

ELEMENTS

THE MYSTERIOUS CASE OF THE COVID-19 LAB-LEAK THEORY

Did the virus spring from nature or from human error?

By Carolyn Kormann

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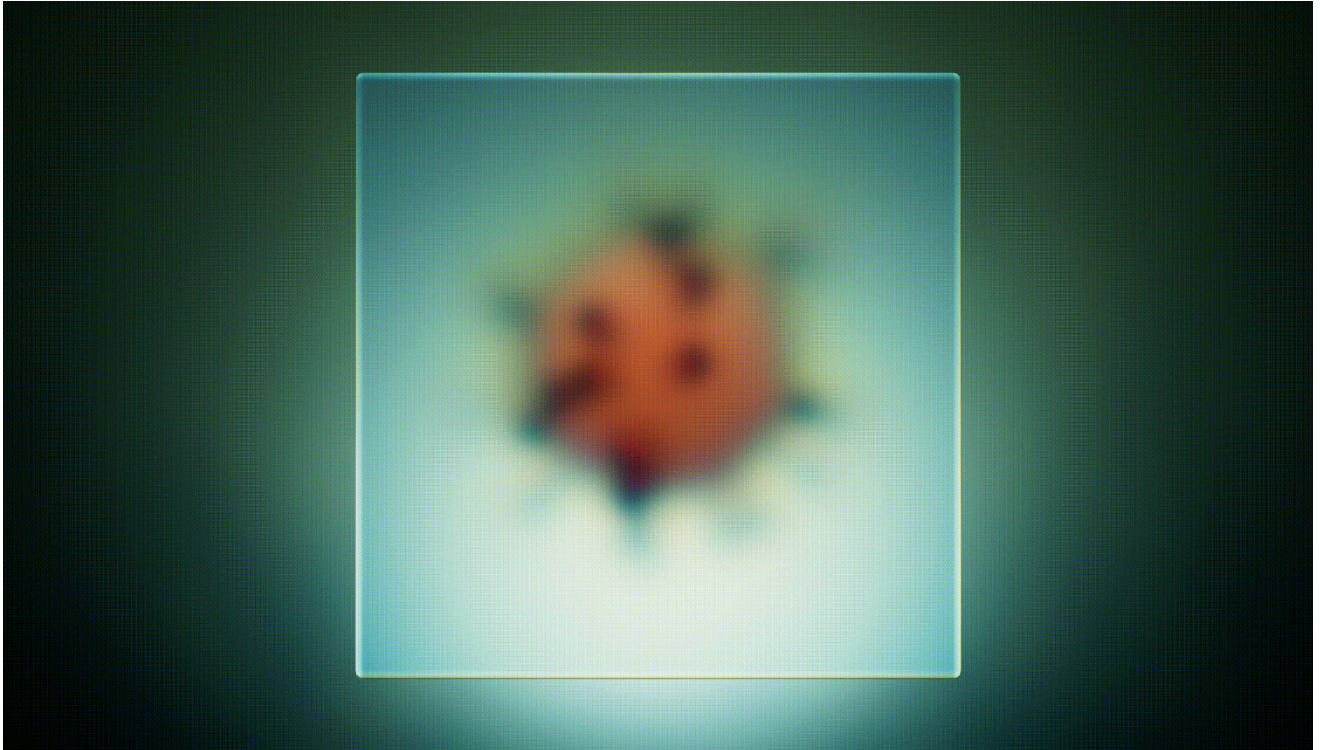


Illustration by Rad Mora

Since the coronavirus first appeared, at the end of 2019, four and a half million people have died, countless more have suffered, whole economies have been upended, schools have been shuttered. Why? Did the virus jump from an animal to its first human host, its patient zero? Or, as some suspect, was the catastrophe the result of a laboratory accident in Wuhan, a city of eleven million people in central China?

Kristian Andersen, an infectious-disease expert at Scripps Research, in San Diego, began tracking the virus in January, 2020. He found the degree of contagion not just scary but unusual. Chinese scientists had already established that it belonged to a genus of coronaviruses commonly found in bats in southern China. It shared eighty per cent of its genome with the first SARS, and was more distantly related to MERS, another bat coronavirus. This new virus, however, was spreading far more quickly, reaching at least

twenty-six countries by the end of the month. “It seemed to be locked and loaded for causing the pandemic,” Andersen told me. Most viruses circulating in the wild, though some can be deadly, are not very good at transmission. They are still animal viruses. “This, almost from Day One,” Andersen said, “appeared like a human virus.”

Andersen, who is originally from Denmark, is wiry and clean cut, with a cleft chin and clipped enunciation. He was working at the post office in Aarhus when he decided he might study molecular biology, and went on to become the first person in his family to attend university. His career took off with investigations into the emergence of West Nile virus, Ebola, and Zika. After the pandemic began, he was among the scientists whom Anthony Fauci, the director of the National Institute of Allergy and Infectious Diseases, consulted regarding the origins of the virus. On January 31, 2020, according to an e-mail obtained by BuzzFeed News, Andersen wrote to Fauci and others that the SARS-CoV-2 genome seemed “inconsistent with expectations from evolutionary theory.”

