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United States Senate Homeland Security and Government Affairs Committee

Senate Dirksen Building, SD-342

ORIGINS OF COVID-19: AN EXAMINATION OF AVAILABLE EVIDENCE

June 18, 2024

Chairman Peters, Ranking Member Paul, distinguished members of the Homeland Security and Governmental Affairs Committee, thank you for inviting me to testify today. I am a Professor and Associate Dean at Tulane University School of Medicine in New Orleans. I am also co-founder of Zalgen Labs and a member of the Global Viral Network. It is important to note that I make these statements today in my personal capacity, and not on behalf of these entities. I have been working in the field of virology for nearly 50 years. Most of my work has been on emerging viruses, including HIV, SARS-CoV, Lassa and Ebola viruses.

On January 10, 2020, Edward Holmes of the University of Sydney, who was representing a consortium led by Yong-Zhen Zhang of Fudan University, Shanghai, became the first person to release the genomic sequence of SARS-Cov-2 (*3*). Shortly after the release of the SARS-CoV-2 genetic sequence I participated in an in-depth molecular and phylogenetic analysis of the virus with a group of other scientists, including Professor Holmes. We wrote a peer-reviewed publication in *Nature Medicine*, titled “The Proximal Origin of SARS-CoV-2 (*1*).”

In the Proximal Origin paper, we discussed several possible SARS-CoV-2 origin pathways. The origin pathways most relevant today are:

1. Direct spillover from a bat to a human
2. Spillover from a bat to an intermediate animal and then to a human.
3. Lab origin

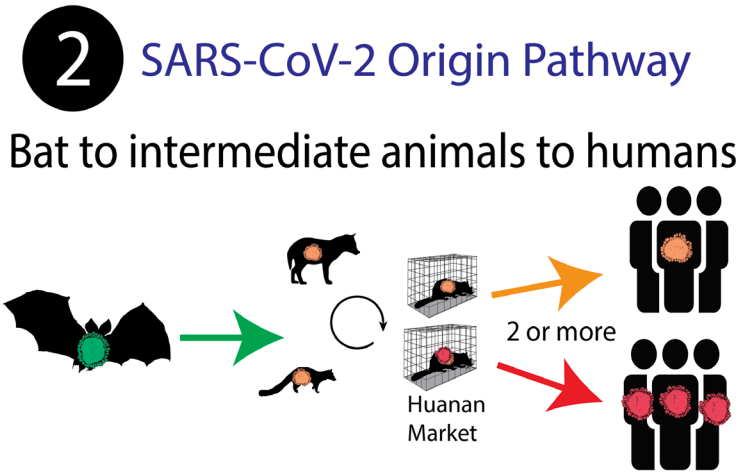

Figure 1. SARS-CoV-2 Origin pathway 2: Bat to intermediate animal to humans. Two or more spillovers at the Huanan Market are likely. Adapted from Andersen et al. (*1*).

At the time of writing the Proximal Origin paper – early February to mid-March 2020 - we did not rule out any of these three pathways. However, already there was sufficient data to conclude that pathway 3: Lab origin was not, in our view, likely or plausible. Based on the available evidence that has since accumulated it is my strong opinion that pathway 3 can be ruled out. In addition, I would like to note that a very specific Lab origin hypothesis involving The University of North Carolina (UNC), EcoHealth Alliance (EHA) and the Wuhan Institute of Virology (WIV) presented by Professors Jeffrey Sachs and Neil Harrison of Columbia University with input from Professor Richard Ebright of Rutgers University (*5*) is highly implausible (*6*). A very similar Lab origin hypothesis was recently outlined in a New York Times Op-Ed by Dr. Alina Chan of the Broad Institute of Harvard and MIT (*7*) and is also highly implausible in my opinion. Similarly, new available evidence, which is discussed in more detail below, indicates that we can also now rule out pathway 1: Direct spread from bat to human.

