CoV⁴. However, it is less clear how the O-linked glycans - if functional - would have been acquired, as these typically suggest the involvement of an immune system, which is not present *in vitro*. In this scenario, it is also unclear how the virus would be linked to the fact that the epidemic seemed to 'take off' at a particular food market, although the exact role of this locality is currently uncertain.

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 a aspects of the initial emergence of 2019	guaranteed tha	t data	can be	obtained	to	conclusively	prove	all
aspects of the initial emergence of 2019	9-nCoV.							

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Progenitor of Severe Acute Respiratory Syndrome Coronavirus. J. Virol. 90, 3253–3256 (2015).

Sent: Thu, 6 Feb 2020 07:18:09 +0000

To: Fauci, Anthony (NIH/NIAID) [E]:Collins, Francis (NIH/OD) [E]

Cc: Josie Golding; Tabak, Lawrence (NIH/OD) [E]

Subject: Re: Prevalence of infection and stage of the epidemic in Wuhan

Perfect, thank you

From: "Fauci, Anthony (NIH/NIAID) [E]" <a (6) (6) >

Date: Wednesday, 5 February 2020 at 22:24

To: Jeremy Farrar (b) (6) Francis Collins (b) (6) Cc: Josie Golding (b) (6), "Tabak, Lawrence (NIH/OD) [E]"

(b) (6)

Subject: RE: Prevalence of infection and stage of the epidemic in Wuhan

Jeremy:

Thanks for the note. Looks like things are moving along with WHO. I will list below a number of names for potential members of the working group to examine the evolutionary origin of the 2019-nCoV in addition to the individuals who were on the call with us last Saturday:

Harold Varmus - Weill Cornell Medical Center - New York City

Feng Zhang – MIT (CRISPR expert)

Joseph DeRisi - Chan Zuckerberg (CZ) BioHub (he's paying close attention to the Wuhan strain vs other bat viruses and the SARS virus)

Don Ganem - University of California at San Francisco (UCSF) and the CZ BioHub (knows more about hepadnaviruses but an outstanding clinical and basic virologist)

John Coffin - Tufts and National Cancer Institute, NIH (worked out the confusion over the alleged Chronic Fatigue Syndrome retrovirus that proved to be a xenotropic MLV)

Eugene Koonin - NCBI/National Libreary of Medicine, NIH;

https://www.ncbi.nlm.nih.gov/research/groups/koonin/)

Wayne Hendrickson – Columbia University and the New York Structural Biology Center Gary Nabel – Sanofi (Boston)

Best regards,

Tony

Anthony S. Fauci, MD Director National Institute of Allergy and Infectious Diseases Building 31, Room 7A-03 31 Center Drive, MSC 2520 National Institutes of Health Bethesda, MD 20892-2520 Phone: (b) (6) FAX: (301) 496-4409

E-mail: (b) (6)

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From: Jeremy Farrar (b) (6)
Sent: Wednesday, February 5, 2020 6:21 AM

To: Fauci, Anthony (NIH/NIAID) [E] (b) (6)>; Collins, Francis (NIH/OD) [E]

(b) (6)

Cc: Josie Golding (b) (6)

Subject: Re: Prevalence of infection and stage of the epidemic in Wuhan

Francis and Tony

Couple of things:

- I spoke again with WHO this morning. I believe they have listened and acted. Let me know if you agree
 - At the WHO meeting next week they will set up the Group who will "look at the origins and evolution of 2019n-CoV"
 - o They have asked for names to sit on that Group please do send any names
 - We can have a call this week with a core group of that to frame the work of the Group including – if you could join?
 - O I think this puts it under the umbrella of WHO, with action this week and into next
 - With names to be put forward into the Group from us and pressure on this group from your and our teams next week.
- The team will update the draft today and I will forward immediately they will add further comments on the glycans

Does that sound reasonable to you?

Jeremy

From: "Fauci, Anthony (NIH/NIAID) [E]" (b) (6)

Date: Tuesday, 4 February 2020 at 13:18

To: Francis Collins (b) (6), Jeremy Farrar (b) (6)

Subject: RE: Prevalence of infection and stage of the epidemic in Wuhan

?? Serial passage in ACE2-transgenic mice

Anthony S. Fauci, MD
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National Institute of Allergy and Infectious Diseases
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From: Collins, Francis (NIH/OD) [E] (b) (6)
Sent: Tuesday, February 4, 2020 6:12 AM
To: Jeremy Farrar (b) (6)

Cc: Fauci, Anthony (NIH/NIAID) [E] (b) (6)

Subject: RE: Prevalence of infection and stage of the epidemic in Wuhan

Yes, I'd be interested in the proposal of accidental lab passage in animals (which ones?).

Francis

From: Jeremy Farrar (b) (6)

Sent: Tuesday, February 4, 2020 6:08 AM

To: Collins, Francis (NIH/OD) [E] (b) (6)

Cc: Fauci, Anthony (NIH/NIAID) [E] (b) (6)

Subject: Re: Prevalence of infection and stage of the epidemic in Wuhan

Being very careful in the morning wording

"Engineered" probably not.

Remains very real possibility of accidental lab passage in animals to give glycans. Will forward immediately or if you want to give Eddie a ring.

Eddie would be 60:40 lab side. I remain 50:50...

On 4 Feb 2020, at 10:58, Collins, Francis (NIH/OD) [E] (b) (6) wrote:

Very thoughtful analysis. I note that Eddie is now arguing against the idea that this is the product of intentional human engineering. But repeated tissue culture passage is still an option – though it doesn't explain the O-linked glycans.

Francis

From: Jeremy Farrar (b) (6)

Sent: Tuesday, February 4, 2020 2:01 AM

To: Fauci, Anthony (NIH/NIAID) [E] (b) (6); Collins, Francis (NIH/OD) [E]

Subject: FW: Prevalence of infection and stage of the epidemic in Wuhan

Please treat in confidence – a very rough first draft from Eddie and team – they will send on the edited, cleaner version later.

Pushing WHO again today

From: Edward Holmes (b) (6)

Date: Tuesday, 4 February 2020 at 06:33 **To:** Jeremy Farrar

(b) (6)

Subject: Re: Prevalence of infection and stage of the epidemic in Wuhan

Here's our summary so far. Will be edited further.

It's fundamental science and completely neutral as written. Did not mention other anomalies as this will make us look like loons. As it stands it is excellent basic science I think, which is a service in itself.

Will finish as soon as we can.

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 (b) (6)

Sent: Thu, 6 Feb 2020 07:17:40 +0000

To: Fauci, Anthony (NIH/NIAID) [E]; Collins, Francis (NIH/OD) [E]

Cc: Josie Golding; Tabak, Lawrence (NIH/OD) [E]

Subject: Re: Prevalence of infection and stage of the epidemic in Wuhan

Thank you. Pardis is great, respected by everyone – best wishes Jeremy

From: "Fauci, Anthony (NIH/NIAID) [E]" (b) (6)

Date: Thursday, 6 February 2020 at 00:00

To: Jeremy Farrar (b) (6), Francis Collins (b) (6)

Cc: Josie Golding (b) (6), "Tabak, Lawrence (NIH/OD) [E]"

Subject: RE: Prevalence of infection and stage of the epidemic in Wuhan

Jeremy:

I left out an important name for the coronavirus evolution working group. Please include her: Pardis Sabeti at the Broad Institute of MIT and Harvard Thanks,

Tony

Anthony S. Fauci, MD

Director

National Institute of Allergy and Infectious Diseases

Building 31, Room 7A-03 31 Center Drive, MSC 2520 National Institutes of Health Bethesda, MD 20892-2520 Phone: (b) (6) FAX: (301) 496-4409

E-mail: (b) (6)

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behalf of the NIAID by one of its representatives.

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

Sent: Wednesday, February 5, 2020 5:25 PM

To: Jeremy Farrar (b) (6) Collins, Francis (NIH/OD) [E] (b) (6) Cc: Josie Golding (b) (6) Tabak, Lawrence (NIH/OD) [E]

(b) (6)

Subject: RE: Prevalence of infection and stage of the epidemic in Wuhan

Jeremy:

Thanks for the note. Looks like things are moving along with WHO. I will list below a number of names for potential members of the working group to examine the evolutionary origin of the 2019-nCoV in addition to the individuals who were on the call with us last Saturday:

Harold Varmus - Weill Cornell Medical Center - New York City

Feng Zhang – MIT (CRISPR expert)

Joseph DeRisi - Chan Zuckerberg (CZ) BioHub (he's paying close attention to the Wuhan strain vs other bat viruses and the SARS virus)

Don Ganem - University of California at San Francisco (UCSF) and the CZ BioHub (knows more about hepadnaviruses but an outstanding clinical and basic virologist)

John Coffin - Tufts and National Cancer Institute, NIH (worked out the confusion over the alleged Chronic Fatigue Syndrome retrovirus that proved to be a xenotropic MLV)

Eugene Koonin - NCBI/National Libreary of Medicine, NIH;

https://www.ncbi.nlm.nih.gov/research/groups/koonin/)

Wayne Hendrickson – Columbia University and the New York Structural Biology Center Gary Nabel – Sanofi (Boston)

Best regards, Tony

E-mail:

Anthony S. Fauci, MD
Director
National Institute of Allergy and Infectious Diseases
Building 31, Room 7A-03
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From: Jeremy Farrar (b) (6)

Sent: Wednesday, February 5, 2020 6:21 AM

To: Fauci, Anthony (NIH/NIAID) [E] (b) (6); Collins, Francis (NIH/OD) [E]

(b) (6)

Cc: Josie Golding (b) (6)

Subject: Re: Prevalence of infection and stage of the epidemic in Wuhan

Francis and Tony

Couple of things:

- . I spoke again with WHO this morning. I believe they have listened and acted. Let me know if you agree
 - o At the WHO meeting next week they will set up the Group who will "look at the origins and evolution of 2019n-CoV"
 - They have asked for names to sit on that Group please do send any names
 - O We can have a call this week with a core group of that to frame the work of the Group including - if you could join?
 - o I think this puts it under the umbrella of WHO, with action this week and into next
 - With names to be put forward into the Group from us and pressure on this group from your and our teams next week.
- The team will update the draft today and I will forward immediately they will add further comments on the glycans

Does that sound reasonable to you?

Jeremy

(b) (6) From: "Fauci, Anthony (NIH/NIAID) [E]"

Date: Tuesday, 4 February 2020 at 13:18

To: Francis Collins (b) (6), Jeremy Farrar (b) (6)

Subject: RE: Prevalence of infection and stage of the epidemic in Wuhan

?? Serial passage in ACE2-transgenic mice

Anthony S. Fauci, MD Director National Institute of Allergy and Infectious Diseases Building 31, Room 7A-03 31 Center Drive, MSC 2520 National Institutes of Health Bethesda, MD 20892-2520 Phone: (b) (6)

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From: Collins, Francis (NIH/OD) [E] (b) (6) Sent: Tuesday, February 4, 2020 6:12 AM (b) (6) > To: Jeremy Farrar Cc: Fauci, Anthony (NIH/NIAID) [E] (b) (6) Subject: RE: Prevalence of infection and stage of the epidemic in Wuhan Yes, I'd be interested in the proposal of accidental lab passage in animals (which ones?). Francis (b) (6) > From: Jeremy Farrar Sent: Tuesday, February 4, 2020 6:08 AM (b) (6) To: Collins, Francis (NIH/OD) [E] Cc: Fauci, Anthony (NIH/NIAID) [E] (b) (6) Subject: Re: Prevalence of infection and stage of the epidemic in Wuhan Being very careful in the morning wording "Engineered" probably not. Remains very real possibility of accidental lab passage in animals to give glycans. Will forward immediately or if you want to give Eddie a ring. Eddie would be 60:40 lab side. I remain 50:50... On 4 Feb 2020, at 10:58, Collins, Francis (NIH/OD) [E] < (b) (6) > wrote: Very thoughtful analysis. I note that Eddie is now arguing against the idea that this is the product of intentional human engineering. But repeated tissue culture passage is still an option - though it doesn't explain the O-linked glycans. Francis From: Jeremy Farrar (b) (6) Sent: Tuesday, February 4, 2020 2:01 AM To: Fauci, Anthony (NIH/NIAID) [E] < (b) (6) >; Collins, Francis (NIH/OD) [E] (b) (6) > Subject: FW: Prevalence of infection and stage of the epidemic in Wuhan Please treat in confidence - a very rough first draft from Eddie and team - they will send on the edited, cleaner version later.

Pushing WHO again today

From: Edward Holmes (b) (6)

Date: Tuesday, 4 February 2020 at 06:33

To: Jeremy Farrar (b) (6)

Subject: Re: Prevalence of infection and stage of the epidemic in Wuhan

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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 (b) (6)

Sent: Wed, 5 Feb 2020 06:57:54 +0000

To: Collins, Francis (NIH/OD) [E];Fauci, Anthony (NIH/NIAID) [E];Edward Holmes

Subject: FW: Origins
Attachments: Summary.pdf

Tony and Francis

The revised draft from Eddie, copied here.

I asked Eddie about the addition of the glycans and where these could be added accidentally by passage in lab animals or of course in the wild – the reply from Bob and Kristian

?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 presense 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 <u>excellent</u> 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..?

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. As rumours have been circulating about this virus being engineered or otherwise created with intent, we wish to make it clear that our analyses show that such scenarios are largely incompatible with the data.

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 around the furin cleavage site.

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 closely related viruses, including 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.

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.

