# News in focus


NOEL CELIS/AFP VIA GETTY

**Police in Wuhan, China, shut down the Huanan Seafood Wholesale Market on 1 January 2020.**

## WUHAN MARKET WAS EPICENTRE OF PANDEMIC'S START, STUDIES SUGGEST

Report authors say that SARS-CoV-2 jumped to people from animals sold at the market on two occasions in late 2019 — but some scientists want more-definitive evidence.

**By Amy Maxmen**

Scientists have released three studies that reveal intriguing new clues about how the COVID-19 pandemic started. Two of the reports trace the outbreak back to a massive market that sold live animals, among other goods, in Wuhan, China[1,2], and a third[3] suggests that the coronavirus SARS-CoV-2 spilled over from animals — possibly those sold at the market — to humans at least twice in November or December 2019. Posted on 25 and 26 February, all three are preprints, and so have not been published in a peer-reviewed journal.

These analyses add weight to original suspicions that the pandemic began at the Huanan Seafood Wholesale Market, which many of the people who were infected earliest with SARS-CoV-2 had visited. The preprints contain genetic analyses of coronavirus samples collected from the market and from people infected in December 2019 and January 2020, as well as geolocation analyses connecting many of the samples to a section of the market where live animals were sold. Taken together, these lines of evidence point towards the market as the source of the outbreak — a situation akin to that seen in the epidemic of severe acute respiratory syndrome (SARS) in 2002–04, for which animal markets were found to be ground zero — says Kristian Andersen, a virologist at Scripps Research in La Jolla, California, and a co-author of two of the reports. "This is extremely strong evidence," he says.

However, none of the studies contains definitive evidence about what type of animal might have harboured the virus before it spread to humans. Andersen speculates that the culprits could be raccoon dogs, squat dog-like mammals used for food and their fur in China. One of the studies he co-authored[2] suggests that raccoon dogs were sold in a section of the market where several positive samples were

collected. And reports[4] show that the animals can harbour other types of coronavirus.

Nevertheless, some virologists say that the evidence pointing to the Huanan market doesn't rule out an alternative hypothesis. They say that the market could just have been the location of a massive amplifying event — in which an infected person spread the virus to many other people — rather than the site of the original spillover.

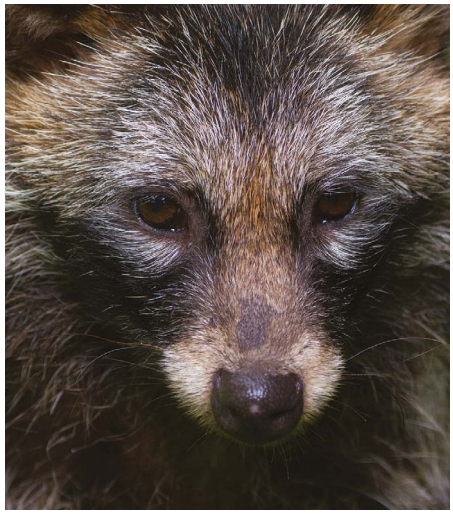
"Analysis-wise, this is excellent work, but it remains open to interpretation," says Vincent Munster, a virologist at the Rocky Mountain Laboratories, a division of the US National Institutes of Health in Hamilton, Montana. He says that searching for SARS-CoV-2 and antibodies against it in blood samples collected from animals sold at the market, and from people who sold animals at the market, could provide more-definitive evidence of COVID-19's origins. The number of positive samples from the market does suggest an animal source, Munster says. But he is frustrated that more-thorough investigations haven't already been conducted: "We are talking about a pandemic that has upended the lives of so many people."

## Ground zero?

In early January 2020, Chinese authorities identified the Huanan market as a potential source of a viral outbreak because most people infected with COVID-19 at that time had been there in the days before they began to show symptoms, or were in contact with people who had been. Hoping to stem the outbreak, the authorities closed the market. Researchers then collected samples from poultry, snakes, badgers, giant salamanders, crocodiles and other animals sold there. They also swabbed drains, cages, toilets and vendors' stalls in search of the pathogen. In March 2021, after an investigation led by the World Health Organization (WHO), researchers released a report showing that all of the nearly 200 samples collected directly from animals were negative, but that around 1,000 environmental samples from the stalls and other areas of the market were positive.

