

On Sun, Feb 9, 2020 at 4:36 PM McNeil Jr, Donald G <> wrote:

got it, thank you.

On Sun, Feb 9, 2020 at 4:00 PM Kristian G. Andersen <> wrote:

These numbers have been discussed on Twitter and (I think) in various news outlets - however, without the data it's difficult to conclude anything from them as it's difficult to know what they mean. E.g., is 99% identity at the nucleotide or amino acid level? Is it 99% across the full genome or is it up to 99% in some parts of the genome? We unfortunately won't know until the data is out so hopefully that'll happen soon.

K

On Sun, Feb 9, 2020 at 12:55 PM McNeil Jr, Donald G <> wrote:

Hmmm. OK, Maybe I misunderstood him. . He's on a plane to Geneva now. He mentioned that there was supposed to be a 99 percent match overall but only a 97 percent match in the receptor binding domain. Do you know where that information could have come from? I don't see it in this Nature article or in the Xinhua writeup of the South China Ag U work.

On Sun, Feb 9, 2020 at 3:48 PM Kristian G. Andersen <> wrote:

No, those are the older sequences from pangolins, and while they're similar to nCoV they don't really provide any new clues - they're further away from nCoV than e.g., RaTG13. The pangolin sequences people have been talking about are supposedly 99% identical to nCoV, which could provide some really important clues - but those unfortunately haven't been released yet and there also isn't a study - just news reports (e.g., <https://www.nature.com/articles/d41586-020-00364-2>).

Best,

Kristian

On Sun, Feb 9, 2020 at 12:44 PM McNeil Jr, Donald G <> wrote:

The sequences haven't been released? Stanley Perlman said he thought they were posted on Genbank back in October. At least, that's what I understood him to say.

On Sun, Feb 9, 2020 at 3:42 PM Kristian G. Andersen <> wrote:

Hi Don,

Thanks for the follow up questions. The pangolin sequences haven't been released and the studies not yet published, so I unfortunately don't have any insights on those sequences. They could provide some very important clues, so I'm excited to see those studies, and importantly, data.

Best,

Kristian

On Sun, Feb 9, 2020 at 10:55 AM McNeil Jr, Donald G <> wrote:

Hello again. A bit more has come out.

Does the pangolin explanation sound like the most plausible now?

Of course, this will now create speculation that the nCoV virus EITHER jumped out of a pangolin into a person in Wuhan OR that the Wuhan Virological Institute had a sample from Guangdong and somehow let it escape.

I don't know if it will ever be possible to prove that one either way -- and if so, how.

Donald

The Oct 2019 study by Liu, Chen and Chen of samples from dying pangolins rescued in March 2019 by the the Guangdong Wildlife Rescue Center. It says they had lots of viruses, including Sendai and several coronaviruses

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6893680/>

Xinhua news release saying virologists from Southern China Agricultural University had found a 99% match between nCoV and one of those coronaviruses. (only 97% in the receptor binding domain, I head later)

http://www.xinhuanet.com/english/2020-02/07/c_138763566.htm

A Nature Med article pulling this together:

<https://www.nature.com/articles/d41586-020-00364-2#ref-CR1>

Now it sounds like a team from Baylor may have also found what the Southern China Ag U people did. (Not clear to me how a South African website realized that first. We are pursuing an interview with the Baylor scientists)

<https://www.dailymaverick.co.za/article/2020-02-07-coronavirus-source-found-in-pangolin-meat/>

On Fri, Feb 7, 2020 at 12:05 PM Kristian G. Andersen <> wrote:

I have only seen the news on Twitter and a Nature reporter who contacted me about it. Eddie Holmes might be a person to contact.

Cheers,
Kristian

On Fri, Feb 7, 2020 at 9:03 AM McNeil Jr, Donald G <> wrote:

Thanks very much -- all I've seen about pangolins is that one line in a press release from Southern China Agricultural University. Is there anything more?

On Fri, Feb 7, 2020 at 11:59 AM Kristian G. Andersen <> wrote:

Hi Don,

To your PS - yeah, unfortunately conspiracy theories will probably never die - every major epidemic will have its own. The question about potential lab escape is not necessarily a crackpot theory though and should always be taken seriously and investigated scientifically.

As to your question - if nCoV had been based on engineered versions previously produced (all of which have been used for basic/vaccine

research), then we would indeed expect to see inserted sequences and some level of high homology between them and nCoV. We don't see that at all so it's not possible that nCoV could have been engineered from those. Somebody who had some sort of malicious intent in making a virus would also be expected to have used e.g., SARS or MERS - since we know they can cause human disease - and not a bat SARS-like CoVs. Again, this is clearly not what we see here - while nCoV is related to both SARS (80% identical) and MERS (50%) they are clearly very distinct viruses.