Read *The New Yorker's* complete news coverage and analysis of the coronavirus pandemic.

Andersen noted that “a really small part” of SARS-CoV-2’s genome had “unusual features.” Its spike—the crucial bit of surface protein that a coronavirus uses to invade a cell—appeared able to bind tightly to a human-cell receptor known as ACE2. This, Andersen told me, “means that it’s more effective at infecting human cells.” The other significant trait, a rare insertion in the genome of twelve nucleotides, called a furin cleavage site, might also increase the virus’s transmissibility, and lower the species barrier, allowing the virus to jump more easily to humans. “One has to look really closely at all the sequences to see that some of the features (potentially) look engineered,” he wrote. There was much more data to analyze, he continued, “so those opinions could still change.”

A day later, Andersen joined a conference call with a group of prominent virologists and government officials, including Fauci and Francis Collins, the director of the National Institutes of Health. Andersen presented a summary of the notable features of the SARS-CoV-2 genome, and asked the group, “Do we think this is unusual?” Fauci recalled that, among the participants, opinions were divided. “Knowledgeable people were saying, It does look like it could be something that might be engineered, because it’s not something you usually see,” he told me. “Then you have somebody else equally as knowledgeable say, Oh, nonsense, you can see that in other situations.”

Some comments about the meeting, e-mailed among the group after the call, were redacted. But three days later, on February 4th, Andersen’s perspective shifted. In an e-mail to a different group of scientists, which was recovered by U.S. Right to Know, an investigative group, Andersen wrote, “The main crackpot theories going around at the moment relate to this virus being somehow engineered with intent and that is demonstrably not the case.”

By March, Andersen and a few of his colleagues had finalized a letter, to be published by *Nature Medicine*, arguing that SARS-CoV-2 had naturally spilled over from a bat, evolving into a pandemic virus either in an animal host or, unnoticed, in humans. “Our analyses clearly show that SARS-CoV-2 is not a laboratory construct or a purposefully manipulated virus,” they wrote. The paper was extremely influential. In the ensuing months, the scientific consensus, echoed by a number of mainstream media outlets, took the same view, that the virus most likely resulted from a natural zoonotic spillover.

On a recent Zoom call, Andersen sat at his desk, overlooking the Pacific Ocean. He told me that his initial suspicions reflected the fact that he hadn’t known enough about coronaviruses. His use of the term “crackpot theories,” he said, was a reference, in part, to an article that was circulating at the time, which claimed that SARS-CoV-2 was engineered with genetic inserts from H.I.V. He also had referred to himself as a crackpot in earlier discussions, he said, since his suspicions about viral engineering were not widely shared. “I think there were people that thought I was an idiot for even suggesting it came from a lab.”

As the pandemic progressed, not everyone was convinced by the natural-origin explanation. A zoonotic spillover would likely require an intermediate animal between bats and humans, but no such species has yet been identified. Initially, the Huanan market, in Wuhan, which sold fish, produce, and meat, seemed like the source of SARS-CoV-2. Nearly a third of the hundred and seventy-four earliest known cases were linked to Huanan. And yet, patient zero likely was not. Chinese officials have said he was a middle-aged accountant, surnamed Chen, who developed symptoms on December 8th, and typically shopped at a supermarket across the river. In May of 2020, George Fu Gao, the director of the Chinese Center for Disease Control and Prevention, said, “At first, we assumed the seafood market might have the virus, but now the market is more like a victim. The novel coronavirus had existed long before.”

Among skeptics, many of them credentialed scientists, others amateur online sleuths—including some full-blown QAnon conspiracy theorists—another theory took shape. Wuhan is home to the Wuhan Institute of Virology (W.I.V.), which, since the first SARS epidemic, has amassed one of the largest libraries of bat coronaviruses in the world; some nineteen thousand samples are stored in its labs. Its scientists have collaborated closely with international teams of virus hunters, published in leading academic journals, and received hundreds of thousands of dollars in research grants from the U.S. government. The W.I.V. also frequently partners with the Wuhan Center for Disease Control and Prevention, which, in the fall of 2019, moved its lab to a new location near the Huanan market.

Circumstantial evidence supporting a new narrative—that the pandemic might have started from a lab accident in Wuhan—began to accumulate in late 2020. Online data sets from the W.I.V. had disappeared, information on a previous outbreak had been elided, and W.I.V. researchers were conducting experiments with engineered viruses. Even Andersen acknowledged that the emergence of the virus in Wuhan is “a crazy coincidence.” In May, 2021, a group of prominent scientists published a letter in *Science*, calling for an origins investigation that took the lab-leak hypothesis seriously. Reports then emerged, from U.S. intelligence sources, that three W.I.V. researchers had fallen ill with COVID-19-like symptoms, and sought hospital care, in November of 2019.