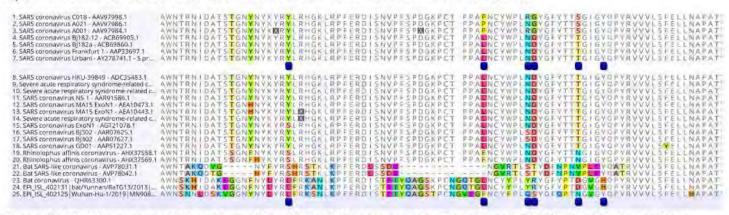


Figure 1 | Mutations in contact residues of the 2019-nCoV spike protein. The spike protein of 2019-nCoV (bottom) was aligned against the most closely related SARS and SARS-like CoVs. Key residues in the spike protein that make contact to the ACE2 receptor have been marked with blue boxes in both 2019-nCoV 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 (<u>RRAR</u>), 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.

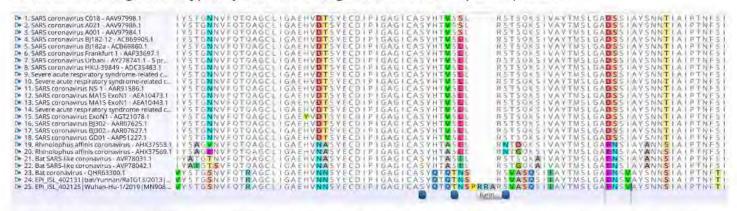


Figure 2 | Acquisition of furin cleavage site and O-linked glycans. The spike protein of 2019-nCoV (bottom) was aligned against the most closely related SARS and SARS-like CoVs. The furin cleavage site is marked in grey with the three adjacent predicted O-linked glycans in blue. Both the furin cleavage 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.

Evolution of 2019-nCoV

As described in the beginning, we believe deliberate engineering can be ruled out with a high degree of confidence as the data is inconsistent with this scenario. In addition, if engineering would have been performed, one would also 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, including those recently posited by various conspiracy theories, based on a 2015 paper in *Nature Medicine*¹⁰.

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.

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

Basic research involving passage of bat SARS-like coronaviruses in cell culture and/or animal models have been ongoing in BSL-2 for many years across the world, including in Wuhan (e.g., 11-14). It is possible that 2019-nCoV could have acquired the RBD mutations and furin cleavage site as part of passage in cell culture, which have been observed in previous studies with e.g., SARS-CoV⁴. However, it is less clear how the O-linked glycans - if functional - would have been acquired, as these typically suggest the involvement of an immune system, which is not present *in vitro*. In this scenario, it is also unclear how the virus would be linked to the fact that the epidemic seemed to 'take off' at a particular food market, although the exact role of this locality is currently uncertain.

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

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- 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.
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- 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).
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- 12. 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).
- 13. Zeng, L.-P. *et al.* Bat Severe Acute Respiratory Syndrome-Like Coronavirus WIV1 Encodes an Extra Accessory Protein, ORFX, Involved in Modulation of the Host Immune Response. *J. Virol.* **90**, 6573–6582 (2016).
- 14. 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).

Sent: Tue, 4 Feb 2020 20:53:09 +0000

To: Collins, Francis (NIH/OD) [E]; Fauci, Anthony (NIH/NIAID) [E]

Subject: Origins

Attachments: Summary.pdf

Tidied up

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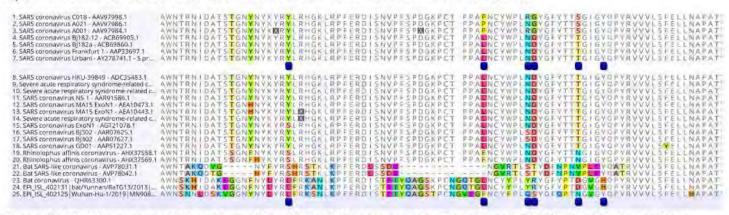


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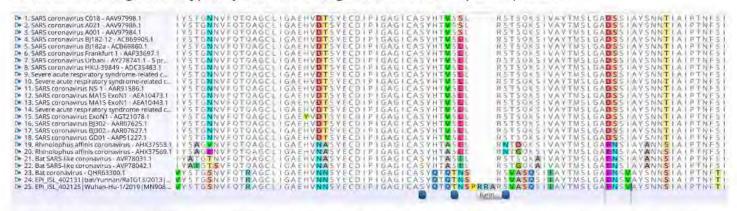


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Three main scenarios could explain how 2019-nCoV acquired the features discussed above: (1) natural selection in humans, (2) natural selection in an animal host, or (3) selection during passage.

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.

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

Basic research involving passage of bat SARS-like coronaviruses in cell culture and/or animal models have been ongoing in BSL-2 for many years across the world, including in Wuhan (e.g., 11-14). It is possible that 2019-nCoV could have acquired the RBD mutations and furin cleavage site as part of passage in cell culture, which have been observed in previous studies with e.g., SARS-CoV⁴. However, it is less clear how the O-linked glycans - if functional - would have been acquired, as these typically suggest the involvement of an immune system, which is not present *in vitro*. In this scenario, it is also unclear how the virus would be linked to the fact that the epidemic seemed to 'take off' at a particular food market, although the exact role of this locality is currently uncertain.

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.
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- 13. Zeng, L.-P. *et al.* Bat Severe Acute Respiratory Syndrome-Like Coronavirus WIV1 Encodes an Extra Accessory Protein, ORFX, Involved in Modulation of the Host Immune Response. *J. Virol.* **90**, 6573–6582 (2016).
- 14. 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).

Sent: Tue, 4 Feb 2020 20:26:23 +0000

To: Collins, Francis (NIH/OD) [E]; Fauci, Anthony (NIH/NIAID) [E]

Subject: Re: Prevalence of infection and stage of the epidemic in Wuhan

Wild West.....

From: Francis Collins (b) (6)

Date: Tuesday, 4 February 2020 at 20:23

To: Jeremy Farrar (b) (6), "Fauci, Anthony (NIH/NIAID) [E]"

(b) (6)

Subject: RE: Prevalence of infection and stage of the epidemic in Wuhan

Surely that wouldn't be done in a BSL-2 lab?

From: Jeremy Farrar (b) (6)

Sent: Tuesday, February 4, 2020 9:03 AM

To: Fauci, Anthony (NIH/NIAID) [E] < (b) (6) Collins, Francis (NIH/OD) [E]

(b) (6)

Subject: Re: Prevalence of infection and stage of the epidemic in Wuhan

Exactly!

From: "Fauci, Anthony (NIH/NIAID) [E]" (b) (6) >

Date: Tuesday, 4 February 2020 at 13:18

To: Francis Collins (b) (6), Jeremy Farrar (b) (6)

Subject: RE: Prevalence of infection and stage of the epidemic in Wuhan

?? Serial passage in ACE2-transgenic mice

Anthony S. Fauci, MD

Director

National Institute of Allergy and Infectious Diseases

Building 31, Room 7A-03
31 Center Drive, MSC 2520
National Institutes of Health
Bethesda, MD 20892-2520
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From: Collins, Francis (NIH/OD) [E] (b) (6) Sent: Tuesday, February 4, 2020 6:12 AM (b) (6) To: Jeremy Farrar Cc: Fauci, Anthony (NIH/NIAID) [E] (b) (6) Subject: RE: Prevalence of infection and stage of the epidemic in Wuhan Yes, I'd be interested in the proposal of accidental lab passage in animals (which ones?). Francis From: Jeremy Farrar (b) (6) Sent: Tuesday, February 4, 2020 6:08 AM To: Collins, Francis (NIH/OD) [E] (b) (6) (b) (6) Cc: Fauci, Anthony (NIH/NIAID) [E] Subject: Re: Prevalence of infection and stage of the epidemic in Wuhan Being very careful in the morning wording "Engineered" probably not. Remains very real possibility of accidental lab passage in animals to give glycans. Will forward immediately or if you want to give Eddie a ring. Eddie would be 60:40 lab side. I remain 50:50... On 4 Feb 2020, at 10:58, Collins, Francis (NIH/OD) [E] (b) (6) wrote: Very thoughtful analysis. I note that Eddie is now arguing against the idea that this is the product of intentional human engineering. But repeated tissue culture passage is still an option - though it doesn't explain the O-linked glycans. Francis From: Jeremy Farrar (b) (6) Sent: Tuesday, February 4, 2020 2:01 AM To: Fauci, Anthony (NIH/NIAID) [E] (b) (6) >; Collins, Francis (NIH/OD) [E] (b) (6) Subject: FW: Prevalence of infection and stage of the epidemic in Wuhan

Please treat in confidence - a very rough first draft from Eddie and team - they will send on the edited,

Pushing WHO again today

cleaner version later.

From: Edward Holmes (b) (6)

Date: Tuesday, 4 February 2020 at 06:33

To: Jeremy Farrar (b) (6)

Subject: Re: Prevalence of infection and stage of the epidemic in Wuhan

Here's our summary so far. Will be edited further.

It's fundamental science and completely neutral as written. Did not mention other anomalies as this will make us look like loons. As it stands it is excellent basic science I think, which is a service in itself.

Will finish as soon as we can.

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 (b) (6)

Fauci, Anthony (NIH/NIAID) [E] From: Sent: Tue, 4 Feb 2020 11:23:44 +0000 Collins, Francis (NIH/OD) [E]; Jeremy Farrar To: Subject: RE: Prevalence of infection and stage of the epidemic in Wuhan Agree. Very thoughtful summary and analysis. We really need to get WHO moving on getting the convening started. From: Collins, Francis (NIH/OD) [E] (b) (6) Sent: Tuesday, February 4, 2020 6:12 AM To: Jeremy Farrar < J. Farrar@wellcome.ac.uk> (b) (6) Cc: Fauci, Anthony (NIH/NIAID) [E] Subject: RE: Prevalence of infection and stage of the epidemic in Wuhan Yes, I'd be interested in the proposal of accidental lab passage in animals (which ones?). Francis From: Jeremy Farrar (b) (6) Sent: Tuesday, February 4, 2020 6:08 AM To: Collins, Francis (NIH/OD) [E] (b)(6)Cc: Fauci, Anthony (NIH/NIAID) [E] (b) (6) Subject: Re: Prevalence of infection and stage of the epidemic in Wuhan Being very careful in the morning wording "Engineered" probably not. Remains very real possibility of accidental lab passage in animals to give glycans. Will forward immediately or if you want to give Eddie a ring. Eddie would be 60:40 lab side. I remain 50:50... On 4 Feb 2020, at 10:58, Collins, Francis (NIH/OD) [E] (b) (6) wrote: Very thoughtful analysis. I note that Eddie is now arguing against the idea that this is the product of intentional human engineering. But repeated tissue culture passage is still an option - though it doesn't explain the O-linked glycans.

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Francis

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Sent: Tue, 4 Feb 2020 07:01:16 +0000

To: Fauci, Anthony (NIH/NIAID) [E];Collins, Francis (NIH/OD) [E]

Subject: FW: Prevalence of infection and stage of the epidemic in Wuhan

Attachments: Summary.docx

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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 (b) (6)

E (b) (6)

Overview

Sequencing of 2019-nCoV revealed two particularly notable features of its genome. We investigate these features and outline some examples for how the virus may have acquired them. As rumours have been circulating about this virus being engineered or otherwise created with intent, we wish to make it clear that our analyses show that such scenarios are largely incompatible with the data.

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 an optimal 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 O-linked glycans around the furin cleavage site.

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 closely related viruses, including RaTG13 (**Figure 1**). Based on modeling¹ and early biochemical experiments².³, 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 often associated with SARS-like viruses, including rodents, civets, and bats¹.

A phenylalanine at F486 in 2019-nCoV corresponds to L472 in the SARS-CoV Ubani strain. In tissue 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 binding⁵. 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.

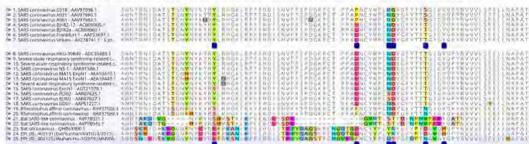


Figure 1 | Mutations in contact residues of the 2019-nCoV spike protein. The spike protein of 2019-nCoV (bottom) was

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.

Acquisition of furin cleavage site and O-linked glycans

An interesting feature of 2019-nCoV is the acquisition of a predicted furin cleavage site in the spike protein (**Figure 2**). In addition to the furin cleavage site (<u>RRAR</u>), a leading P is also inserted so the fully inserted sequence becomes PRRA (**Figure 2**). The addition of a proline in this position is also predicted to create three O-linked glycans at S673, T678, and S686. The addition of 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.

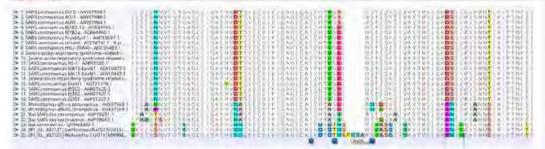


Figure 2 | Acquisition of furin cleavage site and O-linked glycans. The spike protein of 2019-nCoV (bottom) was aligned against the most closely related SARS and SARS-like CoVs. The furin cleavage site is marked in grey with the three adjacent predicted O-linked glycans in blue. Both the furin cleavage 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 virus⁷⁻⁹. The acquisition of furin cleavage sites have also been observed after repeated passage of betacoronaviruses in tissue culture (personal correspondence and NASEM call, February 3, 2020).

A potential function of the three 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.

Evolution of 2019-nCoV

Three main scenarios could explain how 2019-nCoV acquired the features discussed above: (1) natural selection in an animal host, (2) selection during passage, or (3) deliberate engineering. As described in the beginning, engineering (#3) can be ruled out with a high degree of confidence as the data is inconsistent with this scenario. In addition, if engineering would have been performed, one would also 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, including those recently posited by various conspiracy theories, based on a 2015 paper in *Nature Medicine*¹⁰.

