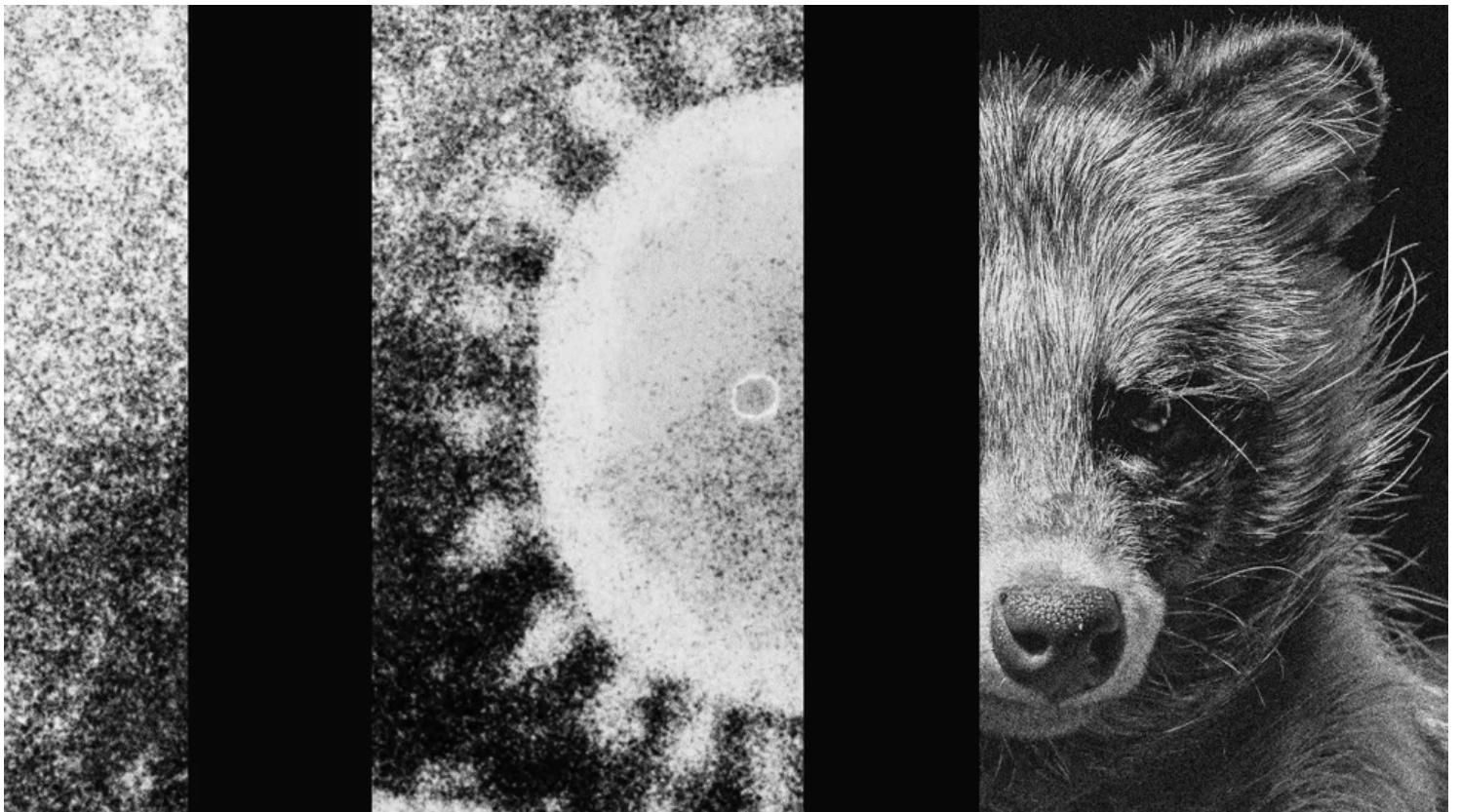


SCIENCE

The Strongest Evidence Yet That an Animal Started the Pandemic

A new analysis of genetic samples from China appears to link the pandemic's origin to raccoon dogs.


By Katherine J. Wu



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For three years now, the debate over the origins of the coronavirus pandemic has ping-ponged between two big ideas: that SARS-CoV-2 spilled into human populations directly from a wild-animal source, and that the pathogen leaked from a lab. Through a swirl of data obfuscation by Chinese authorities and politicalization within the United States, and rampant speculation from all corners of the world, many scientists have stood by the notion that this outbreak—like most others—had purely natural roots. But that hypothesis has been missing a key piece of proof: genetic evidence from the Huanan Seafood Wholesale Market in Wuhan, China, showing that the virus had infected creatures for sale there.