In response, President Biden called for an investigation into the pandemic’s origins. “I have now asked the intelligence community to redouble their efforts to collect and analyze information that could bring us closer to a definitive conclusion,” he said. The National Counterproliferation Center, whose mission is to prevent the spread of weapons of mass destruction, was tapped to facilitate the effort. According to an unclassified summary of the investigation’s findings, released in August, the virus was not developed as a biological weapon, its sudden emergence caught Chinese officials off guard, and it infected humans no later than November, 2019, “with the first known cluster of COVID-19 cases arising in Wuhan, China, in December.” Otherwise, all agencies agreed that two origin hypotheses remained “plausible”: a “natural exposure to an infected animal and a laboratory-associated incident.”

In the spring of 2012, six men who worked clearing bat guano from an abandoned copper mine near the town of Tongguan, in Yunnan Province, fell ill with a severe respiratory disease. They were admitted to a university hospital in Kunming, which sent blood samples from four of the men to the lab of Shi Zhengli, the head of the W.I.V.’s Center for Emerging Infectious Disease. Shi is China’s most famous researcher of bat coronaviruses. Years earlier, she had joined the international team that discovered that horseshoe bats served as a reservoir for a large number of SARS-related viruses. Her lab tested the workers’ serum for possible zoonotic pathogens that Shi and others had previously discovered. Everything came back negative. Three of the workers died.

Between 2012 and 2015, Shi and her team regularly travelled to the Tongguan mine, about a thousand miles from Wuhan. In the evenings, the researchers strung up a mist net at an entrance to the mineshaft, and waited for dusk, when the bats flew out to eat. Throat and fecal swabs were collected from six different species of horseshoe and vesper bats. Ultimately, Shi’s team brought back more than thirteen hundred samples to their lab.

In 2016, Shi and her colleagues published a paper from this work, finding that many of the bats were co-infected by two or more different coronaviruses at the same time. Because the bats live huddled in ever-shifting colonies, they circulate viruses endlessly, even across species, which allows different viruses to recombine, creating novel coronavirus strains: an evolutionary bacchanal. Eventually, Shi's lab would sequence some portion of all nine SARS-related coronaviruses that were found in samples taken from the Tongguan mine.

Three years later, in the final days of 2019, Shi received samples from seven patients sick with a novel virus that was quietly ravaging Wuhan. Once Shi sequenced the virus, SARS-CoV-2, she scoured the W.I.V. databases for any evidence of a genetic match. The closest relative that she found, according to a paper that she and her colleagues published, in *Nature*, in February, 2020, was a bat coronavirus that was ninety-six-per-cent the same as SARS-CoV-2. She called it RaTG13. "Ra" stood for the bat species, *Rhinolophus affinis*, or the intermediate horseshoe bat; "TG" stood for the place, Tongguan; and "13" was the year it was discovered, 2013.

Within a few months, a scientist couple in India, Monali Rahalkar and Rahul Bahulikar, discovered a surprising link—one that Shi had failed to note in her paper. In a preprint journal article posted online, they stated that, according to their genetic analysis, RaTG13 appeared "100% similar" to a novel SARS-like coronavirus sample that Shi had described in her 2016 paper about the abandoned mineshaft, under a different name: RaBtCoV/4991. Oddly, neither of Shi's papers mentioned the sick workers who had led the scientists to the abandoned mineshaft in the first place.

A Twitter user named @TheSeeker268 e-mailed Rahalkar and Bahulikar a link to a 2013 master's thesis about the six workers' illnesses. The author, a medical student at Kunming Medical University, wrote that the six patients were treated with antivirals, antibiotics, and antifungals—similar to treatments for COVID-19. A prominent pulmonologist consulted with two of the patients remotely, and diagnosed them with pneumonia, primarily of viral origin, with a possible secondary fungal infection. The medical student concluded that the pneumonia cases were likely caused by SARS-like coronaviruses that had spilled over from horseshoe bats in the mine. A subsequent chapter in a Ph.D. thesis from 2016 (also unearthed by @TheSeeker268) by a student who was supervised by Gao, China's C.D.C. director, stated that blood samples from four of the patients, which were tested by the W.I.V., had antibodies to SARS-related coronaviruses, suggesting a previous infection.

After these findings were released, *Nature* published an addendum to Shi's RaTG13 paper that acknowledged the link to the mine. Shi clarified that her lab had fully sequenced RaTG13 in 2018, as the "technology and capability in our laboratory had improved." She also provided details about the tests that her lab had conducted on the workers' serum samples, and stated that the lab had recently retested the samples, this time for SARS-CoV-2. They were negative. She also said that no antibodies to a SARS-like coronavirus had been found.

The workers were not infected with SARS-CoV-2, or we would have COVID-12, not COVID-19. But among some scientists, the lack of transparency raised questions. Labs like the W.I.V. are expected to warn the world about viruses that might constitute a threat. In Tongguan, there was a mini outbreak of a life-threatening illness, which looked like SARS but wasn't SARS, in a mine thick with SARS-like bat coronaviruses. The Wuhan Institute of Virology said nothing about the infected workers, even when their cases had direct relevance to the pandemic, until after independent researchers had established the link.