The other two scenarios are largely indistinguishable and current data are consistent with both. It is currently impossible to prove or disprove either, and it is unclear whether future data or analyses will help resolve this issue.

Commented [1]: Is this comment correct? Something Bob said.

Selection in an animal host

Given the similarity of 2019-nCoV to bat SARS-like CoVs, particularly RaTG13, it is highly likely that bats also serve as the reservoir for this virus. However, previous human epidemics caused by betacoronaviruses have involved intermediate (possibly amplifying) hosts such as civets (SARS) and camels (MERS). It is therefore likely that an intermediate host would also exist for 2019-nCoV, although it is currently 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.

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Background:

Bat coronavirus RaTG13 is the closest relative to nCoV-2019. Two recombinant bat viruses are close in some regions of the genomes. Pangolin virus?

Furin cleavage site rough notes about evolutionary origins:

Avian influenza example of natural and spontaneous evolution - get references and details.

There are two scenarios by which we could imagine the furin cleavage site could evolve.

- As a human adaptation during the initial stages of the outbreak. The appearance of the mutation may have then triggered a second phase of rapid transmission. All current genome sequences are from this second phase and thus show limited diversity.
- 2. Adaptation to a non-human host prior to the jump to humans. This mutation is not seen in any bat coronavirus and is thus unlikely to be adaptive in those species.

Thoughts on 1: is it likely to spontaneously appear in a relatively short amount of time (and presumably small number of infections). It didn't happen in SARS with 8000 infections over 6 months. The link to the market would then be spurious - some doubt on that already. Prediction would be that the animal/environmental samples apparently found by China CDC would not have cleavage site.

Thoughts on 2: can we suggest a host where this cleavage site would likely be advantageous. Ferrets/polecats? Rodents - bamboo rats (don't know if they are popular in China)? Circulating in wild populations so limited prior human exposure until infected individual brought to the market.

- 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.
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- 14. Yang, X.-L. et al. Isolation and Characterization of a Novel Bat Coronavirus Closely Related to the



Sent: Sun, 2 Feb 2020 17:47:36 +0000

To: Michael RYAN;Bernhard Schwartländer;Collins, Francis (NIH/OD) [E];Fauci,

Anthony (NIH/NIAID) [E];Dr Tedros **Subject:** 2019nC-V

Mike and Bernhard

Thank you for phoning – very helpful, copying in Francis and Tony as well as Tedros.

Fully agree with your summary.

- Best is if this is addressed under the umbrella of WHO
- Has to be framed as 'To understand the source and evolution of the 2019n-CoV"
 - Within that a number of issues to be addressed including Environmental and animal sampling, human viral genome sequencing and analysis, and more
- Quickest is via a Working Group within an established structure rather than set something new up
- Multiple options for this within WHO
- Mike and Bernhard will work out best approach
- Appreciate the urgency and importance of this issue in midst of a very troubling epidemic
- Gathering interest evident in the science literature and in mainstream and social media to the question of the origin of this virus
- Critical that responsible, respected scientists and agencies get ahead of the science and the narrative of this and are not reacting to reports which could be very damaging.
- I am sure I speak for Francis and Tony when I say we are here and ready to play any constructive role in this
- Do think this is an urgent matter to address (among many we appreciate)
- Fully agree to your comments on the GCM.

Hope that is a reasonable summary

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.

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Sent: Sun, 2 Feb 2020 16:28:29 +0000

To: Fauci, Anthony (NIH/NIAID) [E]; Collins, Francis (NIH/OD) [E]

Cc: Tabak, Lawrence (NIH/OD) [E]

Subject: Re: Teleconference

Tedros and Bernhard have apparently gone into conclave....they need to decide today in my view. If they do prevaricate, I would appreciate a call with you later tonight or tomorrow to think how we might take forward.

Meanwhile....

https://www.zerohedge.com/geopolitical/coronavirus-contains-hiv-insertions-stoking-fears-over-artificially-created-bioweapon

From: "Fauci, Anthony (NIH/NIAID) [E]" (b) (6)

Date: Sunday, 2 February 2020 at 15:30

To: Jeremy Farrar (b) (6) Francis Collins (b) (6)

Cc: "Tabak, Lawrence (NIH/OD) [E]" (6) (6)

Subject: RE: Teleconference

Jeremy:

Sorry that I took so long to weigh in on your e-mails with Francis and me. I was on conference calls. I agree that we really cannot take Ron's suggestion about waiting. Like all of us, I do not know how this evolved, but given the concerns of so many people and the threat of further distortions on social media, it is essential that we move quickly. Hopefully, we can get WHO to convene.

Best regards,

Tony

From: Jeremy Farrar (b) (6)

Sent: Sunday, February 2, 2020 7:13 AM

To: Collins, Francis (NIH/OD) [E] (b) (6)

Cc: Fauci, Anthony (NIH/NIAID) [E] (b) (6) Tabak, Lawrence (NIH/OD) [E]

(b) (6)

Subject: Re: Teleconference

....Really appreciate us thinking through the options.....if Wellcome – I would need 110% support from you all.....it will not be easy!

From: Francis Collins (b) (6)

Date: Sunday, 2 February 2020 at 12:03

To: Jeremy Farrar (b) (6)

Cc: "Fauci, Anthony (NIH/NIAID) [E]" (b) (6), "Tabak, Lawrence (NIH/OD) [E]"

Subject: RE: Teleconference

Hi Jeremy,

Thanks for forwarding these additional reflections from Mike and Bob. I hadn't given much consideration to the idea of lab-based evolution by tissue-culture passage, but that is worth including on the list of options. Waiting a month sounds like a really bad idea. If that's the response from WHO, then another plan will be needed. Would Wellcome be willing to be the host then?

Francis

From: Jeremy Farrar (b) (6)

Sent: Sunday, February 2, 2020 6:53 AM

To: Collins, Francis (NIH/OD) [E] (b) (6)

Cc: Fauci, Anthony (NIH/NIAID) [E] (b) (6) Tabak, Lawrence (NIH/OD) [E]

Subject: Re: Teleconference

Thank you

See thoughts overnight from others.

On a spectrum if 0 is nature and 100 is release – I am honestly at 50! My guess is that this will remain grey, unless there is access to the Wuhan lab – and I suspect that is unlikely!

But grey, from a respected group, under the umbrella of let us say WHO, would in itself help!

A question for you – if WHO say, well maybe, let us think, we might do it in a month. What would be our next step?

Jeremy

From Mike Farzan (discoverer of SARS receptor):

1. The RBD didn't look 'engineered' to him - as in, no human would have selected the individual mutations and cloned them into the RBD (I think we all agree)

- 2. Tissue culture passage can often lead to gain of basic sites including furin cleavage sites (this is stuff they have seen with human coronaviruses)
- 3. He is bothered by the furin site and has a hard time explaining that as an event outside the lab (though, there are possible ways in nature, but highly unlikely)
- 4. Instead of directed engineering, changes in the RBD and acquisition of furin site would be highly compatible with the idea of continued passage of virus in tissue culture
- 5. Acquisition of furin site would likely destabilize the virus, but would make it disseminate to new tissues

So given above, a likely explanation could be something as simple as passaging SARS-like CoVs in tissue culture on human cell lines (under BSL-2) for an extended period time, accidentally creating a virus that would be primed for rapid transmission between humans via gain of furin site (from tissue culture) and adaptation to human ACE2 receptor via repeated passage.

All of this brings it back to a simple conversation about how this virus might have gained a furin site (but with a stretch and series of coincidences you can find a way to explain others - although very odd all together) and there are ways in which that could occur both in nature and in the lab. Nothing seems to specifically suggest whether this virus was most likely to be "adapted", "evolved", or maybe even "engineered". So I think it becomes a question of how do you put all this together, whether you believe in this series of coincidences, what you know of the lab in Wuhan, how much could be in nature accidental release or natural event? I am 70:30 or 60:40.

From Bob

Before I left the office for the ball I aligned nCoV with the 96% bat CoV sequenced at WIV. Except for the RBD the S proteins are essentially identical at the amino acid level - well all but the perfect insertion of 12 nucleotides that adds the furin site. S2 is over its whole length essentially identical. I really can't think of a plausible natural scenario where you get from the bat virus or one very similar to it to nCoV where you insert exactly 4 amino acids 12 nucleotide that all have to be added at the exact same time to gain this function- that and you don't change any other amino acid in S2? I just can't figure out how this gets accomplished in nature. Do the alignment of the spikes at the amino acid level - it's stunning. Of course in the lab it would be easy to generate the perfect 12 base insert that you wanted. Another scenario is that the progenitor of nCoV was a bat virus with the perfect furin cleavage site generated over evolutionary time. In this scenario RaTG13 the wiv virus was generated by a perfect deletion of 12 nucleotides while essentially not changing any other S2 amino acid. Even more implausible imo.

That is the big if.

You were doing gain of function research you would NOT use an existing clone of sars or mersy. These viruses are already human pathogens. What you would do is clone a bat virus they had not yet emerged. Maybe then pass it in human cells for a while to lock in the rbs, then you recloned and put in the mutations you are interested - one of the first a polybasic cleavage site.

From: Francis Collins	(b) (6)	
Date: Sunday, 2 February 2020 at 10:2	.7	
To: Jeremy Farrar	(b) (6)	
Cc: "Fauci, Anthony (NIH/NIAID) [E]"		6) 6) "Tabak, Lawrence (NIH/OD) [E]"
(b) (6)		
Subject: DE: Teleconference		

Jeremy,

Though the arguments from Ron Fouchier and Christian Drosten are presented with more forcefulness than necessary, I am coming around to the view that a natural origin is more likely. But I share your view that a swift convening of experts in a confidence-inspiring framework (WHO seems really the only option) is needed, or the voices of conspiracy will quickly dominate, doing great potential harm to science and international harmony.

I'm available any time today except 3:15 - 5:45 pm EST (on a plane) for a call to Tedros. Let me know if I can help get through his thicket of protectors.

Francis

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(b) (6)
From: Jeremy Farrar
Sent: Sunday, February 2, 2020 4:48 AM
                                           (b) (6)
To: Andrew Rambaut
                                              (b) (6); Fauci, Anthony (NIH/NIAID) [E]
Cc: R.A.M. Fouchier
                  (b) (6) >; Patrick Vallance
                                                                           (b) (6) Drosten, Christian
                           (b) (6) >; M.P.G. Koopmans
                                                                                    (b) (6) Eddie Holmes
                                                        (b) (6) Kristian G. Andersen
Paul Schreier
                                                               (b) (6); Ferguson, Mike
                              (b) (6) Collins, Francis (NIH/OD) [E]
                                                                                    (b) (6); Tabak, Lawrence
                                     (b) (6); Josie Golding
                                                                                    (b) (6)
(NIH/OD) [E]
Subject: Re: Teleconference
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This is a very complex issue.

I will:

- Be in contact with WHO today. I contacted them last night and will speak with them today and set up a broader call with them as soon as possible.
- As discussed on the phone this discussion is not limited to those on this email, it is happening
 wider in the scientific, social and main stream media.
- I believe the best way forward is for a body like the WHO has to ask or commission a group of scientists from around the world to ask the neutral question "To understand the evolutionary origins of 2019-nCoV, important for this epidemic and for future risk assessment and understanding of animal/human coronaviruses".
- That should be done in an open way and quite quickly so that the world can see it is being done,
 it can respect the report when it is available and I think that will help with the growing interest
 of this question.

I suggest we don't get into a further scientific discussion here, but wait for that group to be established.

Jeremy

From:	1000 1000 1000	(b) (6)		
Date: Sunday, 2 Fe	ebruary 2020 at 09:38			
To: Jeremy Farrar	(b) (6)			
Cc:		(b) (6)	'Fauci, Antho	ony (NIH/NIAID) [E]"
The same of the sa	(b) (6), Patrick Vallance		(b) (6	, "Drosten,
Christian"	(b) (6), M	arion Koopmans	1	(b) (6)
Edward Holmes			(b) (б	5)
	(b) (6), "Kristian G. Anderser	1"	(b) (6), Pa	aul Schreier
Time .			(b)	(6) Michael FMedSci
	(b) (6) Francis Colli	ns	(b) (6) _,	
L		(b) (6) Josie (Golding	
4 - 1 14 - 17	A land			

<<u>J.Golding@wellcome.ac.uk</u>>

Subject: Re: Teleconference

Dear Jeremey, Ron and all,

Thanks for inviting me on the call yesterday. I am also agnostic on this - I do not have any experience of laboratory virology and don't know what it is likely or not in that context. From a (natural) evolutionary point of view the only thing here that strikes me as unusual is the furin cleavage site. It strongly suggests to me that we are missing something important in the origin of this virus. My inclination would be that it is a missing host species in which this feature arose because it was selected for in that host. We can see this insertion has resulted in an extremely fit virus in humans - we can also deduce that it is not optimal for transmission in bat species.

The alternative is that it arose early in the human outbreak, perhaps during a longer period of hidden transmission and then the current epidemic is the result of this mutation but this seems less likely to me (it didn't happen in SARS for example).

Perhaps this needs to be discussed urgently, not only because of the lurid claims on Twitter but because if it is in a non-human host, pre-adapted, it may threaten control efforts through new zoonotic jumps (although perhaps we are beyond this point now).