Thus, pathway 2, which involves two steps: (1) a spillover from a bat to an intermediate animal, and (2) from the intermediate animal to a human (Fig. 1), is the only scientifically supported hypothesis. Specifically, there is a large body of available scientific evidence – clinical, epidemiological, serological, and phylogenetic evidence – for this two-step spillover from bats via an intermediate animal to humans. Simply put, Pathway 2 is the only parsimonious pathway, one that is fully consistent with all the available scientific evidence.

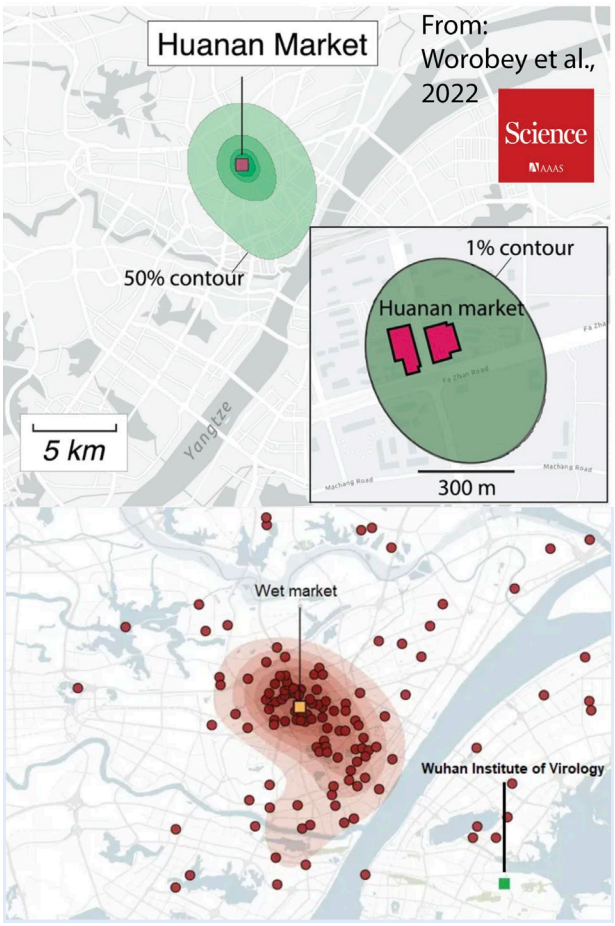

Figure 2. Clustering of the December 2019 COVID-19 cases paints a bullseye on the Huanan Market. Top: Probability density contours showing the spatial pattern of COVID-19 cases in Wuhan in December 2019. Cases are from hospital records of the entirety of Wuhan. Only cases from December 2019, which is before COVID-19 was described, are included. Ascertainment bias does not account for these results. Bottom: A heat map of early cases is centered on the Huanan Market, not the Wuhan Institute of Virology laboratory across the river or the WIV BSL-4 facility further south (not shown)(*2*).

The Huanan Market in Wuhan was the early epicenter of the COVID-19 pandemic (Worobey, 2021; Worobey et al., 2022; Holmes et al., 2021)

The geographic location of the earliest documented SARS-COV-2 infections supports the two-step spillover hypothesis. The earliest documented human case of COVID-19 was a vendor in the Huanan Wholesale Seafood Market (hereafter, "Huanan Market") who fell ill December 10, 2019, (*8*). Of the initial 41 people hospitalized with the previously undescribed pneumonia, 27 (66%) had direct exposure to the Huanan Market (*9*) . Other diagnoses of what would later be named COVID-19 were made independently in several hospitals in the city of Wuhan up to the end of December 2019. These diagnoses were made before it was known that a new disease was spreading (*10*). Worobey et al. (*2*) showed that the earliest documented COVID-19 cases from December 2019, including those without reported direct links to the Market, lived close to the Huanan market (Fig. 2). In contrast here was no cluster of early cases near the Wuhan Institute of Virology (WIV) laboratory across the river from the Market or the WIV BSL-4 facility located even further from the Market. It is misleading to say that these results can explained by ascertainment bias (*11*). The early reports of cases

were based on their unique signs and symptoms and not a link to the Huanan Market (*2, 8*). Holmes et al. (*12*) also showed clustering of early cases spreading in the neighborhood of the Huanan Market and noted that excess pneumonia deaths in early January 2020 were likewise occurring near the Huanan Market, not near either WIV campus.