@TheSeeker268 is a member of DRASTIC, or Decentralized Radical Autonomous Search Team Investigating COVID-19, which formed on Twitter and has been among the most aggressive advocates of the lab-leak theory. (Rahalkar and Bahulikar are loosely connected with the group as well.) In a tweet about the W.I.V. researchers and the Tongguan mine, @TheSeeker268 wrote, "In a nutshell: They haven't been forthcoming about their trips to the mine, the motive behind their trips, & all the CoVs they sampled."

Shi has firmly denied that she tried to suppress anything about the Tongguan mine. “I’ve just downloaded the Kunming Hospital University student’s master’s thesis and read it,” Shi told the BBC. “The conclusion is neither based on evidence nor logic. But it’s used by conspiracy theorists to doubt me.” Instead, she said in an interview with *Scientific American* last year, a fungus was the pathogen that had sickened the miners. “Bat guano, covered in fungus, littered the cave,” Shi said. Fungal infections are certainly a risk for spelunkers. But they are also a common secondary infection in pneumonia cases, as seen in some COVID-19 patients.

Linfu Wang, the director of the Programme in Emerging Infectious Diseases, at Duke-N.U.S. Medical School, in Singapore, is one of the world’s leading bat-virus experts, and has frequently collaborated with Shi. He had helped analyze the samples that were collected from the workers in 2012, and dismissed accusations that Shi kept data secret. “We wanted to prove that a coronavirus caused the deaths,” Wang told Science. “If we proved that another SARS-like virus was in humans in China that would have been scientifically brilliant.”

DRASTIC also exposed another mystery related to the W.I.V. In September, 2019, according to Web pages that DRASTIC archived, a W.I.V. database that was once publicly available was made inaccessible. It contained records pertaining to roughly twenty-two thousand samples, including, presumably, the sequences from Tongguan. When asked about it by the BBC, Shi said that the W.I.V. had “nothing to hide,” and that its Web site and staff e-mail “had been attacked,” so the database “was taken offline for security reasons.” The data still has not been made available.

There are twelve hundred different mutations between the genomes of RaTG13 and SARS-CoV-2—scattered variations that demonstrate the messiness of evolution. The number and distribution of these mutations are too large for RaTG13 to be the direct progenitor of SARS-CoV-2; they split from a common ancestor at least twenty years ago. But its genetic proximity means “we should look for the ancestors of SARS-CoV-2 in locations where relatives like RaTG13 are found,” Jesse Bloom, an evolutionary biologist at Fred Hutchinson Cancer Research Center, told me in September. “At this point, the closest relatives of SARS-CoV-2 are known to have existed in two locations: bat caves in Yunnan, and at the Wuhan Institute of Virology.”

Geography aside, the nature of the experiments undertaken by the W.I.V. and its partners has raised concerns. In 2015, Shi was a co-author on a groundbreaking study, in *Nature*, with Ralph Baric, a coronavirus expert at the University of North Carolina. Through the use of pioneering genetic technology, Baric examined which viral structures could give a coronavirus the ability to infect humans. The work involved synthesizing what is known as a chimeric virus, named for the mythical beast with its parts taken from various animals; in this case, a modified clone of SARS was combined with a spike protein taken from one of the bat coronaviruses that Shi had discovered in Yunnan.

Their research took place during a fraught time for virologists. Four years earlier, a Dutch scientist named Ron Fouchier decided to see if he could make the lethal avian influenza virus, H5N1, more transmissible. After failing to genetically reengineer the virus, Fouchier turned to a classic method: he passaged the virus through live ferrets repeatedly, forcing the virus to evolve in its new host. After ten rounds, the virus was airborne. He had created a pandemic-ready pathogen in his lab.

The experiment, which constituted a type of research known as “gain-of-function,” provoked alarm. There were high-level meetings, op-eds, and reports decrying such work as far riskier than it was valuable. In 2014, President Barack Obama mandated a pause on gain-of-function studies involving influenza, SARS, and MERS, until a new regulatory process could be created. Baric, however, was in the middle of his chimeric-virus experiment. He petitioned the N.I.H. biosecurity board, which granted him, and other researchers, an exemption from the pause.

When Baric tested the chimeric virus in a culture of human airway cells, its spike protein proved able to bind to the cell receptor ACE2, suggesting that the virus was now poised to jump species. In live mice, it caused disease. Given this unexpected outcome,

Baric concluded, “scientific review panels may deem similar studies building chimeric viruses based on circulating strains too risky to pursue.”