The biggest hindrance at the moment (for this and more generally) is the lack of data and information. There have been no genome sequences from Wuhan for cases more recent than the beginning of January and reports, but no information, about virus from non-human animals in Wuhan. If the evolutionary origins of the epidemic were to be discussed, I think the only people with sufficient information or access to samples to address it would be the teams working in Wuhan.

Best, Andrew

On 2 Feb 2020, at 08:40, Jeremy Farrar (6) (6) wrote:

Thanks Ron

My view is completely neutral on this. The evolutionary origins on this virus are clearly important.

I do know these questions are being asked by politicians, starting in the scientific literature, certainly on social and main stream media. If, and I stress if, this does spread further, pressure and tensions rise, j fear these questions will get louder and more polarised and people will start to look who to blame. We live in a polarised world where there is a quick reaction to try and deflect issues by blaming someone somewhere. That may only increase tension and reduce cooperation.

A respected body convening a group now to consider the evolutionary origins of this, with an open mind, neutral, and in a transparent way is I think an approach that may prevent wild claims being made.

Such a group needs the best minds, from around the world, not just US-Europe-Australia. It needs to be transparent and respected.

I am not sure your thoughts on "short time frame". I am concerned if this is not done quite quickly it will be reacting to what may be lurid claims.

Thoughts on that very welcome.

On 2 Feb 2020, at 08:30, R.A.M. Fouchier

(b) (6) wrote

Dear Jeremy and others,

This was a very useful teleconference. Given the evidence presented and the discussions around it, I would conclude that a follow-up discussion on the possible origin of 2019-nCoV would be of much interest. However, I doubt if it needs to be done on very short term, given the importance of other activities of the scientific community, WHO and other stakeholders at present. It is my opinion that a non-natural origin of 2019-nCoV is highly unlikely at present. Any conspiracy theory can be approached with factual information. I have written down some of the counter-arguments. It is a bit long (below) but wanted to share it with you anyway.

Thanks for organizing this on such short notice, Kind regards Ron

Ron's notes:

An accusation that nCoV-2019 might have been engineered and released into the environment by humans (accidental or intentional) would need to be supported by strong data, beyond reasonable doubt. It is good that this possibility was discussed in detail with a team of experts. However, further debate about such accusations would unnecessarily distract top researchers from their active duties and do unnecessary harm to science in general and science in China in particular. At present, the arguments that nCoV-2019 could have emerged from an animal source is much stronger than other possibilities.

Observations about the genome that were inferred to be suggestive for a non-animal origin:

- 1. HIV-like sequences in the spike protein.
- Level of mutations in the spike protein region.

- 3. Presence of a furin cleavage site in the middle of spike
- 4. BamH1 restriction site at the end of the spike sequence
- 5. An F-to-Y substitution in the receptor-binding domain of spike
- 6. Potential O-linked glycan sites protecting the cleavage site of spike
- The biorxiv publication by Prashant Pradhan and colleagues from Delhi ("Uncanny similarity of unique inserts in the 2019-nCoV spike protein to HIV-1 gp120 and Gag") has already been heavily debated on biorxiv and <u>virological.org</u>. The similarity between the inserts in 2019-nCoV spike and sequences of HIV-1 is accidental. These are very short insert sequences that are highly similar to many Genbank entries. Such similarities are explained by pure chance alone.
- 2. Andrew Rambaut analyzed the level of mutations in the spike region of SARS-CoV with that of its closest bat virus relative and of 2019-nCoV and its closest bat virus relative. The level of mutations between the two pairs of viruses was in the same range. Thus, this level of mutations can arise under circumstances of natural emergence.
- 3. Bat coronaviruses generally do not have a furin cleavage site in the spike protein. Some human coronaviruses do have a furin cleavage site in spike, which must have evolved naturally. As animal reservoir and spill-over hosts are highly under-sampled, the presence of a furin cleavage site in spike in such species is unknown. When coronaviruses jump host barriers, this frequently involved adaptation of cleavage sites that may be targeted by various proteases. Given the presence of furin-like sites in human coronavirus and the mutation of protease cleavage sites upon coronavirus host-jumps in general, a natural origin of the furin site is certainly not impossible.
- 4. The BamHI restriction endonuclease site evolved due to a single (silent) nucleotide substitution as compared to the closest relative bat virus genome sequence. Restriction sites of 6 nucleotides can be found in every sequence, all over the genome, when 1 of the 6 positions is allowed to vary. We now find BamHI, next time it might be one of the plethora of other 6-nucleotide sequence motifs. This can be explained by pure chance.
- 5. The F-Y substitution in the spike receptor binding domain was observed in mouse-adapted SARS-CoV and in 2019-nCoV. It is generally absent in bat coronaviruses. This substitution is associated with host adaptation in mice. It may point to (natural) host adaption of 2019-nCoV (in mice, humans or unknown hosts) as well. It is possible that scientists would like to test the effect of F-Y because it was found in a mouse adaptation experiment. However, the logical way to test it would be in the original (SARS-CoV) virus backbone. There is no other reason to insert the F-Y substitution in an engineered virus.
- 6. It is unclear if the potential O-linked glycosylation sites 1) are used during glycosylation; 2) have a functional role for the spike protein; 3) were present in the ancestral virus from the original host. This is not an argument in the discussion on the origin of 2019-nCoV.

Additional arguments:

- A. All focus is on spike. Spike is a highly variable protein in general, crucial for host adaptation and under strong natural selection.
- B. The virus backbone (beyond spike) is not an indicator of a human source of 2019-nCoV emergence. The virus itself has not been described or characterized previously and no reverse genetics system has been described for this virus. Any scientist wanting to investigate spike function (e.g. to study protease cleavage or the receptor-binding domain) would have used a well-characterized reverse genetics system that is already available (making accidental labescape unlikely). Anyone with malicious intend would have used a well-characterized virulent strain (SARS-CoV, MERS-CoV) described and characterized (by others) in the literature.

- C. The patterns of mutations we observe in the receptor-binding domain and the protease cleavage sites of spike are typical for host-switched naturally evolving viruses. We can infer it for the naturally evolved human coronaviruses, we have seen it for the natural zoonoses of SARS-CoV and MERS-CoV. Convergent (parallel) evolutionary events are common in virology. Also for influenza, we see the same mutations emerge during the pandemics of 1918 (H1N1), 1957 (H2N2) and 1968 (H3N2), in the 2013 zoonotic H7N9 virus and e.g. an epizootic in seals in 2014 (H10N7). Regardless of the divergent subtype, we see identical substitutions in the receptor-binding domains, identical substitutions in polymerase, and non-identical substitutions with identical phenotypic consequences (e.g. stability) in the genome. The fact that we (think we) see recognizable traits in spike does not mean it must be man-made.
- D. We do not know the source of 2019-nCoV. There is "~30 years of evolutionary gap" between 2019-nCoV and the closest bat virus relative. These 30 years may have been in any host. We have no idea what might have happened (in evolutionary sense) between BatCov/RaTG13 and 2019-nCoV. We should rest our case until we have a close relative of 2019-nCoV.

Van: Jeremy Farrar	(b) (6) >			
Datum: zaterdag 1 februari 2	020 om 21:59			
Aan: "Fauci, Anthony (NIH/NI	AID) [E]"	⊛ @ Patrick Val	lance	
	(b) (6)			
CC: Christian Drosten	(b) (c), "M. Koopmans"		
(b)	(6), "R.A.M. Fouchier" <	r.fouchier@erasmusr	nc.nl>, Edward	
Holmes		The second second	(b)	(6)
Andrew Rambaut	டு டு, "Kristian (3. Andersen"	(b) (6)	, Paul
Schreier			(b) (6)	
"Ferguson, Mike"	(b) (6)	rancis Collins	(b) (6) >,	0-
	Ф	6 Josie Golding		
(b) (6)				
Onderwern: Re: Teleconferer	nce			

Thank you to everyone for joining.

There is clearly much to understand understand in this. This call was very helpful to hear some of our current understanding and the many gaps in our knowledge. I do not believe this is a question of a binary outcome, it is more a question of "What are the evolutionary origins of 2019-nCoV, important for future risk assessment and understanding of animal/human coronaviruses".

I do know there are papers being prepared, there will media interest and there is already chat on Twitter/WeChat.

We on this call are not the only ones with scientific expertise in this area and this was an ad hoc group that came together to air some thoughts. It is clearly not the sole group to take this forward, that will need a broader range of imput and a respected international body to ask an expert group to explore this, with a completely open mind. In order to stay ahead of the conspiracy theories and social media I do think there is an urgency for a body to convene such a group and commission some work to – (draft)

"To understand the evolutionary origins of 2019-nCoV, important for this epidemic and for future risk assessment and understanding of animal/human coronaviruses".

In other words a completely open minded and neutral question bringing in the best minds, and under the umbrella of a respected international agency

I hope that is a reasonable approach, please send any thoughts or suggestions.

Once again, thank you for making time over a weekend and for such an informed discussion on a complex issue.

Thank you and best wishes Jeremy

From: Jeremy Farrar	(b) (6)		
Date: Saturday, 1 February 2020 at 15:34			
To: "Fauci, Anthony (NIH/NIAID) [E]"		(b) (6), Patrick Vallance	
(b) (6)			
Cc: "Drosten, Christian"		(b) (6) Marion Koopmans	
		(ъ) (б	0)
Edward Holmes		(b) (6)	
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(b) (6), Paul Schreier		(b)	(6)
<rfgarry@tulane.edu>, Michael FMedSci</rfgarry@tulane.edu>		(b) (6)	_
Subject: Teleconference			

1st February (2nd Feb for Eddie)

Information and discussion is shared in total confidence and not to be shared until agreement on next steps.

Dial in details attached.

Please mute phones.

I will be on email throughout – email Paul or I Paul if any problems If you cannot make it, I will phone you afterwards to update.

One Hour

6am Sydney 8pm CET 7pm GMT 2pm EST 11am PST (Hope I have the times right!)

Thank you for the series of calls and for agreeing to join this call.

Agenda

- · Introduction, focus and desired outcomes JF
- Summary KA
- Comments EH
- · Q&A All
- Summary and next steps JF

Kristian Anderson

Bob Garry - I have not been able to contact Bob. Please forward if you can.

Christian Drosten

Tony Fauci

Mike Ferguson

Ron Fouchier

Eddie Holmes

Marion Koopmans

Stefan Pohlmann

Andrew Rambaut

Paul Schreier

Patrick Vallance

Andrew Rambaut

Institute for Evolutionary Biology

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

contact - (b) (6) http://tree.bin.ed.ac.uk (b) (6)

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Sent:	Sat, 1 Feb 2020 22:06:		
To:	Jeremy Farrar; Collins,	Francis (NIH/OD) [E]	
Subject:	RE: Teleconference		
Thanks, Jeremy.	We really appreciate who	at you are doing here.	Pleasure to work with you.
Best,			
Tony			
From: Jeremy Farr		(6)	
	bruary 1, 2020 4:00 PM		
To: Collins, Francis		(b) (6)	
Cc: Fauci, Anthony		(b) (6)	
Subject: Re: Telec	onterence		
We are altogether great working with		is with you and Tony, an	d Patrick and others – always
From: Francis Co	ollins (6) (6 1 February 2020 at 20:50	5)	
To: Jeremy Farra		b) (6)	
	ony (NIH/NIAID) [E]"	(b) (6)	
Subject: Re: Tele		.,,,,	
- 205 4 - 124 Mar 1 0 - 205	22000323033		
Hi Jeremy,			
	available at any time 24/7 for		ust let me know.
marginal days and area are	adership on this critical and	sensitive issue.	
Francis			
Sent from my iPho	one		
0+ 0 0 0 expr	/		N.A.
On Feb 1, 2020, at	3:07 PM, Jeremy Farrar	(b) (6)	wrote:
I have rejoined so	a line is open if any help to r	rejoin.	
From: Jeremy Fa	rrar	(b) (6)	
Date: Saturday, 1	1 February 2020 at 19:56		
To: "Fauci, Antho	ony (NIH/NIAID) [E]"	(b) (6), Fr	ancis Collins
100000000000000000000000000000000000000	(b) (6) Michael FMedSci		(b) (6), Patrick Vallance
	(b) (6)		2.1.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2
Subject: Re: Tele	conference		

Fauci, Anthony (NIH/NIAID) [E]

From:

Can I suggest we shut down the call and then redial in?

Just for 5-10mins?

From: Marion Koopmans	(b) (6	0	
Date: Saturday, 1 February 2020 at 19	:43	•	
To: Jeremy Farrar	(b) (6)		
Cc: "Fauci, Anthony (NIH/NIAID) [E]"		(b) (6), Patrick Vallance	
(b) (6) , "Dr	osten, Christian"		(b) (6)
	(b) (6	, Edward Holmes	
			(b) (6)
Autoria de la compansión de la compansió	(b) (б) "Kristiar	G. Andersen"	(b) (б)
Paul Schreier	100000	DOMESTIC OF THE PARTY OF THE PA	(b) (6)
Michael FMedSci	(b) (6) Franc	cis Collins	(b) (6)
Subject: Re: Teleconference			

Re the pangolin sequence: there are sections of the genome that have higher homology, and there is suggestion of recombinant history. And how much of the observation could be explained by having the wrong comparator?

Finally, we see in coronaviruses very similar functional domains in highly dissimilar core structures

On 1 Feb 2020, at 19:12, Jeremy Farrar (b) (6) wrote:

Kristen and Eddie have shared this and will talk through it on the call. Thank you.

Hope it will help frame the discussions.

From: Jeremy Farrar (b) (6)

Date: Saturday, 1 February 2020 at 15:34

1st February (2nd Feb for Eddie)

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Dial in details attached.