Now, an international team of virologists, genomicists, and evolutionary biologists may have finally found crucial data to help fill that knowledge gap. A new analysis of genetic sequences collected from the market shows that raccoon dogs being illegally sold at the venue could have been carrying and possibly shedding the virus at the end of 2019. It's some of the strongest support yet, experts told me, that the pandemic began when SARS-CoV-2 hopped from animals into humans, rather than in an accident among scientists experimenting with viruses.

“This really strengthens the case for a natural origin,” says Seema Lakdawala, a virologist at Emory University who wasn't involved in the research. Angela Rasmussen, a virologist involved in the research, told me, “This is a really strong indication that animals at the market were infected. There's really no other explanation that makes any sense.”

The findings won't fully convince the entrenched voices on either side of the origins debate. But the new analysis may offer some of the clearest and most compelling

evidence that the world will *ever* get in support of an animal origin for the virus that, in just over three years, has killed nearly 7 million people worldwide.

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The genetic sequences were pulled out of swabs taken in and near market stalls around the pandemic's start. They represent the first bits of raw data that researchers outside of China's academic institutions and their direct collaborators have had access to. A few weeks ago, the data appeared on an open-access genomic database called GISAID, after being quietly posted by researchers affiliated with the country's Center for Disease Control and Prevention. By almost pure happenstance, scientists in Europe, North America, and Australia spotted the sequences, downloaded them, and began an analysis.

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The samples were already known to be positive for the coronavirus, and had been scrutinized before by the same group of Chinese researchers who uploaded the data to GISAID. But that prior analysis, released as a preprint publication in February 2022, asserted that “no animal host of SARS-CoV-2 can be deduced.” Any motes of coronavirus at the market, the study suggested, had most likely been chauffeured in by infected humans, rather than wild creatures for sale.

The new analysis, led by Kristian Andersen, Edward Holmes, and Michael Worobey—three prominent researchers who have been looking into the virus’s roots—shows that that may not be the case. Within about half a day of downloading the data from GISAID, the trio and their collaborators discovered that several market samples that tested positive for SARS-CoV-2 were also coming back chock-full of animal genetic material—much of which was a match for the common raccoon dog, a small animal related to foxes that has a raccoon-like face. Because of how the samples were gathered, and because viruses can’t persist by themselves in the environment, the scientists think that their findings could indicate the presence of a coronavirus-infected raccoon dog in the spots where the swabs were taken. Unlike many of the other points of discussion that have been volleyed about in the origins debate, the genetic data are “tangible,” Alex Crits-Christoph, a computational biologist and one of the scientists who worked on the new analysis, told me. “And this is the species that everyone has been talking about.”

Finding the genetic material of virus and mammal so closely co-mingled—enough to be extracted out of a single swab— isn't perfect proof, Lakdawala told me. "It's an important step; I'm not going to diminish that," she said. Still, the evidence falls short of, say, isolating SARS-CoV-2 from a free-ranging raccoon dog or, even better, uncovering a viral sample swabbed from a mammal for sale at Huanan from the time of the outbreak's onset. That would be the virological equivalent of catching a culprit red-handed. But "you can never go back in time and capture those animals," says Gigi Gronvall, a senior scholar at the Johns Hopkins Center for Health Security. And to researchers' knowledge, "raccoon dogs were not tested at the market and had likely been removed prior to the authorities coming in," Andersen wrote to me in an email. He underscored that the findings, although an important addition, are not "direct evidence of infected raccoon dogs at the market."

Still, the findings don't stand alone. "Do I believe there were infected animals at the market? Yes, I do," Andersen told me. "Does this new data add to that evidence base? Yes." The new analysis builds on extensive previous research that points to the market as the source of the earliest major outbreak of SARS-CoV-2: Many of the earliest known COVID-19 cases of the pandemic were clustered roughly in the market's vicinity. And the virus's genetic material was found in many samples swabbed from carts and animal-processing equipment at the venue, as well as parts of nearby infrastructure, such as storehouses, sewage wells, and water drains. Raccoon dogs, creatures commonly bred for sale in China, are also already known to be one of many mammal species that can easily catch and spread the coronavirus. All of this left one main hole in the puzzle to fill: clear-cut evidence that raccoon dogs and the virus were in the exact same spot at the market, close enough that the creatures might have been infected and, possibly, infectious. That's what the new analysis provides. Think of it as finding the DNA of an investigation's main suspect at the scene of the crime.