That didn’t happen. Baric’s experiments, which the N.I.H. had determined were not gain-of-function, continued at the University of North Carolina. Shi’s lab developed its own platform for creating chimeric viruses. She crossed another bat coronavirus from Yunnan—named wiv1—with clones of different novel spike proteins, and tested the creation in humanized mice. The viruses quickly replicated. One made the mice emaciated, a sign of severe pathogenesis. What made this work especially risky was that wiv1 was already known to be potentially dangerous to humans. Baric himself had made this clear in a [2016 study](#) titled “SARS-Like WIV1-CoV Poised for Human Emergence.”

Some of these experiments at the W.I.V. were funded by the U.S. government, according to Shi’s published papers, as well as N.I.H.-funded grant applications and progress reports obtained by the Intercept. In 2014, N.I.H. had awarded a New-York-based nonprofit called the EcoHealth Alliance a five-year, \$3.7-million grant, a portion of which—roughly six hundred thousand dollars—went to the W.I.V. Fauci and the N.I.H. have maintained that the W.I.V.’s work, like Baric’s, did not qualify as gain-of-function research, and so did not violate the Obama-era pause. (The Trump Administration lifted the pause in 2017, after three years of workshops and deliberations across multiple agencies resulted in a new regulatory process.) “Don’t mislead people by saying we haven’t taken this seriously for years,” Fauci told me, his voice rising. “According to our definition, it was not gain-of-function, period. If you don’t like the definition, let’s change the definition.”

In recent months, skeptics of natural origins have pointed to the fact that Shi was running her chimeric-virus experiments in a Biosafety Level 2 lab, which, compared with Biosafety Level 3, doesn’t require the same precautions, such as full P.P.E., medical surveillance for researchers, mandatory biosafety cabinets, controlled airflow, and two sets of self-closing, locking doors. (Shi did conduct live-animal experiments in a BSL-3 lab at a separate facility.) Because they were working with novel bat viruses rather than viruses known to infect humans directly, the low biosecurity setting was in accordance with Chinese laws. But Susan Weiss, a coronavirus expert at the University of Pennsylvania’s medical school, who co-authored a recent paper with Andersen and others that outlines the evidence for a natural origin, was surprised when I told her that they had been working in BSL-2. “That’s not a good idea,” she said.

Still, none of Shi’s documented work on chimeric viruses resulted in the creation of SARS-CoV-2. (“If you’re trying to say that that particular experiment could have led to SARS-CoV-2, that’s completely impossible,” Fauci said.) The chimeric viruses that the W.I.V. engineered are far from SARS-CoV-2 on the coronavirus family tree. According to Shi, the W.I.V. has only isolated and grown in culture three novel coronaviruses out of their nineteen thousand samples. What this chapter of her work demonstrates, however, is a high tolerance for risk. “They were essentially playing Russian roulette with the virus that the world’s expert had labelled poised for human emergence,” David Relman, a microbiologist at Stanford, said. “It’s the willingness to manipulate them without due concern.”

In January, the World Health Organization sent a team of international scientists to Wuhan to conduct the first phase of a search for SARS-CoV-2’s origins. The group’s report, published in March, ranked a zoonotic spillover—from a bat, through an intermediate animal, to a human—as the most likely origin pathway. They ruled a lab incident as “extremely unlikely,” dedicating just three of more than a hundred pages in the primary report to the theory. As Andersen frequently says when surveying the evidence, “Anything is possible, but I’m interested in what’s plausible.”

First, a natural origin has historic precedence. SARS spilled over from bats to civets at an urban market in November, 2002. MERS, which emerged in Saudi Arabia, in 2012, went from bats to camels to people. The civet was identified as the most probable source of SARS within four months of the outbreak; camels were identified within nine months of MERS. And yet, SARS-CoV-2’s

intermediate animal—among the only things, at this point, that could definitively prove that it did not originate in the Wuhan labs—has not been found. Such a discovery is becoming less likely, too. As members of the W.H.O. mission wrote in an August letter to *Nature*, “The window is rapidly closing on the biological feasibility of conducting the critical trace-back of people and animals inside and outside China.”

One member of the W.H.O. team was Peter Daszak, the president of the EcoHealth Alliance, which is dedicated to mitigating the emergence of infectious diseases. Since the first SARS outbreak, he has been one of the W.I.V.’s closest partners, facilitating the N.I.H. subcontracts and working extensively with Shi and her team in the field. He has unwaveringly vouched for Shi, and led the charge to call any suggestion of a lab accident a conspiracy theory. “The problem with this lab-release hypothesis,” he told me, “is that it depends on a critical thing: that the virus was in the lab before it got out. But I know that that virus was not in the lab.”

Daszak, a widely published disease ecologist, also knows that the diversity of viruses in nature is nearly limitless. Most recently, he and other EcoHealth scientists built a model analyzing how frequently coronaviruses might spill over from bats to people across southern China and southeast Asia. They overlaid the habitats of all twenty-three bat species known to harbor SARS-related coronaviruses with maps of human populations. Based on bat-human contact and antibody data, they estimated that roughly four hundred thousand people could be infected with SARS-related coronaviruses annually. “People are getting exposed to them every year,” Daszak told me. “They may not know it. They may even get sick and die.”