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Tony Fauci

Mike Ferguson

Ron Fouchier

Eddie Holmes

Marion Koopmans

Stefan Pohlmann

Andrew Rambaut

Paul Schreier

Patrick Vallance

<Coronavirus sequence comparison[1].pdf>

From: Jeremy Farrar Sent: Sat, 1 Feb 2020 20:13:15 +0000 Collins, Francis (NIH/OD) [E]; Fauci, Anthony (NIH/NIAID) [E]; Ferguson, To: Mike; Patrick Vallance Subject: Re: Teleconference sure From: Francis Collins Date: Saturday, 1 February 2020 at 20:12 To: Jeremy Farrar (b) (6), "Fauci, Anthony (NIH/NIAID) [E]" (b) (6), Patrick Vallance (b) (6), Michael FMedSci (b) (6) > Subject: RE: Teleconference Just saw this, still want me to call in? From: Jeremy Farrar (b) (6) Sent: Saturday, February 1, 2020 2:56 PM To: Fauci, Anthony (NIH/NIAID) [E] (b) (6) Collins, Francis (NIH/OD) [E] (b) (6) >; Ferguson, Mike (b) (6) Patrick Vallance (b) (6) Subject: Re: Teleconference Can I suggest we shut down the call and then redial in? Just for 5-10mins? From: Marion Koopmans (b) (6) Date: Saturday, 1 February 2020 at 19:43 (b) (6) To: Jeremy Farrar

To: Jeremy Farrar (b) (6)

Cc: "Fauci, Anthony (NIH/NIAID) [E]" (b) (6) >, Patrick Vallance (b) (6),

(b) (6) Edward Holmes (b) (6)

(b) (6) "Kristian G. Andersen" (b) (6),

Paul Schreier (b) (6)

Michael FMedSci (b) (6), Francis Collins (b) (6)

Subject: Re: Teleconference

Re the pangolin sequence: there are sections of the genome that have higher homology, and there is suggestion of recombinant history. And how much of the observation could be explained by having the wrong comparator?

Finally, we see in coronaviruses very similar functional domains in highly dissimilar core structures

On 1 Feb 2020, at 19:12, Jeremy Farrar (b) (6) wrote:

Kristen and Eddie have shared this and will talk through it on the call. Thank you.

Hope it will help frame the discussions.

From: Jeremy Farrar (6) (6)

Date: Saturday, 1 February 2020 at 15:34

1st February (2nd Feb for Eddie)

Information and discussion is shared in total confidence and not to be shared until agreement on next steps.

Dial in details attached.

Please mute phones.

I will be on email throughout – email Paul or I Paul if any problems

If you cannot make it, I will phone you afterwards to update.

One Hour

6am Sydney 8pm CET 7pm GMT 2pm EST 11am PST (Hope I have the times right!)

Thank you for the series of calls and for agreeing to join this call.

Agenda

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- Summary KA
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- Q&A All
- Summary and next steps JF

Kristian Anderson

Bob Garry - I have not been able to contact Bob. Please forward if you can.

Christian Drosten

Tony Fauci

Mike Ferguson

Ron Fouchier

Eddie Holmes

Marion Koopmans

Stefan Pohlmann

Andrew Rambaut

Paul Schreier

Patrick Vallance

<Coronavirus sequence comparison[1].pdf>

From: Fauci, Anthony (NIH/NIAID) [E]
Sent: Sat, 1 Feb 2020 20:03:12 +0000

To: Jeremy Farrar
Subject: RE: Teleconference

Yes

From: Jeremy Farrar (b) (6)

Sent: Saturday, February 1, 2020 2:56 PM

To: Fauci, Anthony (NIH/NIAID) [E] (b) (6) Collins, Francis (NIH/OD) [E] (b) (6) Ferguson, Mike (b) (6) Patrick Vallance (b) (6)

Subject: Re: Teleconference

Can I suggest we shut down the call and then redial in?

Just for 5-10mins?

(b) (6) From: Marion Koopmans Date: Saturday, 1 February 2020 at 19:43 (b) (6) To: Jeremy Farrar Cc: "Fauci, Anthony (NIH/NIAID) [E]" (b) (6) Patrick Vallance (b) (6) "Drosten, Christian" (b) (6) (b) (6) Edward Holmes (b) (6) (b) (6) "Kristian G. Andersen" Paul Schreier (b) (6) Michael FMedSci (b) (6), Francis Collins

Subject: Re: Teleconference

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Mike Ferguson
Ron Fouchier
Eddie Holmes
Marion Koopmans
Stefan Pohlmann
Andrew Rambaut
Paul Schreier
Patrick Vallance

<Coronavirus sequence comparison[1].pdf>

From: Jeremy Farrar

Sent: Sat, 1 Feb 2020 19:09:05 +0000

To: Fauci, Anthony (NIH/NIAID) [E];Patrick Vallance

Cc: Drosten, Christian; Marion Koopmans; R.A.M. Fouchier; Edward

Holmes (b) (6)u;Andrew Rambaut;Kristian G. Andersen;Paul

Schreier (b) (6); Ferguson, Mike; Collins, Francis (NIH/OD) [E]; Tabak, Lawrence (NIH/OD)

[E];Josie Golding

Subject: Re: Teleconference

If any issues come up, please email me and I will try and adjust or try and help.

From: Jeremy Farrar (b) (6)

Date: Saturday, 1 February 2020 at 15:34

To: "Fauci, Anthony (NIH/NIAID) [E]" (b) (6) Patrick Vallance (b) (6)

Cc: "Drosten, Christian" (b) (6), Marion Koopmans (b) (6)

Edward Holmes (b) (6)

(b) (6) "Kristian G. Andersen" (b) (6) Michael FMedSci (b) (6)

Subject: Teleconference

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Tony Fauci

Mike Ferguson

Ron Fouchier

Eddie Holmes

Marion Koopmans

Stefan Pohlmann

Andrew Rambaut

Paul Schreier

Patrick Vallance

From: Jeremy Farrar

Sent: Sat, 1 Feb 2020 18:12:57 +0000

To: Fauci, Anthony (NIH/NIAID) [E]; Patrick Vallance

Cc: Drosten, Christian; Marion Koopmans; R.A.M. Fouchier; Edward

Holmes; (b) (6) u;Andrew Rambaut;Kristian G. Andersen;Paul Schreier (b) (6) ;Ferguson, Mike;Collins, Francis (NIH/OD) [E]

Subject: Re: Teleconference

Attachments: Coronavirus sequence comparison[1].pdf

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Hope it will help frame the discussions.

From: Jeremy Farrar (b) (6)

Date: Saturday, 1 February 2020 at 15:34

1st February (2nd Feb for Eddie)

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Mike Ferguson

Ron Fouchier

Eddie Holmes

Marion Koopmans

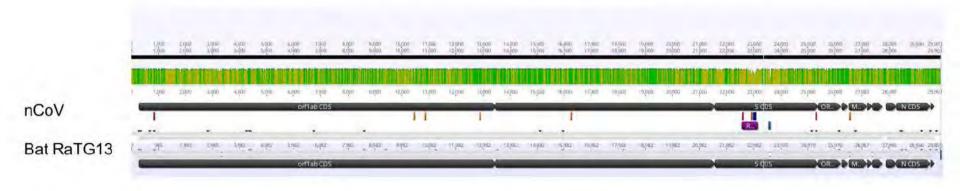
Stefan Pohlmann

Andrew Rambaut

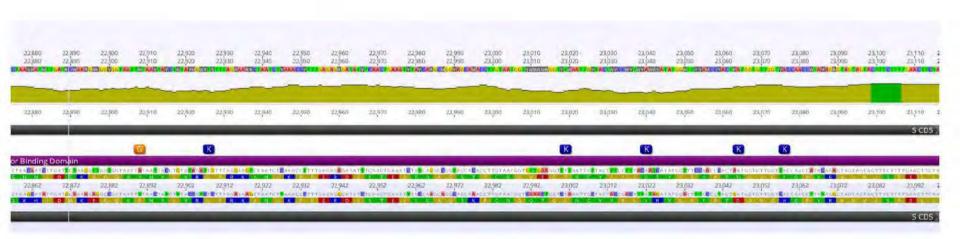
Paul Schreier

Patrick Vallance

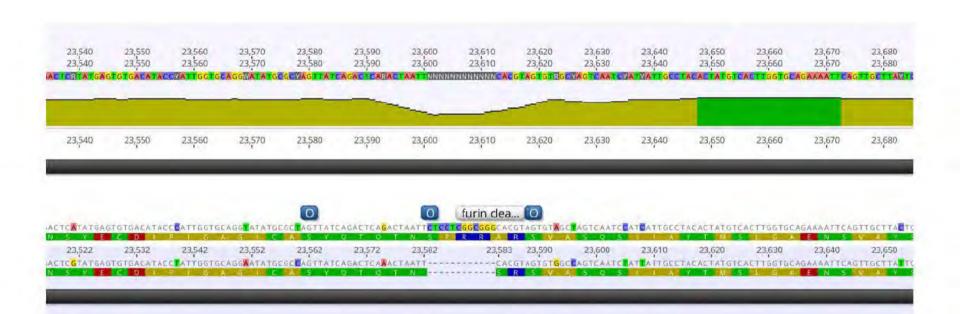
Main comparison is between 2019-nCoV (top) and bat SARS-like coronavirus RaTG13 (96% identical; bottom)



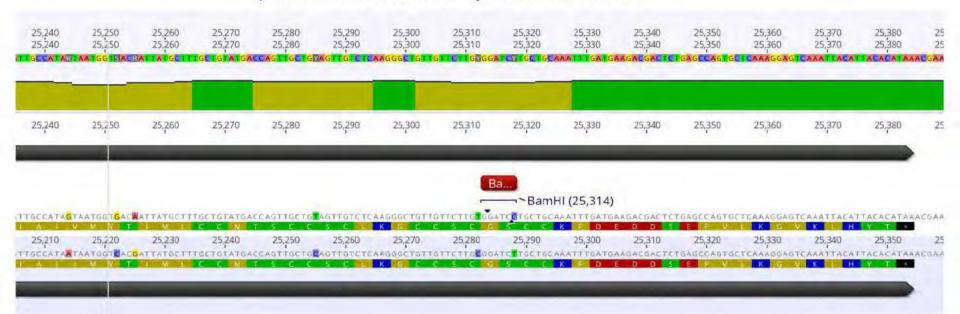
High level of mutations around key residues in the receptor binding domain



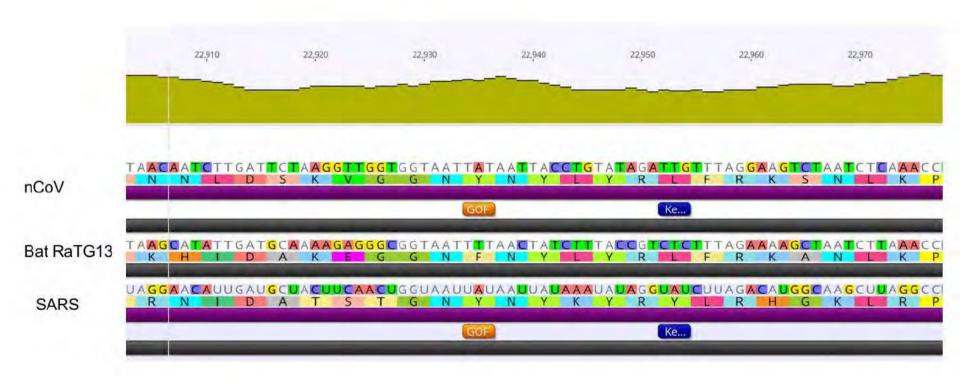
Gain of furin cleavage site in nCoV - not present in bat coronaviruses, SARS, or MERS



Gain of BamHI restriction site in nCoV at the very end of the spike protein. Note, diversity upstream of site, followed by none downstream



A "gain of function" (PMID: 17222058) in spike reverts to SARS sequence in RBD



A few references - to be significantly updated

A SARS-like cluster of circulating bat coronaviruses shows potential for human emergence; https://www.ncbi.nlm.nih.gov/pubmed/26552008

A mouse-adapted SARS-coronavirus causes disease and mortality in BALB/c mice; https://www.ncbi.nlm.nih.gov/pubmed/17222058

SARS-like WIV1-CoV poised for human emergence; https://www.ncbi.nlm.nih.gov/pubmed/26976607

Modeling pathogenesis of emergent and pre-emergent human coronaviruses in mice; https://www.ncbi.nlm.nih.gov/pubmed/30043100

Receptor recognition by novel coronavirus from Wuhan: An analysis based on decade-long structural studies of SARS; https://www.ncbi.nlm.nih.gov/pubmed/31996437

Molecular determinants of severe acute respiratory syndrome coronavirus pathogenesis and virulence in young and aged mouse models of human disease; https://www.ncbi.nlm.nih.gov/pubmed/22072787

From:

Jeremy Farrar

Sent:

Sat, 1 Feb 2020 16:12:51 +0000

To:

Fauci, Anthony (NIH/NIAID) [E]; Patrick Vallance

Cc:

Drosten, Christian; Marion Koopmans; R.A.M. Fouchier; Edward

Holmes Schreier (b) (6);Andrew Rambaut;Kristian G. Andersen;Paul

Subject:

(b) (6); Ferguson, Mike; Collins, Francis (NIH/OD) [E]

Re: Teleconference

Dial in details

+44 208 322 2629

Participant Code - 565941

From: Jeremy Farrar

(b) (6)

Date: Saturday, 1 February 2020 at 15:34

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

(b) (6), Patrick Vallance

(b) (6)

Cc: "Drosten, Christian"

(b) (6), Marion Koopmans

Edward Holmes

(b) (6)

(b) (6)

(b) (6)

Zamara majores

0.7.5.7

(b) (6) , Paul Schreier

Michael FMedSci

(b) (6)

Subject: Teleconference

1st February (2nd Feb for Eddie)

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Kristian Anderson

Bob Garry - I have not been able to contact Bob. Please forward if you can.