The findings don't rule out the possibility that other animals may have been carrying SARS-CoV-2 at Huanan. Raccoon dogs, if they were infected, may not even be the creatures who passed the pathogen on to us. Which means the search for the virus's many wild hosts will need to plod on. "Do we know the intermediate host was raccoon dogs? No," Andersen wrote to me, using the term for an animal that can ferry a pathogen between other species. "Is it high up on my list of potential hosts? Yes, but it's definitely not the only one."

On Tuesday, the researchers presented their findings at a hastily scheduled meeting of the World Health Organization's Scientific Advisory Group for the Origins of Novel Pathogens, which was also attended by several of the Chinese researchers responsible for the original analysis, according to multiple researchers who were not present but were briefed about it before and after by multiple people who were there. Shortly after the meeting, the Chinese team's preprint went into review at a Nature Research journal—suggesting that a new version was being prepared for publication.

At this point, it's still unclear why the sequences were so recently posted to GISAID. They also vanished from the database shortly after the international team of researchers notified the Chinese researchers of their preliminary findings, without explanation. When I emailed George Gao, the former China CDC director-general and the lead author on the original Chinese analysis, asking for his team's rationale, I didn't immediately receive a response—though he later [told Jon Cohen at *Science* magazine](#) that this latest analysis represent "nothing new." Given what was in the GISAID data, it does seem that raccoon dogs could have been introduced into and clarified the origins narrative far sooner—at least a year ago, and likely more. On Friday, at a press briefing, Tedros Adhanom Ghebreyesus, WHO's director general, addressed the disappearing data, as well as the extreme lag with which it was posted to GISAID in the first place. "These data could have and should have been shared three years ago," he told reporters. "We continue to call on China to be transparent in sharing data and to conduct the necessary investigations to share the results." Maria Van Kerkhove, WHO's COVID-19 technical lead, also told me that the rapid unfolding of these events "is an indication to me in recent days that there is more data that exists" that could further clarify the pandemic's origins. And if that's the case,

those data, especially any that speak to what has unfolded within China's borders, need "to be made available immediately."

China has, for years, been keen on pushing the narrative that the pandemic didn't start within its borders. In early 2020, a Chinese official suggested that the novel coronavirus may have emerged from a U.S. Army lab in Maryland. The notion that a dangerous virus sprang out from wet-market mammals echoed the beginnings of the SARS-CoV-1 epidemic two decades ago—and this time, officials immediately shut down the Huanan market, and vehemently pushed back against assertions that live animals being sold illegally in the country were to blame; a WHO investigation in March 2021 took the same line. "No verified reports of live mammals being sold around 2019 were found," the report stated. But just three months later, in June 2021, a team of researchers published a study documenting tens of thousands of mammals for sale in wet markets in Wuhan between 2017 and late 2019, including at Huanan. The animals were kept in largely illegal, cramped, and unhygienic settings—conditions conducive to viral transmission—and among them were more than 1,000 raccoon dogs. Holmes himself had been at the market in 2014 and snapped a photo at Stall 29, clearly showing a raccoon dog in a cage; another set of images from the venue, captured by a local in December 2019 and later shared on Weibo, caught the animals on film as well—right around the time that the first recorded SARS-CoV-2 infections in humans occurred.

And yet, Chinese researchers maintained their stance. As Cohen reported last year, scientists from several of China's largest academic institutions posted a preprint in September 2021 concluding that a massive nationwide survey of bats—the likeliest original source of the coronavirus before it jumped into an intermediate host, such as raccoon dogs, and then into us—had turned up no relatives of SARS-CoV-2. The implication, the team behind the paper asserted, was that relatives of the coronavirus were “extremely rare” in the region, making it unlikely that the pandemic had started there. The findings directly contradicted others showing that cousins of SARS-CoV-2 were indeed circulating in China's bats. (Local bats have also been found to harbor viruses related to SARS-CoV-1.)