In other words, spillovers happen far more often than anyone realizes. People are exposed to bats when they shelter in caves, harvest bat guano—the world’s best fertilizer—and hunt, butcher, and eat bats, which is a well-documented practice in various pockets across the region. “These small villages are at the edge of disappearing forests,” Kendra Phelps, a bat biologist with the EcoHealth Alliance and a co-author on the recent study, told me. “Inside that forest is densely packed wildlife, which is super stressed by things like encroaching palm oil and rice monocultures.” Stressed animals (just like us) are more likely to get sick and shed virus.

Before the pandemic, President Xi Jinping promoted wildlife farms as a means of poverty alleviation, and the industry, which was largely unregulated, employed more than fourteen million people. “There’s this incredible network of people involved in farming and raising animals and trying out new ideas,” Daszak told me last year. “It’s entrepreneurial, it’s chaotic, it’s the sort of farms that are half falling apart, with mixed species in them.” The W.H.O. report stated that some wild-meat suppliers to Wuhan were located in south China, where horseshoe bats that host SARS-like coronaviruses primarily reside. Perhaps that is where the virus crossed from bats to animals, and those sickened animals were brought to Wuhan, where they were sold in Huanan and the city’s three other known live-animal markets. “The big missed opportunity, clearly,” Andersen said, “was testing potential reservoirs—intermediate hosts at these markets, not just at Huanan market but across Wuhan, as well as the farther-flung farms where these animals came from, which, to my knowledge, was officially not done.”

The Chinese government shuttered and sanitized the Huanan market on January 1, 2020, essentially destroying a crime scene. China’s officials told W.H.O. investigators that no live mammals were sold there—a position they still maintain. But a virologist at Hubei University of Traditional Chinese Medicine had been, he wrote, “serendipitously” conducting monthly surveys to identify the source of a severe tick-borne disease. In June, he published a study containing documentary evidence that, in the two years prior to the emergence of SARS-CoV-2, nearly fifty thousand live animals representing thirty-eight wild species—many of which are now known to be susceptible to SARS-CoV-2—were sold and butchered in Wuhan markets, including Huanan.

In February, 2020, China banned the trade and consumption of live wild animals. Tens of thousands of farms were shut down throughout the country. A farmer in Yunnan said that the government had bought and killed his mischief of bamboo rats. Chinese officials have not shared the extent to which they tested the farm animals and workers before the mass slaughter. This makes “any evidence of early coronavirus spillover increasingly difficult to find,” the W.H.O. mission noted in its report. Chinese officials told

the W.H.O. that their scientists did test more than eighty thousand livestock, poultry, and wild-animal samples, across thirty-one provinces, collected both before and after the outbreak, but found no evidence of SARS-CoV-2.

The world's most trafficked animal, the pangolin, was initially thought to be a likely contender in the intermediate-animal search, not because they were sold at Huanan market but because, in early 2020, tissue samples from a group of pangolins—confiscated from smugglers at China's southern border—tested positive for a coronavirus. There are coronaviruses particular to all sorts of animals, but this one was weird. Part of its spike protein, the receptor binding domain, could bind more tightly to human ACE2 than SARS-CoV-2's. Back in February, 2020, Andersen had been suspicious of SARS-CoV-2's ACE2 binding strength. The pangolin-coronavirus discovery helped change his mind. If the pangolin had naturally evolved a coronavirus primed for binding to ACE2, then SARS-CoV-2 could have naturally evolved such a feature as well. (The rest of the pangolin coronavirus was too distinct from SARS-CoV-2 to be its source.)

Since then, close relatives of SARS-CoV-2 have been identified in China, Thailand, Cambodia, and Japan. But the most significant finding supporting a natural origin was announced in September. Scientists in Laos—just south of the border from Yunnan—found a horseshoe-bat coronavirus that is genetically closer to SARS-CoV-2 than the virus from the Tongguan mine. It might have split from a common ancestor with SARS-CoV-2 sometime in the last decade or so. Alarming, their spikes are identical and bind with equal efficiency to human ACE2 receptors. The discovery “completely blows away many of the main lab-leak arguments about Yunnan being special,” Andersen said. “These types of viruses are much more widespread than we initially realized.”

Bloom questioned the significance of the discoveries in Laos. “I don't think it really, again, tells us exactly how these viruses got to Wuhan,” he said. But China's wildlife trade could have been both an incubator and a transit system for a virus like SARS-CoV-2, which has proved not so necessarily adapted to humans but to mammals more generally. Coughing tigers tested positive for COVID-19 at the Bronx Zoo, then eight congested gorillas at the San Diego Zoo. White-tailed deer have SARS-CoV-2 antibodies. In the Netherlands, the virus devastated mink farms, infecting sixty-eight per cent of farm workers and hastening a permanent end to the country's fur trade. China is the world's largest fur producer. Could mink farms have been the problem? Raccoon dogs, another source of fur and exotic meat in China, are susceptible. “We've seen this virus jump into all kinds of animals with no adaptation, no evolution,” Andersen told me. “It's a generalist. It had to be, otherwise it probably couldn't cause a pandemic. It's a unique beast.”