Christian Drosten

Tony Fauci

Mike Ferguson

Ron Fouchier

Eddie Holmes

Marion Koopmans

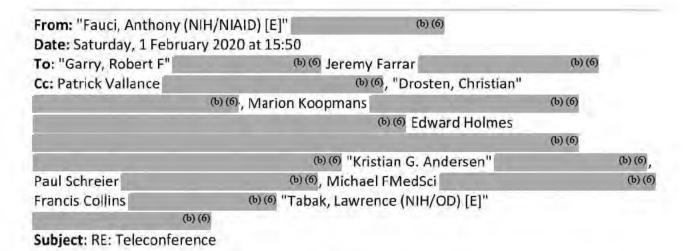
Stefan Pohlmann

Andrew Rambaut

Paul Schreier

Patrick Vallance

From:	Jeremy Farrar
Sent:	Sat, 1 Feb 2020 15:51:54 +0000
To:	Fauci, Anthony (NIH/NIAID) [E]; Garry, Robert F
Cc:	Patrick Vallance; Drosten, Christian; Marion Koopmans; R.A.M. Fouchier; Edward
Holmes	(b) (6);Andrew Rambaut;Kristian G. Andersen;Paul Schreier;Ferguson,
Mike;Collins, Fra	ancis (NIH/OD) [E];Tabak, Lawrence (NIH/OD) [E]
Subject:	Re: Teleconference
Francis	
Call me on	



Please include Francis Collins (copied here) on all subsequent correspondence regarding this call. Thanks.

```
(b) (6)
From: Garry, Robert F
Sent: Saturday, February 1, 2020 10:49 AM
To: Jeremy Farrar
                                           (b) (6)
Cc: Fauci, Anthony (NIH/NIAID) [E]
                                                       (b) (6); Patrick Vallance
                                                                                             (b) (6)
                                                                 (b) (6); Marion Koopmans
                ; Drosten, Christian
                            (b) (6) R.A.M. Fouchier
                                                                            (b) (6); Edward Holmes
                                                       (b) (6) Andrew Rambaut
                                                                                         (b) (6) Ferguson,
Kristian G. Andersen
                                         (b) (6); Paul Schreier
Mike
                                  (b) (6)
```

Subject: Re: Teleconference

Thanks Jeremy

I will be on the call

Bob Garry

Sent from my iPhone

On Feb 1, 2020, at 9:34 AM, Jeremy Farrar

(b) (6) wrote:

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

1st February (2nd Feb for Eddie)

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Kristian Anderson Bob Garry - I have not been able to contact Bob. Please forward if you can. Christian Drosten Tony Fauci Mike Ferguson Ron Fouchier Eddie Holmes Marion Koopmans Stefan Pohlmann Andrew Rambaut Paul Schreier Patrick Vallance

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.

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<Teleconference Dial In.jpg>

From: Jeremy Farrar

 Sent:
 Sat, 1 Feb 2020 15:50:28 +0000

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

 Cc:
 Collins, Francis (NIH/OD) [E]

Subject: Re: Teleconference

excellent

From: "Fauci, Anthony (NIH/NIAID) [E]" (b) (6) >

Date: Saturday, 1 February 2020 at 15:48

To: Jeremy Farrar

(b) (6)

Cc: Francis Collins (b) (6)

Subject: RE: Teleconference

Jeremy:

Francis will be on the call. He is trying to phone you.

Tony

From: Jeremy Farrar (b) (6)
Sent: Saturday, February 1, 2020 10:34 AM

To: Fauci, Anthony (NIH/NIAID) [E] (b) (6) Patrick Vallance (b) (6)

Cc: Drosten, Christian (b) (6) >; Marion Koopmans

(b) (6); R.A.M. Fouchier (b) (6); Edward Holmes

(b) (6) Andrew Rambaut (b) (6)
Kristian G. Andersen (b) (6) Paul Schreier (b) (6)

(b) (6); Ferguson, Mike (b) (6)

Subject: Teleconference

1st February (2nd Feb for Eddie)

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11am PST (Hope I have the times right!)

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From: Jeremy Farrar

Sent: Sat, 1 Feb 2020 13:27:42 +0000
To: Fauci, Anthony (NIH/NIAID) [E]

Subject: Re: Conf details

Thanks Tony!

I will make sure we have the correct times.

On 01/02/2020, 13:26, "Fauci, Anthony (NIH/NIAID) [E]" (b) (6) > wrote:

Jeremy:

I can be on the 2:00 PM EST call (8:00 PM CET). Note for West Coast callers, that 2:00 PM EST equal 11:00 AM West Coast and not 9:00 AM West Coast

Thanks, Tony

----Original Message----

From: Jeremy Farrar (b) (6)>

Sent: Saturday, February 1, 2020 5:55 AM
To: Fauci, Anthony (NIH/NIAID) [E] (b) (6)>

Subject: Re: Conf details

Could you join?

Trying to set up an initial call with

Kristian Anderson

Bob Garry

Christian Drosten

Tony Fauci

Ron Fouchier

Eddie Holmes

Marion Koopmans

Patrick Vallance - Chief Scientist UK

Time zones a challenge

Suggestion - Today 1st February (2nd Feb for Eddie) - I Will confirm later today. If you cannot make it, we will phone you afterwards to update.

6am Sydney

8pm CET

7pm GMT

2pm EST

9am West Coast

My preference is to keep this really tight group.

To listen to the work Eddie, Bob and Kristian have done.

Question it

And think through next steps.

Obviously ask everyone to treat in total confidence.

From: Jeremy Farrar

Sent: Sat, 1 Feb 2020 10:55:15 +0000 **To:** Fauci, Anthony (NIH/NIAID) [E]

Subject: Re: Conf details
Attachments: IMG_1781[2].JPG

Could you join?

Trying to set up an initial call with

Kristian Anderson Bob Garry Christian Drosten Tony Fauci Ron Fouchier Eddie Holmes Marion Koopmans

Patrick Vallance - Chief Scientist UK

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wellcometrust

Chairman's Office

MeetingSpace No:

International No:

Participant Access Code:

Host Access Code:

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

Sent: Sat, 1 Feb 2020 02:47:39 +0000

To: Jeremy Farrar; Kristian G. Andersen

Subject: FW: Science: Mining coronavirus genomes for clues to the outbreak's origins

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] (b) (6

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 Guandong.

EcoHealth Alliance

Mining coronavirus genomes for clues to the outbreak's origins

By Jon CohenJan. 31, 2020, 6:20 PM

attaaaggtt tataccttcc caggtaacaa accaaccaac tttcgatctc ttgtagatct ...

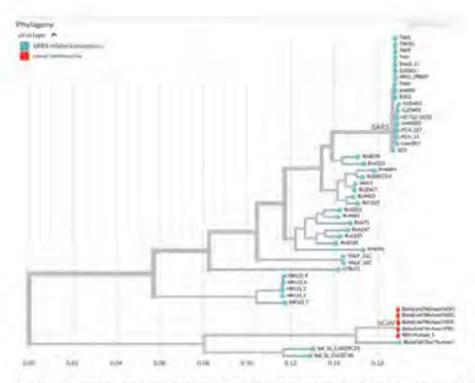
That string of apparent gibberish is anything but: It's a snippet of a DNA sequence from the viral pathogen, dubbed 2019 novel coronavirus (2019-nCoV), that is overwhelming China and frightening the entire world. Scientists are publicly sharing an ever-growing number of full sequences of the virus from 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.)

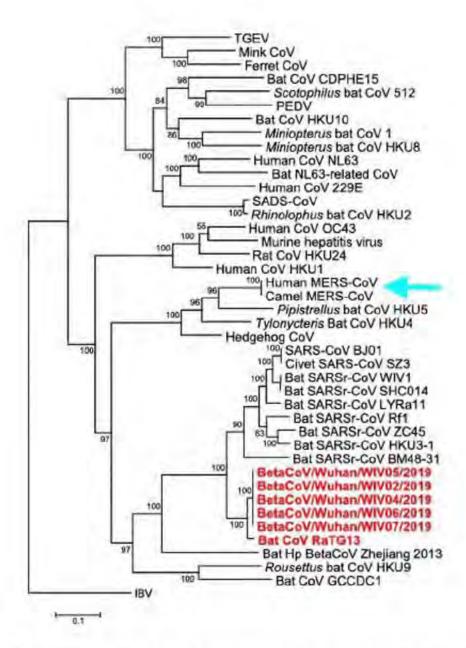
When the first 2019-nCoV sequence became available, researchers placed it on a family tree of known coronaviruses—which are abundant and infect many species—and found that it was most closely related to relatives found in bats. A team led by Shi Zheng-Li, a coronavirus specialist at the Wuhan Institute 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 cofounded, 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 <u>first group</u> 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, <u>pilloried it</u>. 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 <u>SARS</u> in <u>Beijing</u>. Ebright, who has a long history of raising red flags about studies with

dangerous pathogens, also in 2015 <u>criticized an experiment</u> 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 <u>questioned the accuracy</u> 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 *Science*Insider 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

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Fauci, Anthony (NIH/NIAID) [E] From: Sent: Sat, 1 Feb 2020 00:38:35 +0000

To: Jeremy Farrar Cc: Kristian G. Andersen

Conrad, Patricia (NIH/NIAID) [E]; Mascola, John (NIH/VRC) [E]; Conrad, Patricia Bcc:

(NIH/NIAID) [E]

RE: Phone call Subject:

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 Building 31, Room 7A-03 31 Center Drive, MSC 2520 National Institutes of Health Bethesda, MD 20892-2520 Phone: (b) (6)

FAX: (301) 496-4409

(b) (6) E-mail:

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From: Jeremy Farrar (b) (6)

Sent: Friday, January 31, 2020 5:57 PM

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

Subject: Re: Phone call

Thanks Tony

Can you phone Kristian Anderson

(b) (6)

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

(b) (6)

Eddie Holmes

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

From: "Conrad, Patricia (NIH/NIAID) [E]" (b) (6) > on behalf of "Fauci,

Anthony (NIH/NIAID) [E]" (b) (6)

Date: Friday, 31 January 2020 at 22:34

To: Jeremy Farrar (b) (6)

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
31 Center Drive, MSC 2520 - Room 7A03
Bethesda, Maryland 20892
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From: Jeremy Farrar	(b) (6)		
Sent: Friday, January 31, 2020 5;2	23 PM		
To: Fauci, Anthony (NIH/NIAID) [E	E]	(b) (6)	
Subject: Phone call			
Tony			
Really would like to speak with yo	ou this evening		
It is 10pm now UK			
Can you phone me on	(b) (6)		
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.

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From: Fauci, Anthony (NIH/NIAID) [E]
Sent: Thu, 30 Jan 2020 14:26:15 +0000

To: Jeremy Farrar
Cc: Patrick Vallance
Subject: Re: Contacts

Thanks, Jeremy. Great chatting with you and Patrick. Will stay in close touch, Best,
Tony

> On Jan 30, 2020, at 7:13 AM, Jeremy Farrar
> Tony
> Prefect timing - thank you. Great to catch up.
> Patrick Vallance
> Chief Scientific Advisor UK
> (6) (6)
> You have mine
> Keep in touch
> J
> J
> >

> 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.

(b) (6) wrote:

> The Wellcome Trust is a charity registered in England and Wales, no. 210183. Its sole trustee is The Wellcome Trust Limited, a company registered in England and Wales, no. 2711000 (whose registered office is at 215 Euston Road, London NW1 2BE, UK)

From:

Jeremy Farrar

Sent:

To:

Wed, 29 Jan 2020 20:43:32 +0000 Fauci, Anthony (NIH/NIAID) [E]

Subject:

Re: Informal coronavirus teleconference, 29 January, 19.00 CET

So kind!!

From: "Conrad, Patricia (NIH/NIAID) [E]"

(b) (6) on behalf of "Fauci,

Anthony (NIH/NIAID) [E]"

(b) (6)

Date: Wednesday, 29 January 2020 at 20:42 To: Jeremy Farrar

Subject: RE: Informal coronavirus teleconference, 29 January, 19.00 CET

Ok - we will try to call you early morning our time tomorrow. Thanks.

Patricia L. Conrad Public Health Analyst and Special Assistant to the Director National Institute of Allergy and Infectious Diseases The National Institutes of Health 31 Center Drive, MSC 2520 - Room 7A03

Bethesda, Maryland 20892

(b) (6)

301-496-4409 fax

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From: Jeremy Farrar

Sent: Wednesday, January 29, 2020 3:40 PM

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

Subject: Re: Informal coronavirus teleconference, 29 January, 19.00 CET

Will probably run over at the WH. Thank you and him so much!

Tomorrow is fine.

On 29 Jan 2020, at 20:38, Fauci, Anthony (NIH/NIAID) [E] (b) (6) wrote:

Dr Fauci is in meeting at the WH until about 5 pm ET so he would likely call you between 5 pm - 7 pm ET - is that too late today?