A team in China including researchers at China's Center for Disease Control and Prevention (CDC) has now sequenced genetic material recovered from those positive samples, and released the results in a preprint posted on 25 February[1]. The scientists confirm that the samples contain SARS-CoV-2 sequences almost identical to those that have been circulating in humans. Furthermore, they show that the two original virus lineages circulating at the start of the pandemic, called A and B, were both present at the market.

"It's a nice piece of work," says Ray Yip, an epidemiologist and a former director of the China branch of the US Centers for Disease Control and Prevention. "They've confirmed that the Huanan market was indeed a very important spreading location."



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**Raccoon dogs have been sold at the Huanan market.**

As soon as the report from China had been posted online, Andersen and his colleagues rushed to post manuscripts they had been working on for weeks.

In one[2], the team zeroed in on the southwestern section of the Huanan market, where live animals were sold as recently as 2019, as being the potential epicentre of the outbreak. The researchers arrived at this conclusion by compiling information on the first known COVID-19 cases in China, as reported by various sources, including the WHO investigation, newspaper articles and audio and video recordings of doctors and patients in Wuhan. This geospatial analysis found that 156 cases that occurred in December 2019 were clustered tightly around the market, with cases gradually becoming more dispersed across Wuhan during January and February 2020.

The authors also examined the locations of the positive samples collected in the market, as reported in the WHO study. One major finding reported by Andersen and his colleagues is the mapping of five positive samples from the market to a single stall that sold live animals, and, more specifically, to a metal cage, to carts used to move animals and to a machine used to remove birds' feathers[2]. One of the report's co-authors, virologist Eddie Holmes at the University of Sydney in Australia, had been to this stall in 2014 and snapped photographs — included in the study — of a live raccoon dog in a metal cage, stacked above crates of poultry, with the whole assembly sitting on top of sewer drains. Notably, in the study by researchers at the China CDC, sewage at the market tested positive for SARS-CoV-2.

In a second report[3], Andersen and his colleagues concluded that, genetically, lineage A and lineage B of SARS-CoV-2 are too different from one another for one to have evolved into the other quickly in humans. Therefore, they suggest that the coronavirus must have evolved in non-human animals and that the two lineages spread to humans separately. For several reasons, including the fact that lineage B was much more prevalent in January 2020, the authors suggest that it spilled over into humans before lineage A. Other outbreaks of coronaviruses, such as the SARS and Middle East respiratory syndrome epidemics, also resulted from repeated introductions from wildlife, the paper notes.

## 'As good as it gets'

Over the past year, Michael Worobey, a virologist at the University of Arizona in Tucson and a co-author of the papers with Andersen[2,3], says that his thinking on the origins of COVID-19 has shifted. In May 2021, he led a letter published in *Science*[5] in which he and others pressed the scientific community to keep an open mind about whether the pandemic had come from a laboratory, a controversial hypothesis suggesting that SARS-CoV-2 was either created in a lab or was accidentally or intentionally released by researchers at the Wuhan Institute of Virology. "You want to take this kind of thing seriously," he explains.

But since then, other evidence has come to light that supports a zoonotic origin story similar to those of HIV, Zika virus, Ebola virus and multiple influenza viruses, he says. "When you look at all of the evidence, it is clear that this started at the market." Separate lines of analysis point to it, he says, and it's extremely improbable that two distinct lineages of SARS-CoV-2 could have been derived from a laboratory and then coincidentally ended up at the market.

Nonetheless, Munster is not completely convinced that there were two spillover events, because the virus might have evolved from one lineage into the other in a person with a compromised immune system. He says that more data collected from people and animals are needed to answer this question, and to show that the first spillover occurred at the Huanan market.

Holmes fears that additional samples from early human cases and from animals might never materialize. Last July, for example, Chinese officials said that they planned to analyse patient blood samples from 2019, stored at the Wuhan Blood Center — but if that study has been conducted, it has yet to be made public. "This is as good as it gets," Holmes says. "What we should focus on now is trying to keep these events from happening again."


1. Gao, G. *et al*. Preprint at Research Square https://doi.org/10.21203/rs.3.rs-1370392/v1 (2022).
2. Worobey, M. *et al*. Preprint at Zenodo https://doi.org/10.5281/zenodo.6299600 (2022).
3. Pekar, J. E. *et al*. Preprint at Zenodo https://doi.org/10.5281/zenodo.6291628 (2022).
4. He, W.-T. *et al*. *Cell* https://doi.org/10.1016/j.cell.2022.02.014 (2022).
5. Bloom, J. D. *et al*. *Science* **372**, 694 (2021).