On September 21st, DRASTIC published a startling new revelation. In 2018, Daszak, at EcoHealth Alliance, in partnership with Shi, Baric, and Wang, had submitted a \$14.2-million grant proposal to the U.S. Defense Advanced Research Projects Agency (DARPA). The proposal—which was obtained from an anonymous whistle-blower—detailed an ambitious plan to identify, model, and test the spillover risk of novel SARS-related bat coronaviruses, then develop vaccines for the horseshoe bats themselves, to preempt viruses from jumping into other animals or people. What stood out was their plan to insert “human-specific” furin cleavage sites into SARS-like bat coronaviruses. The furin cleavage site is the single most distinguishing feature of SARS-CoV-2. It's “the magic sauce of this virus,” Michael Worobey, an evolutionary biologist at the University of Arizona, said recently. “Whether it's natural or genetically modified, this is why *this* virus is circulating in humans.”

Before SARS-CoV-2 emerged, research suggested that a furin cleavage site broadens the range of host species that a virus can successfully infect, and increases its contagiousness (a hypothesis that the pandemic has confirmed). In order for a coronavirus to enter a cell, its spike must undergo a fragile metamorphosis, in which it is cut into two pieces. Only then can the virus fuse to the host cell's membrane, and unload its genetic material, or RNA. A virus with a furin cleavage site can use a host's furin—an enzyme that the human body readily produces—to quickly cut apart its spike. Worobey said that this “kind of puts the virus on a hair trigger so that once it binds to the cell, it can get in and be very effective.”

The DARPA proposal stated that scientists would introduce furin cleavage sites into lab-created versions of SARS-related coronaviruses, recovered from bats in Yunnan. They planned to fully sequence and generate clones of three to five novel bat viruses each year. Then they would test the altered viruses in human respiratory cells, and, potentially, in humanized mice. “This describes work that is, like, ‘Let’s go out and discover new viruses,’” Andersen said, “and do things like furin cleavage sites. So, yes, that’s why this is relevant to the wider conversation.”

SARS-CoV-2 is the only virus known to possess a furin cleavage site in its section of the coronavirus family tree. “We now know that there are full-length bat CoVs similar to SARS-CoV-2 that bind well to human ACE2,” Bloom said, referring to the Laos viruses, “but only lack the furin cleavage site.” The W.I.V. was collecting many viruses each year. What if researchers had found one even more similar to SARS-CoV-2, with the same binding affinity for human ACE2, then swapped a furin cleavage site into a clone of that virus in the lab? Such work could have led directly to the creation of SARS-CoV-2. “A novel furin cleavage site might have been the extra ingredient for a natural virus to spill over from animals to humans and cause a pandemic,” Alina Chan, a postdoc in molecular biology and gene therapy at the Broad Institute of M.I.T. and Harvard, tweeted recently. “It could also have been the extra ingredient for a lab virus to jump into a researcher and be carried out of the lab unnoticed.”

Chan is the co-author of the forthcoming book “Viral: The Search for the Origin of COVID-19,” and has been, since the spring of 2020, one of the most tenacious researchers of a possible lab accident. “The question has to be asked,” she tweeted, “why people in the know didn’t think it was urgent & important, in Jan 2020, to let the world know there was research that could have plausibly led to the emergence of SARS2 in Wuhan.”

The proposal was rejected. A DARPA project manager explained that its “key strengths are the experienced team and the selected coronavirus hotspot caves that show high prevalence for novel bat coronaviruses.” But, they wrote, the team “does not mention or assess potential risks of Gain of Function (GoF) research.” That is, the group didn’t have a plan for the event that their experiments created a novel, pandemic-ready virus. Reviewers within DARPA “were really shocked” by the “irresponsible” nature of the proposal, and its lack of consideration for the risks that gain-of-function research would entail, an official, who was not authorized to speak to reporters, told me.

In the spring of 2020, when President Donald Trump started promoting the lab-leak theory, hijacking it from any reasonable discussion, someone told him that EcoHealth’s N.I.H. grant funded the W.I.V. The N.I.H. abruptly cancelled the grant. I spoke to Daszak at that time about the politicization of science and how the decision would affect his organization’s ability to function. He said that it halted collaboration with the W.I.V. on important work that was directly related to developing drugs for COVID-19, tracing the origin of the virus, and preventing the next pandemic. It also meant, he said, that EcoHealth scientists would no longer have access to the W.I.V.’s data. “It’s a very complex thing,” he said, describing EcoHealth’s work in China, “Chinese scientists will try and do my work, but it won’t be the same work, and it won’t be the work that we need to really understand the next one.”