Patricia L. Conrad
Public Health Analyst and
Special Assistant to the Director
National Institute of Allergy and Infectious Diseases
The National Institutes of Health
31 Center Drive, MSC 2520 - Room 7A03
Bethesda, Maryland 20892

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From: Jeremy Farrar Sent: Wednesday, January 29, 2020 2:35 PM To: Fauci, Anthony (NIH/NIAID) [E] (b) (6)> Subject: Re: Informal coronavirus teleconference, 29 January, 19.00 CET Sure (b) (6) Anytime -Tonight from 5pm would be fine, but tomorrow also possible.... From: "Conrad, Patricia (NIH/NIAID) [E]" (b) (6) on behalf of "Fauci, (b) (6) Anthony (NIH/NIAID) [E]" Date: Wednesday, 29 January 2020 at 19:29 (b) (6), "Fauci, Anthony (NIH/NIAID) [E]" To: Jeremy Farrar Subject: RE: Informal coronavirus teleconference, 29 January, 19.00 CET

Is there a cell number to reach you? or best number?

Patricia L. Conrad
Public Health Analyst and
Special Assistant to the Director
National Institute of Allergy and Infectious Diseases

The National Institutes of Health
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Bethesda, Maryland 20892

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From: Jeremy Farrar (b) (6) Sent: Wednesday, January 29, 2020 2:21 PM

To: Fauci, Anthony (NIH/NIAID) [E] (b) (6)

Subject: Re: Informal coronavirus teleconference, 29 January, 19.00 CET

I could not make it until 5pm CET today. But next few days also OK.

From: "Conrad, Patricia (NIH/NIAID) [E]" (b) (6) on behalf of "Fauci,

Anthony (NIH/NIAID) [E]" (b) (6)

Date: Wednesday, 29 January 2020 at 18:54

To: Jeremy Farrar (b) (6)

Subject: RE: Informal coronavirus teleconference, 29 January, 19.00 CET

Dr Fauci is in back to back meetings but hopes to be able to step out and call you between 3:00 pm ET - 4:00 pm ET. Is that time ok and what is the best number to reach you at that time?

Best,

Patricia L. Conrad
Public Health Analyst and
Special Assistant to the Director
National Institute of Allergy and Infectious Diseases
The National Institutes of Health
31 Center Drive, MSC 2520 - Room 7A03
Bethesda, Maryland 20892

(b) (6)
301-496-4409 fax

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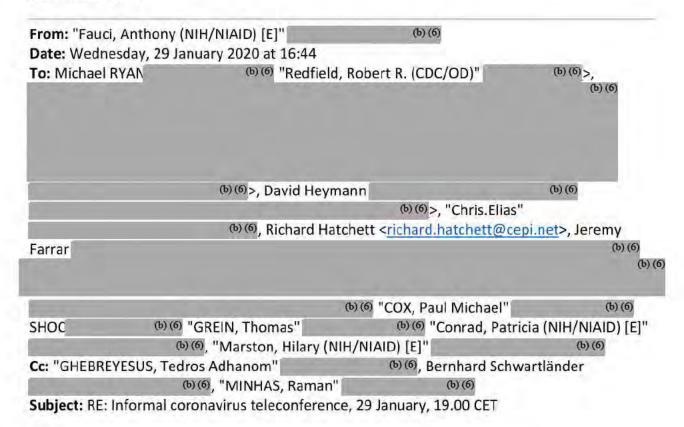
From: Jeremy Farrar (b) (6)
Sent: Wednesday, January 29, 2020 1:32 PM

To: Fauci, Anthony (NIH/NIAID) [E] (6) (6)

Subject: Re: Informal coronavirus teleconference, 29 January, 19.00 CET

Tony - Would be very keen to hear your personal views on n-CoV. If you have 5 mins for a phone call.

Best wishes Jeremy



Mike:

I am sorry but I have an important meeting with Secretary Azar that is a prep meeting for another important meeting at the White House. These overlap with the 19:00 CET time frame of your call. Unless something changes I cannot be on the call. If that is the case, I will ask Hilary Marston from my staff to fill in for me and report back to me. Please send the call in information to my Special Assistant, Patty Conrad, and me just in case something changes. Thanks,

Tony

Anthony S. Fauci, MD
Director
National Institute of Allergy and Infectious Diseases
Building 31, Room 7A-03
31 Center Drive, MSC 2520
National Institutes of Health
Bethesda, MD 20892-2520
Phone:
(b) (6)
FAX: (301) 496-4409

E-mail: (b) (6)

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(b) (6) From: RYAN, Michael J. Sent: Wednesday, January 29, 2020 10:45 AM To: Redfield, Robert R. (CDC/OD) (b) (6) (D) (6) (b) (6); Chris. Elias (b) (6) (b) (6) Fauci, Anthony (NIH/NIAID) [E] (b) (6); (b) (6); COX, Paul Michael (b) (6) >; SHOC (b) (6); GREIN, Thomas (b) (6) Cc: GHEBREYESUS, Tedros Adhanom (b) (6); SCHWARTLANDER, Bernhard F. (b) (6); MINHAS, Raman < Subject: Informal coronavirus teleconference, 29 January, 19.00 CET

Dear colleagues,

Dr Tedros would like to take the opportunity to informally discuss with you the ongoing 2019 novel coronavirus.

We are planning to host a teleconference today at 19.00 CET and will provide a dial-in number with a passcode.

If you face any difficulties with the dial-in number, please provide us with a contact number and we will attempt to dial you in.

Best,

Mike

From: Fauci, Anthony (NIH/NIAID) [E]
Sent: Wed, 29 Jan 2020 11:36:40 +0000

To: Dzau, Victor J.;'GPMB Secretariat';As Sy Elhadj;Brundtland Gro Harlem;Chris.Elias;Farrar Jeremy;Fore Henrietta;Gao Fu;Gashumba Diane;Kaag Sigrid;llona Kickbusch;Suzuki Yasuhiro;Vega Morales Jeanette;Vega Morales Jeanette;VijayRaghavan Krishnaswamy;'Skvortsova Veronika'

Statement on 2019-novel coronavirus

Attachments: Draft GPMB Statement nCOV 28Jan for Bd member review NIAID.docx

Looks fine. Please see my comments in attached document. Thanks,
Tony

From: Dzau, Vio	ctor	(b) (6)				
Sent: Tuesday,	January 28, 20	20 11:46 PM				
To: 'GPMB Secr	retariat'		(b) (6) As Sy	Elhadj	(b) (6); Brundtland Gro
Harlem	(b) (6) Chris. Elias	Street, Street	(1	(6)>; Farra	ar Jeremy
	(b) (6);	Fauci, Anthon	y (NIH/NIAID) [E		(b) (6);	Fore Henrietta
Marie and Marie	(b) (6) Gao Fu	1	(b) (6); Gashur	mba Diane		(b) (6) >; Kaag
Sigrid	(b) (6); Ilona	Kickbusch	The second second	(b) (டு; Suzuki	Yasuhiro	(b) (6)
	Vega	Morales Jean	nette <j< td=""><td></td><td>(b) (6); Veg</td><td>ga Morales Jeanette</td></j<>		(b) (6); Veg	ga Morales Jeanette
	(b) (б) Vijay	Raghavan Kris	shnaswamy		(b) (6); 'Skv	ortsova Veronika'
	(b) (6)					
Cc: MAHJOUR,	Jaouad	(ъ) (); MINHAS, Ram	nan	(b) (6);	Toomas Palu
	(b) (6); Pat	e Muhamed		(b) (6); RYAN	N, Michael J	
(b	6; SCHWAR	TLANDER, Ber	nhard F.		(b) (6); Alex	k Harris
	(b) (6);	Alveberg, Ben	edikte Louise			(b) (6) Chiaki
NOGUCHI		(b) (6)>; Esveld Marja	ALC: NO PERSONAL PROPERTY AND P	(6) (6) Esveld Marja
	(b) (6); Esveld N	/larja	(b) (6) >; Gon	ggrijp Mette	A	(b) (6)
Julie.HALL	(ъ	(6); Kanarek,	Morgan	(b) (6	; Marston,	Hilary (NIH/NIAID)
[E]	(b) (6	; Omar Abdi		(b) (6); Amelie F	RIOUX	
-	(b) (6) To	re Godal		6 GABEDAVA,		(b) (6);
		Banks Lynn			(b) (6) Block	Bruce
<bblock@nas.e< td=""><td></td><td></td><td>(b) (6) Co</td><td>nrad, Patricia</td><td>(NIH/NIAID</td><td>) [E]</td></bblock@nas.e<>			(b) (6) Co	nrad, Patricia	(NIH/NIAID) [E]
		el Sol Dinia		டு டுDiao Fay		(b) (6)
Gahungu Zacha	rie		(b) (6); Harik	cumar M K		(b) (6)
Harikumar M K		(b) (6) Kabag	ire Christine		(b) (6)>; KITA Yosuke

(b) (6);	(b) (6) Miller de Vega Teresa		
(b) (6) MURIUKI, Hilda	(b) (6) MURIUKI, Hilda Wairimu		
(b) (6); Sarah Belmir	(b) (6); YU Bai	(b) (6); Kirsi Madi	
(b) (6) 'Oleg So	onin'	(b) (6)	

Subject: RE: TIME SENSITIVE Message from GPMB Co-Chairs: review of draft GPMB Statement on 2019novel coronavirus

The message is clear and appropriate, I support it.

```
(b) (6)
From: GPMB Secretariat
Sent: Tuesday, January 28, 2020 7:09 AM
                                 (b) (6); Brundtland Gro Harlem
To: As Sy Elhadj
                                                                                     (b) (6); Dzau, Victor J.
               (b) (6); Chris. Elias
                                                                 (b) (6); Farrar Jeremy
                                                                  (b) (6) Fore Henrietta
                       (b) (6) >; Fauci Anthony
                                                                                                         (b) (6)
                           (b) (6) Gashumba Diane
                                                                     (b) (6) >; Kaag Sigrid
                                                                                                      (b) (6)
Gao Full
                                                                                         (b) (6) >; Vega
Ilona Kickbusch
                                       (b) (6) Suzuki Yasuhiro
                                                (b) (6); Vega Morales Jeanette
Morales Jeanette
                                                                                                   (b) (6)
VijayRaghavan Krishnaswamy
                                                     (b) (6) 'Skvortsova Veronika'
                                                                                  (b) (6); Toomas Palu
Cc: MAHJOUR, Jaouad
                                        (b) (6)>; MINHAS, Raman
                    (b) (6); Pate Muhamed
                                                                   (b) (6) RYAN, Michael J.
              (b) (6); SCHWARTLANDER, Bernhard
                                                                               (b) (6) Alex Harris
                        (b) (6) Alveberg, Benedikte Louise
                                                                                              (b) (6); Chiaki
NOGUCHI
                                          (b) (6); Esveld Marja
                                                                                         (b) (6) Esveld Marja
                                                   (b) (6); Gonggrijp Mette
                (b) (6); Esveld Marja
                                                                                                         (b) (6)
Julie.HALL
                             (b) (6); Kanarek, Morgan
                                                                          (b) (6) Marston Hilary
                     (b) (6) >; Omar Abdi
                                                           (b) (6); Amelie RIOUX
                                                                                                        (b) (6)
                              (b) (6); GABEDAVA, Tsira
                                                                          (b) (6); ROSS, Alex
Tore Godal
                                                                  (b) (6) Block, Bruce
             (b) (6); Banks Lynn
                                                                                                     (b) (6)
                                                                             (b) (6)>; Del Sol Dinia
Conrad Jane
                                (b) (6); Conrad Patricia
                                                     (b) (6); Gahungu Zacharie
                              (b) (6) >; Harikumar M K
                                                                               (b) (6) Harikumar M K < (b) (6)
                                                                (b) (6) >; KITA Yosuke (b) (6)
           >; Kabagire Christine
                                                            (b) (6) Miller de Vega Teresa
                       >;
                                (b) (6); MURIUKI, Hilda Wairimu
                                                                                   (b) (6) Muzenda Sindiso
                         (b) (6); Sarah Belmir
                                                               (b) (6) >; YU Bai
                                                                                            (b) (6); Kirsi Madi
                                          (b) (6) 'Oleg Sonin'
                                                                                      (b) (6)
Subject: TIME SENSITIVE Message from GPMB Co-Chairs: review of draft GPMB Statement on 2019-
novel coronavirus
```

Dear Board members,

Importance: High

Thank you to all who participated in yesterday's teleconference call regarding the novel 2019-Coronavirus outbreak.

We received excellent updates from WHO and from Professor Gao.

There was consensus for the GPMB to issue a statement supportive of countries' (especially China) and WHO response efforts, and to call for urgent actions to further strengthen global preparedness and response to this outbreak.

Please find attached a draft GPMB Statement.

We ask that you please send us any feedback (preferably in track change mode) no later than <u>1700</u> Wednesday 29 January, Geneva time

Thank	you	very	muc	h.

Kinds regards,

Gro and As

<u>DRAFT 0</u> - Statement from the Global Preparedness Monitoring Board on the Outbreak of 2019novel Coronavirus (2019-nCoV) - DRAFT - 27 January 2020

Xx January 2020, Geneva — The Global Preparedness Monitoring Board (GPMB) convened on 27 January 2020 to discuss the current outbreak of 2019-nCoV which was first detected in Wuhan, China and has now reached fourteen countries as of 28 January 2020. The Board praises the speed of the response so far by countries and the World Health organization (WHO), the transparency of China in rapidly sharing information and the genome sequence,—and commends the strong collaboration between China and affected countries and with WHO. The Board would recommend that China invite and WHO facilitate expert epidemiologic and other assistance. The Board however is concerned that many countries remain unprepared and urges leaders in all countries to take immediate action to ensure that they have the necessary capacities in place.

