



Raccoon dogs are susceptible to SARS-CoV-2 and were sold at many markets in Wuhan, China.

# DID THE CORONAVIRUS JUMP FROM ANIMALS TO PEOPLE TWICE?

An unverified analysis of viral genomes suggests that the pandemic might have multiple animal origins.

By Smriti Mallapaty

**S**ARS-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 the pandemic originated in multiple markets in Wuhan, China, and make the hypothesis that SARS-CoV-2 escaped from a laboratory less likely, say some researchers. But the data need to be verified, and the analysis has not yet been peer reviewed.

The earliest viral sequences, taken from people infected in late 2019 and early 2020, are split into two broad lineages, known as A and B, which have key genetic differences.

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, 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 (see [go.nature.com/399feg](https://go.nature.com/399feg)).

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 lineages and there were two spillovers, it all but eliminates the idea that it came from a lab.”

The findings are “consistent with there being at least two introductions of SARS-CoV-2 into

the human population”, says David Robertson, a virologist at the University of Glasgow, UK.

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 latest 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,” says study co-author Michael Worobey, an evolutionary biologist at the University of Arizona, in Tucson.

Such sequencing errors are not unusual, say researchers. Software can sometimes fill in gaps in the raw data with incorrect sequences, and viral samples can become contaminated, notes Richard Neher, a computational biologist at the University of Basel in Switzerland. “Such mishaps are not surprising,” he says. “Especially early in the pandemic, when protocols weren’t very established and people tried to generate data as fast as they could.”

Several researchers who sequenced samples included in the study told *Nature* 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 ‘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

GREG BAKER/AFP VIA GETTY

“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 that multiple individual animals, of one or more species, that were carrying a progenitor of SARS-CoV-2 could have been transported across Wuhan, infecting people in at least two locations.

A study published in June found that live animals susceptible to SARS-CoV-2, such as raccoon dogs and mink, were sold in numerous markets in Wuhan (X. Xiao *et al. Sci. Rep.* **11**, 11898; 2021). Previous studies of the virus

that caused severe acute respiratory syndrome (SARS) have concluded that it, too, probably jumped multiple times from animals to people (L. F. Wang and B. T. Eaton *Curr. Top. Microbiol. Immunol.* **315**, 325–344; 2007).

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 had its origins in the wildlife trade, he says.

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

plume of carbon might have been indirectly sucked up by a gigantic phytoplankton bloom in the Southern Ocean.

The unprecedented fires burnt across as much as 74,000 square kilometres of mostly eucalyptus, or gum, forest in southeast Australia – an area larger than Sri Lanka.

Previous estimates from global databases of wildfire emissions based on satellite data suggested that the fires released about 275 million tonnes of CO<sub>2</sub> during their zenith, between November 2019 and January 2020.

But the latest analysis indicates that this figure was a gross underestimate, says Ivar van der Velde, lead author of the first paper. “These models often lack the spatio-temporal detail to explain the full impact these fires have,” says van der Velde, an environmental scientist at the SRON Netherlands Institute for Space Research, in Utrecht, and at the Free University of Amsterdam.

He and his team set out to get a better estimate, based on more-granular data from the tropospheric monitoring instrument TROPOMI on the European Space Agency's Sentinel-5 Precursor satellite.

TROPOMI takes daily snapshots of carbon monoxide levels in the atmospheric column beneath it. The researchers used these data to calculate a more accurate estimate of the carbon monoxide emissions from the bush fires, which they used as a proxy for calculating CO<sub>2</sub> emissions.

Their final figure – 715 million tonnes – is nearly 80 times the typical amount of CO<sub>2</sub> emitted from fires in southeast Australia during the three peak months of the summer bush-fire season.

Bowman says the figure is similar to what his team calculated from the area of forests burnt<sup>3</sup>, but much higher than figures based on previous satellite measurements of emissions.

The key question is how these forests will recover, says Cristina Santín, a wildfire researcher at the Spanish National Research Council in Asturias. Wildfires have long been considered net-zero-carbon events, because the emissions they release are recaptured when the vegetation regrows – but if fires “threaten the recovery of the ecosystem, then we really need to worry”, she says.

The second paper, also published last week, could give researchers reason to hope, however. It suggests that the emissions generated by the bush-fire crisis were nearly offset by gigantic phytoplankton blooms in the Southern Ocean, recorded over the summer of 2019–20.

The findings demonstrate how wildfires can directly influence ocean processes, says study co-author Richard Matear, a climate scientist based in Hobart with the Australian government's Commonwealth Scientific and Industrial Research Organisation. “The systems are connected.”

# AUSTRALIAN BUSH FIRES BELCHED OUT IMMENSE QUANTITY OF CARBON

Plankton mopped some of it up, but scientists might have to rethink the climate impact of extreme blazes.

By Smriti Mallapaty

**T**he extreme fires that blazed across southeastern Australia in late 2019 and early 2020 released 715 million tonnes of carbon dioxide into the air – more than double the emissions previously estimated from satellite data, according to an analysis<sup>1</sup> published last week in *Nature*.

“That is a stupendous amount,” says David Bowman, a fire ecologist at the University of Tasmania in Hobart, who adds that scientists might have to rethink the impact on global climate of extreme blazes, which have now raged not just across Australia, but across the western United States and Siberia.

It's not all bad news, however. Another paper<sup>2</sup> in *Nature* reports that much of this



Sydney is encircled by huge bush fires that shroud it in smoke on 21 December 2019.