Despite the fact that furin cleavage sites have been the subject of much debate for the past year and a half, Shi, Baric, and Wang never publicly mentioned that they had proposed these experiments. Daszak, despite being a member of the W.H.O. investigation, said nothing. (“All of that sort of furin-cleavage-site work was supposed to be done in North Carolina, not at the Wuhan Institute of Virology,” an EcoHealth spokesman said.) Andersen emphasized that there is no evidence to suggest that any of the work described in the proposal was actually done. But he added, “I was quite appalled, actually, to see it released now. I think the U.S.-based researchers that were on this particular grant have done a huge disservice by not releasing this information earlier.” (The EcoHealth spokesman told me that “the DARPA proposal was not funded” and that “the work described was not ever done.”)

Wang, at Duke-N.U.S. Medical School, was the first member of the DARPA proposal to publicly discuss it. He recently joined Bloom, Worobey, and Chan for a debate hosted by *Science* and live-streamed online. Both Bloom and Chan asked why the proposal’s existence was not shared earlier. Wang, who was born and raised in China, holds Australian citizenship, and now lives in

Singapore, said that he didn't know "the proper procedure of releasing the information" from a failed DARPA grant. When Jon Cohen, a writer for *Science* and the moderator of the debate, pressed him on transparency, Wang said the furin cleavage sites were not his part of the proposal. "From Day One, I said, to engineer a coronavirus in a lab, technically that is possible. But to engineer SARS-CoV-2 from existing knowledge? That's not possible."

It used to strike me as strange that, with current technology, virologists couldn't look at the SARS-CoV-2 genome and determine whether it had been engineered. When I mentioned this to a French virologist who studies coronaviruses, he said, deadpan, "The secret is if you just look closely enough, you can see a tiny Wuhan Institute of Virology signature." Proponents of a lab leak rest most of their arguments on the assumption that Chinese officials, the W.I.V., and Shi Zhengli are lying about the viruses they had, and the work they did, in a massive coverup. The natural-origin proponents assume that the W.I.V. has shared everything. "It's not that the scientists would not have wanted to share," Relman, who has refrained from taking a position on the question of SARS-CoV-2's origin, said. "It's that they wouldn't have been allowed."

The stakes are high on all sides. From one perspective, proving the virus has a natural origin is even worse for China. If wildlife farms were responsible for the pandemic, that would implicate the policies of President Xi Jinping. If there was a lab leak, just one, or a few, scientists are culpable of an accident. Either way, it is likely that the Chinese government prefers a storm of swirling theories, within which they can continue to push their own: that U.S. soldiers brought the virus to Wuhan in October, 2019, during the World Military Games, or that the American government manufactured the virus in Fort Detrick, Maryland. Or they can blame imported frozen food. The conspiracy theories branch out from there, in their own kind of evolutionary tree.

Without greater transparency from China, it will be difficult, if not impossible, to find the truth. Beijing "continues to hinder the global investigation, resist sharing information and blame other countries, including the United States," the intelligence community states, in the declassified summary. "These actions reflect, in part, China's government's own uncertainty about where an investigation could lead as well as its frustration the international community is using the issue to exert political pressure." President Biden, in a statement, said that the U.S. and its allies would continue to "press the P.R.C. to fully share information," and to cooperate in the second phase of the W.H.O.'s investigation, both of which, so far, Beijing has refused to do.

For now, the battle between two theories rolls onward. As a friend said to me recently, "Why does it seem like we have to pick a side?" Both camps share a desire to understand the origins in order to prevent the emergence of the next pandemic. But, between them, there are some differences of emphasis.

The lab leakers tend to be more interested in biosecurity, transparency, and human hubris. They exhibit an admirable drive to follow the money, to upend centralized power, to overturn academic hierarchy, and to expose the injustices of oppressive governments. Some are China hawks. By and large, they have not done virus-hunting field or lab work.

On the natural-origin side, most people have done the kind of field and lab work that the W.I.V. pursued—and are regularly bowled over by nature's endless diversity. They believe in scientific precedent, as opposed to uncertainties that have yet to be resolved. Many people in this camp have devoted their careers to conservation, biodiversity, and public health, and have been warning about a future pandemic for years. Spillovers most often happen because of land-use change, or human encroachment into previously wild places, which is happening on pretty much the entire planet, but particularly in areas that are developing rapidly, like south China and southeast Asia.

More than one virologist reminded me that nature is the best bioterrorist. It's far more creative than humans are. With enough time, evolution is capable of anything we can imagine, and everything we can't. "If you look at a platypus, you can very clearly realize that that's not something somebody would have designed, right?" Andersen said. "Because it's too absurd. It's a bit of a

disaster. But it works pretty well.” It occupies its own ecological niche. Some of the notable features of SARS-CoV-2, Andersen said, make it “the platypus of coronaviruses.”

Still, humans have changed the equation. Calling viruses zoonotic obscures the role we play in their evolution, whether in the wilderness, a wet market, or a lab. What is an ecological niche when humans have their hands in everything? Nature’s staggering diversity includes human nature. Somehow, SARS-CoV-2 found its ecological niche in us.

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