The Board recommends the following urgent actions:

- 1) Countries, institutions, communities and partners should ensure that all relevant information about the outbreak is shared fully and freely, in a timely manner, to support the response (in accordance with the International Health Regulations (IHR (2005);
- 2) Countries should support and enable WHO's central role in the response, including by fully financing WHO's preparedness and response activities through voluntary contributions and replenishment of the WHO Contingency Fund for Emergencies, and to strengthen its communication capacity. The WHO should ensure that it provides timely, accurate and easily accessible information on the outbreak status and best practices in responding.;
- 3) The research & development community, including national research institutions, the Coalition for Epidemic Preparedness Innovations (CEPI) and related dedicated efforts in the public and private sectors, should urgently accelerate the development of a vaccine, diagnostics and therapeutics against the coronavirus. This could be facilitated through, *inter alia*, the <u>prompt and unrestricted</u> sharing of coronavirus specimens <u>and clinical samples</u>. Countries and the international community should expand understanding of potential trajectories of the epidemic and its social-economic impact;
- 4) Ensuring that communities are properly informed and trust the response is crucial to controlling the outbreak. Countries, <u>institutions and the WHO</u> should regularly <u>and pro-actively</u> communicate information about the outbreak in a transparent and open manner, and should find ways to engage local organizations and communities in the planning and implementation of response activities;
- 5) All countries, including those that have not yet been affected, must urgently dedicate resources to building their essential preparedness capacities (as described in the IHR (2005) to prevent, detect, inform about and respond to the outbreak and to strengthen their health systems. All donors and international financing institutions should financially support lower resourced countries, including using existing instruments. Donor and development partners should prioritize Emphasis must be given to providing financial and technical support to low- and middle-income countries at risk to assist them in building these capacities, notably to improve early detection of the virus and to take actions to limit the risk of transmission.

About the GPMB

As an independent monitoring and advocacy body, the <u>GPMB</u> urges political action to prepare for and mitigate the effects of global health emergencies. Co-convened by the World Bank Group and the WHO, the GPMB works independently to provide expert assessments and recommendations on the

Commented [A1]: Please note: we fill finalise this figure prior to release of the Statement

Commented [A2]: May want to consider an additional sentence that calls for WHO action: WHO should lead the global response through effective action to minimize risks of transmission, support care for people who are infected, share critical risk and event information and counter misinformation, and engage with governments to support their preparedness and response efforts.

Commented [A3]: Not sure why CEPI in particular should be singled out here

Commented [A4R4]: Agree especially because so far they are primarily vaccines

Commented [A5]: Prompt data sharing and harmonization of clinical protocols (as was done in the Zika response) should be encouraged and facilitated by WHO.



Jeremy Farrar From:

Sent: Tue, 28 Jan 2020 21:13:22 +0000

To: Jeanette Vega Morales; GPMB Secretariat; As Sy Elhadi; Brundtland Gro Harlem; Dzau Victor; Chris. Elias; Fauci, Anthony (NIH/NIAID) [E]; Fore Henrietta; Gao Fu; Gashumba Diane; Kaag Sigrid; Ilona Kickbusch; Suzuki Yasuhiro; Vega Morales Jeanette; Vega Morales

Jeanette; Vijay Raghavan Krishnaswamy; 'Skvortsova Veronika'

Cc: MAHJOUR, Jaouad; MINHAS, Raman; Toomas Palu; Pate Muhamed; RYAN, Michael J.; SCHWARTLANDER, Bernhard F.; Alex Harris; Alveberg, Benedikte Louise; Chiaki NOGUCHI; Esveld Marja; Esveld Marja; Esveld Marja; Gonggrijp Mette; Julie. HALL; Kanarek Morgan; Marston, Hilary (NIH/NIAID) [E]; Omar Abdi; Amelie RIOUX; Tore Godal; William Hall; GABEDAVA, Tsira; ROSS, Alex; Banks Lynn; Block Bruce; Conrad Jane; Conrad, Patricia (NIH/NIAID) [E]; Del Sol Dinia; Diao Fay; Gahungu Zacharie; Harikumar M K; Harikumar M K; Kabagire Christine; KITA Yosuke; ;Teresa Miller de Vega;MURIUKI, Hilda Wairimu;Muzenda Sindiso;Sarah Belmir;YU Bai;Kirsi

(b) (6); 'Oleg Sonin'; Alice Jamieson; Alex Harris Madi

Re: TIME SENSITIVE Message from GPMB Co-Chairs: review of draft GPMB Subject:

Statement on 2019-novel coronavirus

Attachments: Draft GPMB Statement nCOV 28Jan for Bd member review JF.docx

Suggestions - thank you

F ((b) (6)			
From: Jeanette Vega Morales	-	(b) (6)			
Date: Tuesday, 28 January 20	120 at 14:38		2 3 5 5 4		
To: GPMB Secretariat		(b) (6), As	Sy Elhadj		(ъ) (б)
Brundtland Gro Harlem		(b) (6), Victor	Dzau	0	6) (6), "Chris.Elias"
	(b) (6) , Jerem	y Farrar		(b)	(6), Fauci Anthony
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Diane Gashumba	(b) (6), h	Kaag Sigrid		(b) (6), Ilona	Kickbusch
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	The second second	(b) (6) Teres	a de Vega
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Sindiso	(b)(6), Sarah Be	lmir	(b) (6), YU Bai
(b) (6)	, Kirsi Madi	100	(b) (6)
The second second	(b) (6), 'Oleg Sonin '	(b) (б)	
Subject: RE: TIME	SENSITIVE Message from GF	MB Co-Chairs: review	v of draft GPMB Statement

on 2019-novel coronavirus

Dear Gro and As

As requested please see attached

Best,

Jeanette

From: GPMB Secretar	iat	(b) (6)			
Sent: martes, 28 de en	nero de 2020 9:09				
To: As Sy Elhadj	(b) (6) Brundt	land Gro Harlem	Commence of the last of the la	(b) (6) D	zau Victor
(b) (6); CI	nris.Elias		(b) (6) Farrar Jere	my	
	(b) (6); Fauci Anthony		(b) (6); Fore Hen	rietta	(b) (6)
Gao Fu	(b) (6) Gashumba Dia	ane	(b) (6); Kaag	Sigrid	(b) (6)
Ilona Kickbusch	(b) (6); St	zuki Yasuhiro		(b) (6)	>; Vega
Morales Jeanette	19	(b) (6) Vega Mora	les Jeanette		(b) (6);
VijayRaghavan Krishna	aswamy	(b) (б); 'Skvor	tsova Veronika'		(b) (6) >
Cc: MAHJOUR, Jaouad	(b) (6);	MINHAS, Raman	The second	(b) (6); Too	mas Palu
(b)	(6); Pate Muhamed	Contract Contract	(b) (6) RYAN, Mi	ichael J.	
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	(b) (6); Alveberg, Bened	dikte Louise			(b) (6) Chiaki
NOGUCHI	(b) (6) >	; Esveld Marja	N. W. Land	(b) (6	Esveld Marja
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Julie.HALL	(b) (6); Kanarek M	organ	(b) (6); Ma	rston Hilar	У
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Tore Godal	(b) (6) GABEDAV	A, Tsira	(b) (6); R	OSS, Alex	
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(b) (6); Sarah Belmir		(b) (6) ; YU Bai	(b) (6) >; Kirsi Madi
(b) (6)	(b) (6) 'Oleg Sonin '	Land of the land	(b) (6)

Subject: TIME SENSITIVE Message from GPMB Co-Chairs: review of draft GPMB Statement on 2019-

novel coronavirus Importance: High

Dear Board members,

Thank you to all who participated in yesterday's teleconference call regarding the novel 2019-Coronavirus outbreak.

We received excellent updates from WHO and from Professor Gao.

There was consensus for the GPMB to issue a statement supportive of countries' (especially China) and WHO response efforts, and to call for urgent actions to further strengthen global preparedness and response to this outbreak.

Please find attached a draft GPMB Statement.

We ask that you please send us any feedback (preferably in track change mode) no later than <u>1700</u> Wednesday 29 January, Geneva time

Thank you very much.

Kinds regards,

Gro and As

<u>DRAFT 0</u> -- Statement from the Global Preparedness Monitoring Board on the Outbreak of 2019novel Coronavirus (2019-nCoV) – DRAFT – 27 January 2020

Xx January 2020, Geneva — The Global Preparedness Monitoring Board (GPMB) convened on 27 January 2020 to discuss the current outbreak of 2019-nCoV which was first detected in Wuhan, China and has now reached fourteen countries as of 28 January 2020. The Board praises the speed of the response so far by countries and the World Health organization (WHO), the transparency of China in rapidly sharing information and the genome sequence of the virus, and commends the strong collaboration between China and affected countries and with WHO. The Board however is concerned that many countries remain unprepared and urges leaders in all countries to take immediate action to ensure that they have the necessary capacities in place.

The Board recommends the following urgent actions:

- 1)—Countries, institutions, communities and partners should ensure that all relevant information about the outbreak is shared fully and freely, in a timely manner openly and rapidly, to support the response (in accordance with the International Health Regulations (IHR (2005):
- 2) The research & development community, including national research institutions, the Coalition for Epidemic Preparedness Innovations (CEPI) and related dedicated efforts in the public and private sectors, should urgently accelerate the coordinated development of a vaccine, diagnostics and therapeutics against the coronavirus. The rapid sharing of coronavirus specimens is essential to advancing this research & development, early detection and the global public health response. To ensure rapid access to emerging findings, all peer-reviewed research publications relevant to the outbreak should be made open access immediately. Research findings relevant to the outbreak should be shared rapidly with WHO, In line with recent commitments by some journals¹. Countries and the international community should expand understanding of potential trajectories of the epidemic and its social-economic impact;
- 2) Countries should support and enable WHO's central role in the response, including by fully financing WHO's preparedness and response activities through voluntary contributions and replenishment of the WHO Contingency Fund for Emergencies, and to strengthen its communication capacity;
- 3) The research & development community, including national research institutions, the Coalition for Epidemic Preparedness Innovations (CEPI) and related dedicated efforts in the public and private sectors, should urgently accelerate the development of a vaccine, diagnostics and therapeutics against the coronavirus. This could be facilitated through, inter alia, the sharing of coronavirus specimens. Countries and the international community should expand understanding of potential trajectories of the epidemic and its social economic impact;
- 4) Ensuring that communities are properly informed and trust the response is crucial to controlling the outbreak. Countries and WHO should regularly communicate information about the outbreak in a transparent and open manner, and should find ways to engage local organizations and communities in the planning and implementation of response activities;

Commented [RA1]: Please note: we fill finalise this figure prior to release of the Statement

Medical Journals and the 2019-nCqV Outbreak, NEJM https://www.nejm.org/doi/full/10.1056/NEJMe2001329?query=featured_home

5) All countries, including those that have not yet been affected, must urgently dedicate resources to building their essential preparedness capacities (as described in the IHR (2005) to prevent, detect, inform about and respond to the outbreak and to strengthen their health systems. All donors and international financing institutions should financially support lower resourced countries, including using existing instruments. Emphasis must be given to providing financial and technical support to low- and middle-income countries to assist them in building these capacities, notably to improve early detection of the virus, to enhance their ability to respond.

About the GPMB

As an independent monitoring and advocacy body, the <u>GPMB</u> urges political action to prepare for and mitigate the effects of global health emergencies. Co-convened by the World Bank Group and the WHO, the GPMB works independently to provide expert assessments and recommendations on the state of global preparedness. The opinions and recommendations contained in the GPMB report are those of the Board and do not necessarily represent the views of the World Bank Group and WHO.

From: Fauci, Anthony (NIH/NIAID) [E]
Sent: Fri, 24 Jan 2020 11:16:47 +0000

To: Jeremy Farrar

Cc: Collins, Francis (NIH/OD) [E] (b) (6)

Subject: RE: nCo-V

Jeremy:

Thank you for letting me know. Very sad and a great loss. Every day is a blessing.

Best, Tony

From: Jeremy Farrar (b) (6)

Sent: Friday, January 24, 2020 6:08 AM

To: Fauci, Anthony (NIH/NIAID) [E] (b) (6)
Cc: Collins, Francis (NIH/OD) [E] (b) (6)

Subject: Re: nCo-V

Tragic news - Pete Salama died last night, life is very fragile - what a loss.

On 23 Jan 2020, at 20:32, Fauci, Anthony (NIH/NIAID) [E] (b) (6) > wrote:

Jeremy:

I hope that all is well with you. Happy New Year! I, like you, am somewhat baffled by the recommendation of the Emergency Committee at WHO. They are probably hesitating to declare a PHEIC because they have not seen "sustained" human-to-human transmission in other countries that have cases such as Japan, Thailand, South Korea. I do not necessarily agree with that opinion. We have a rapidly evolving outbreak with the epicenter in Wuhan, but with multiple cities in China and multiple countries in Asia involved. To me, that would be enough for a PHEIC. But then again, I am not the one that decides.

Best regards,

Tony

Anthony S. Fauci, MD
Director
National Institute of Allergy and Infectious Diseases
Building 31, Room 7A-03
31 Center Drive, MSC 2520
National Institutes of Health
Bethesda, MD 20892-2520

Phone: (b) (6) FAX: (301) 496-4409

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From: Jeremy Farrar (6) (6)

Sent: Thursday, January 23, 2020 2:03 PM

To: Fauci, Anthony (NIH/NIAID) [E] (b) (6); Richard Hatchett

(b) (6)

Subject: nCo-V

Tony

Happy New Year!

Difficult to understand the advice from the Emergency Ctte at WHO.

Reach out if anything – best wishes 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.

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