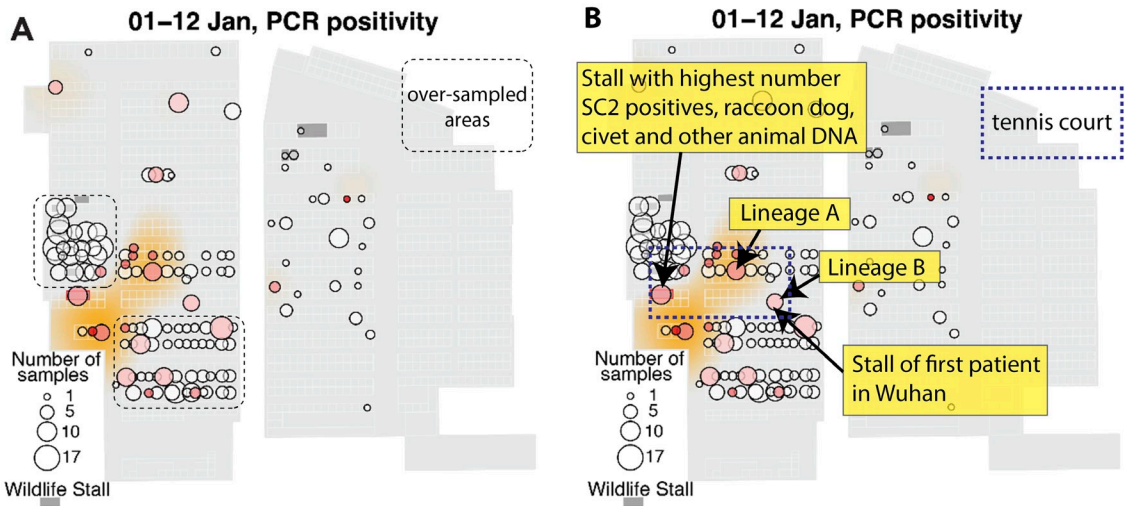

Figure. 3. Testing of surfaces for SARS-CoV-2 RNA. A. SARS-CoV-2 positive samples cluster in the southwest corner of the Huanan Market. Ascertainment bias does not account for these results. Most positive samples are in relatively under-sampled areas. B. SARS-CoV-2 RNA from both lineages A and B, susceptible animal DNA, and the FIRST known patient in Wuhan are present in the Huanan Market in an area smaller than a tennis court (*4*).

Challenges to Worobey et al. 2022

Several recent studies have challenged the Worobey paper's original findings, including by misleading dismissing the results as a case of ascertainment bias (*11*). For example, Stoyan and Chiu (*13*) challenged the centrality of the Huanan Market in maps of December 2019 COVID-19 case residential locations as shown by Worobey et al. (*2*). They proposed a statistical test based on the premise that the central tendency of a sample of case locations must coincide with the point from which local transmission began. Debarre and Worobey (*14*) countered by showing that Drs. Stoyan and Chiu's concerns about the use of centre-points are inconsequential. Even using Stoyan and Chiu's stringent statistical test, the mode still falls at the entrance of a parking lot at

the market and the 95% confidence region still includes the Market. In addition, Weissman (*15*) recently claimed to find "*internal evidence*" of major ascertainment bias. This is also unsupported (*16*). The pattern of early case clusters shown in Worobey et al. (*2*) can be explained by places of infection not being limited to residential neighborhoods without requiring any ascertainment bias (*16*). Moreover, the early reports of cases were based on their unique signs and symptoms, not scientists looking to create a link to the Huanan Market (*2, 8*).

