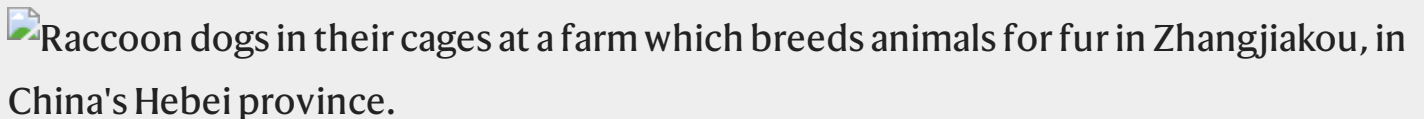


NEWS | 16 September 2021

Did the coronavirus jump from animals to people twice?

A preliminary analysis of viral genomes suggests the COVID-19 pandemic might have multiple animal origins – but the findings still have to be peer reviewed.

Smriti Mallapaty

 Raccoon dogs in their cages at a farm which breeds animals for fur in Zhangjiakou, in China's Hebei province.

Raccoon dogs — pictured here at a fur farm in China's Hebei province — are susceptible to SARS-CoV-2 and were sold at multiple markets in Wuhan. Credit: Greg Baker/AFP via Getty

SARS-CoV-2, the virus that causes COVID-19, could have spilled from animals to people multiple times, according to a preliminary analysis of viral genomes sampled from people infected in China and elsewhere early in the pandemic.

If confirmed by further analyses, the findings would add weight to the hypothesis that

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WHO report into COVID pandemic origins zeroes in on animal markets, not labs

Lineage B has become the dominant lineage globally and includes samples taken from people who visited the Huanan seafood market in Wuhan, which also sold wild animals. Lineage A spread within China, and includes samples from people linked to other markets in Wuhan.

A crucial question is how the two viral lineages are related. If viruses in lineage A evolved from those in lineage B, or vice versa, that would suggest that the progenitor of the virus jumped just once from animals to people. But if the two lineages have separate origins, then there might have been multiple spillover events.

Dagger in the heart

The latest analysis – posted on the [virological.org discussion forum](#) – adds weight to the second possibility by questioning the existence of genomes linking the lineages.

The finding could be the “dagger into the heart” of the hypothesis that SARS-CoV-2 escaped from a lab, rather than originating from the wildlife trade, says Robert Garry, a virologist at Tulane University in New Orleans, Louisiana. But others say that more research is needed, especially given the limited genomic data from early in the pandemic.

“It is a very significant study,” says Garry. “If you can show that A and B are two separate

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The COVID lab-leak hypothesis: what scientists do and don't know

Lineages A and B are defined by two key nucleotide differences. But some of the earliest genomes have a combination of these differences. Researchers previously thought that these genomes could be those of viruses at intermediate stages of evolution linking the two lineages.

But the researchers behind the new analysis looked at them in detail and noticed some problems.

Fine-tooth comb

They analysed 1,716 SARS-CoV-2 genomes in a popular online genome repository called GISAID that were collected before 28 February 2020, and identified 38 such 'intermediate' genomes.

But when they looked at the sequences more closely, they found that many of these also contained mutations in other regions of their genomes. And they say that these mutations are definitively associated with either lineage A or lineage B – which discredits the idea that the corresponding viral genomes date to an intermediate stage of evolution between the two lineages.

The authors suggest that a laboratory or computer error probably occurred in sequencing one of the two mutations in these 'intermediate' genomes. "The more we dug, the more it looked like, maybe we can't trust any of the 'transitional' genomes,"

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pandemic, when protocols weren't very established and people tried to generate data as fast as they could."



After the WHO report: what's next in the search for COVID's origins

Several researchers contacted by *Nature*, who sequenced some of the samples included in the study, say it is unlikely that their sequences include errors in the two key nucleotides. But the study authors counter that even if some of the genomes were sequenced correctly, other parts of the same genomes, or the locations from which the samples were collected, still clearly indicate that they belong to only one or the other lineage.

"It is very unlikely" that any of the so-called intermediate genomes are actually transitional genomes, says study co-author Joel Wertheim, a molecular epidemiologist at the University of California, San Diego.

Xiaowei Jiang, an evolutionary biologist at Xi'an Jiaotong-Liverpool University in Suzhou, China, says that the team behind the study must verify the findings by getting "the original raw sequencing data for as many genomes as possible".

Many markets

If the virus did jump between animals and people on several occasions, the fact that lineages A and B are linked to people who visited different markets in Wuhan suggests

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The latest study, if verified, would mean that the scenario of a researcher accidentally being infected in a lab, and then spreading the virus to the population at large, would have had to happen twice, says Garry. It's much more likely that the pandemic has its origins in the wildlife trade, he says.

To gather more evidence, the team behind the new analysis now plans to run computer simulations to test how well multiple spillovers would fit with the diversity of known SARS-CoV-2 genomes.

doi: <https://doi.org/10.1038/d41586-021-02519-1>

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