The original Chinese analysis of the Huanan market swabs, from February 2022, also stuck with China's party line on the pandemic. One of the report's graphs suggested that viral material at the market had been mixed up with genetic material of *multiple* animal species—a data trail that should have led to further inquiry or conclusions, but that the Chinese researchers appear to have ignored. Their report noted only humans as being linked to SARS-CoV-2, stating that its findings “highly” suggested that any viral material at the market came from people (at least one of whom, presumably, picked it up elsewhere and ferried it into the venue). The Huanan market, the study's authors wrote, “might have acted as an amplifier” for the epidemic. But “more work involving international coordination” would be needed to suss out the “real origins of SARS-CoV-2.”

The wording of that report baffled many scientists in Europe, North America, and Australia, several of whom had, almost exactly 24 hours after the release of the China CDC preprint, published early versions of their own studies, concluding that the Huanan market was the pandemic's probable epicenter—and that SARS-CoV-2

might have made its hop into humans from the venue *twice* at the end of 2019. Itching to get their hands on China CDC's raw data, some of the researchers took to regularly trawling GISAID, occasionally at odd hours. Last Thursday evening, after spotting the sequences, Florence Débarre, an evolutionary biologist at the French National Centre for Scientific Research, alerted her colleagues about their availability. Stumbling across the data, which she was not expecting to pop up, was “a total surprise,” Débarre told me.

Within hours of downloading the data and starting their own analysis, the researchers found their suspicions confirmed. Several surfaces in and around one stall at the market, including a cart and a defeathering machine, produced virus-positive samples that also contained genetic material from raccoon dogs—in a couple of cases, at higher concentrations than of human genomes. It was Stall 29—the same spot where Holmes had snapped the photo of the raccoon dog, nearly a decade before.

Slam-dunk evidence for a raccoon-dog host—or another animal—could still emerge. In the hunt for the wild source of MERS, another coronavirus that caused a deadly outbreak in 2012, researchers were eventually able to identify the pathogen in camels, which are thought to have caught their initial infection from bats—and which still harbor the virus today; a similar story has played out for Nipah virus, which hopscotched from bats to pigs to us.

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Proof of that caliber, though, may never turn up for SARS-CoV-2. (Nailing wild origins is rarely simple: Despite a years-long search, the wild host for Ebola still has

not been definitively pinpointed.) Which leaves just enough ambiguity to keep debate about the pandemic's origins running, potentially indefinitely. Skeptics will likely be eager to poke holes in the team's new findings—pointing out, for instance, that it's technically possible for genetic material from viruses and animals to end up slogged together in the environment even if an infection didn't take place. Maybe an infected human visited the market and inadvertently deposited viral RNA near an animal's crate.

But an infected animal, with no third-party contamination, still seems by far the most plausible explanation for the samples' genetic contents, several experts told me; other scenarios require contortions of logic and, more important, additional proof. Even prior to the reveal of the new data, Gronvall told me, "I think the evidence is actually more sturdy for COVID than it is for many others." The strength of the data might even, in at least one way, best what's available for SARS-CoV-1: Although scientists have isolated SARS-CoV-1-like viruses from a wet-market-traded mammal host, the palm civet, those samples were taken months after the outbreak began—and the viral variants found weren't exactly identical to the ones in human patients. The versions of SARS-CoV-2 tugged out of several Huanan-market samples, meanwhile, are a dead ringer for the ones that sickened humans with COVID early on.

The debate over SARS-CoV-2's origins has raged for nearly as long as the pandemic itself—outlasting lockdowns, widespread masking, even the first version of the COVID vaccines. And as long as there is murkiness to cling to, it may never fully resolve. While evidence for an animal spillover has mounted over time, so too have questions about the possibility that the virus escaped from a laboratory. When President Joe Biden asked the U.S. intelligence community to review the matter, four government agencies and the National Intelligence Council pointed to a natural

origin, while two others guessed that it was a lab leak. (None of these assessments were made with high confidence; a bill passed in both the House and the Senate would, 90 days after it becomes a law, require the Biden administration to declassify underlying intelligence.)

If this new level of scientific evidence does conclusively tip the origins debate toward the animal route, it will be, in one way, a major letdown. It will mean that SARS-CoV-2 breached our borders because we once again mismanaged our relationship with wildlife—that we failed to prevent this epidemic for the same reason we failed, and could fail again, to prevent so many of the rest.

This article originally stated that the raw data appeared on GISAID late last week. In fact, some of the data appeared even earlier.