As I mention in my previous email, many less subtle scenarios (e.g., culture) would be expected to look much the same as spillover, so it's going to be very hard/impossible to distinguish between those sorts of scenarios. Some news broke last night that researchers in China had identified viruses that are 99% identical to nCoV from pangolins, so it's likely that they might have served as an intermediate host. I haven't seen any of that data yet, but it seems highly plausible as there are already a few public sequences from SARS-like CoVs from pangolins and they do indeed look very similar to nCoV (not full genomes so hard to say exactly how identical - but I expect more data to come shortly).

Best,
Kristian

On Fri, Feb 7, 2020 at 4:25 AM McNeil Jr, Donald G <> wrote:

Kristian:

Thank you very much. That's very helpful. Can you elaborate a bit on one thing you said?

You said that, if it was an engineered virus "we would have been able to easily pick that up if that were the case."

Can you tell me what you might have seen in the sequences that would betray the fact that it was engineered? Inserted sequences from other viruses? Sections of the genome missing that don't go missing in nature? Deletions in areas that are always conserved? Something else?

(I'm pressing because I have to explain this to editors who are reading the conspiracy theories and then probably write a piece making clear why they are probably wrong.)

Thanks, Donald

PS: I'm now getting notes, including from MDs, reviving all the old conspiracy theories about Zika that I thought I'd debunked five years ago. It never ends....

On Thu, Feb 6, 2020 at 11:37 PM Kristian G. Andersen <> wrote:

Dear Don,

It's good to hear from you, and yes I of course remember our great conversations about Zika and Ebola. It's an interesting question you're asking, but I'm afraid I might not be the best person to answer, as we are mostly looking at what's going on during the epidemic (not before). Mostly, unless the virus was a really obvious recombinant virus, a virus from culture vs an intermediate host would probably be indistinguishable.

A couple of things I can say based on the data so far though:

1. A lot of the conspiracy theories are talking about this being either a lab strain that had previously been engineered (Nature Medicine paper) or some new recombinant. These rumours are demonstratively false - we would have been able to easily pick that up if that were the case, however it is not.
2. The virus is highly related to bat SARS-like coronaviruses so we can with strong evidence say that the reservoir host is also a bat. Likely there was an amplifying host involved before the virus got into humans, but we don't yet know what it might be. I'm sure there's a lot of investigations going on addressing that exact question.
3. As you mention, we can clearly see from the sequence data produced so far that the introduction into the human population was a single event. This could either be from a single infected host to a single human, or a small cluster of hosts into a small cluster of people. The virus has then been spreading human to human ever since.
4. While the RaTG13 bat sequence is interesting, it still too divergent from nCoV to have anything to do with the current epidemic - the genetic distance is simply too great.
5. From a genomics perspective, the theories Richard Ebright lay out would likely look the same - there would be no way to distinguish between them.

I hope some of these answers were helpful.

Best,
Kristian

On Thu, Feb 6, 2020 at 2:10 PM McNeil Jr, Donald G <> wrote:

PS: Since I wrote that, Richard Ebright explained to me that the virus is 96.2 percent identical to bat coronavirus RaTG13, which he said was collected by Wuhan Institute of Virology in a cave in Yunnan in 2003, and that has been stored at the institute since then.

So, he argued, it could have entered humans from the cave in Yunnan or another cave, or a wet market. Or, alternatively, it could have escaped into a human from the lab

Right now, with the available data, he says, there is no way to tell. But he points out that SARS got into humans the first time in 2002 from a civet, and the second, third and fourth times from laboratory accidents in 2003.

Do you agree with that analysis?

Thanks, Donald

On Thu, Feb 6, 2020 at 4:48 PM McNeil Jr, Donald G <> wrote:

Dear Kristian:

Hello again. I hope you remember us talking about Zika and microcephaly in 2017. I'm now part of our team covering the Wuhan coronavirus, of course.. Happily for me, I was on an extended fishing trip when it started, so I missed many of the initial stories. But now I'm back and trying to be helpful.

I'm trying to check out a rumor that an editor got from a government source -- that the US government is trying to seriously investigate the possibility that the nCoV came out of the Wuhan Virus Laboratory rather than out of a wet market.

I know that's part of a lot of silly conspiracy theories circling.

But is there any possibility that: it could be from the Wuhan lab?

And, if it was -- would there be any way to tell? (I mean, I assume the lab has a large library of coronaviruses, some of

which came from animal samples. If a lab tech got infected with one, I imagine it wouldn't be very different from one that a wet market worker picked up from the same animal.)

Is there anything in the sequences posted so far that suggests the virus has been manipulated by human hands in any way? (Sequences from another virus inserted, deletions that seem unlikely to occur in nature, anything like that?)

And is it the consensus now that all the known human cases stem from a single introduction of the virus into humans? Would that make it more likely that it was a lab accident rather than an animal spillover? One imagines that if one animal had it, a lot of its fellow animals had it before it adapted to a human host -- and I haven't heard any evidence of that...

Sorry if these questions seem naive, but I have editors with bits between their teeth for a "bioweapons escape" story and am wondering.

Thanks, Donald

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Donald G. McNeil Jr.
Science Correspondent