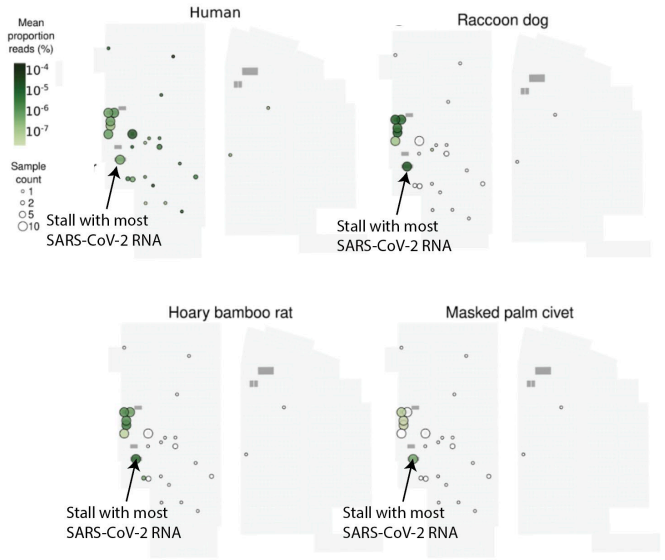

Figure 4. **Figure 3: The spatial distribution of human and animal DNA/RNA in the Huanan market**. Nucleic acids of SARS-CoV-2 susceptible animals is co-mingled with SARS-CoV-2 RNA in the stall containing the most SARS-CoV-2 positive samples in the market (*4*).

Genetic tracing of Market wildlife and viruses at the epicenter of the COVID-19 pandemic (Crits-Christoph et al. 2023)

Genetic tracing of wildlife in the Market around the time of the first outbreak further supports the two-step spillover hypothesis. Huanan means 'South China' and the Huanan market features items purchased via its trade routes to Southern China (*10*). The Huanan Market was one of only four locations that sold live wildlife in Wuhan (*17*). It is likely that many live animals in the Huanan Market were farmed or trapped in South China or other Southeast Asia countries. Available evidence indicates that all of the live animals were removed from the Huanan Market before it was shuttered on January 1, 2020. However, samples were collected from various surfaces in the Market and its drainage system after the Market was closed (*2, 4, 18*). Those Market surface samples that tested positive for

SARS-CoV-2 were specifically clustered in the southwest corner of the West side of the Huanan Market, where live SARS-CoV-2 susceptible mammals were sold. (Fig. 3A).

Although WHO investigators in 2021 were told that no life wildlife was sold at the Huanan Market (*10*) an important study by Xiao et al. (*17*) demonstrated that this conclusion was not supported. Instead, many animals known to be susceptible to SARS-CoV-2 were sold at the Market. Xiao et al.'s conclusion was confirmed when the complete genetic sequencing files from the Huanan market were analyzed, including by Crits-Christoph et al. (*4, 18*). As expected, the sampling picked up not only the SARS-CoV-2 RNA but DNA And RNA from all of the organisms present, including humans (Fig. 4). Raccoon dog and civet cat DNA and RNA were co-mingled in several samples from the wildlife stall that contained the highest number of SARS-CoV-2 positive samples in the Market (*4*) (Fig. 3B). Other potential animal hosts were present, but importantly no bat nucleic acids were found. The SARS-CoV-2 positive samples included those from an iron cage and two carts commonly used to transport animal cages (*2, 4*). Both raccoon dogs and civets were implicated in the outbreak of SARS-CoV, the first SARS virus. Spillovers of SARS- CoV from raccoon digs and civets occurred in China via the wildlife trade in 2002-2004 (*19-21*). As I said in my prior testimony to the Covid Select subcommittee of the House Oversite Committee on July 11, 2023 - this is equivalent to finding a smoking gun carrying the main suspects' DNA at the exact scene of the crime.

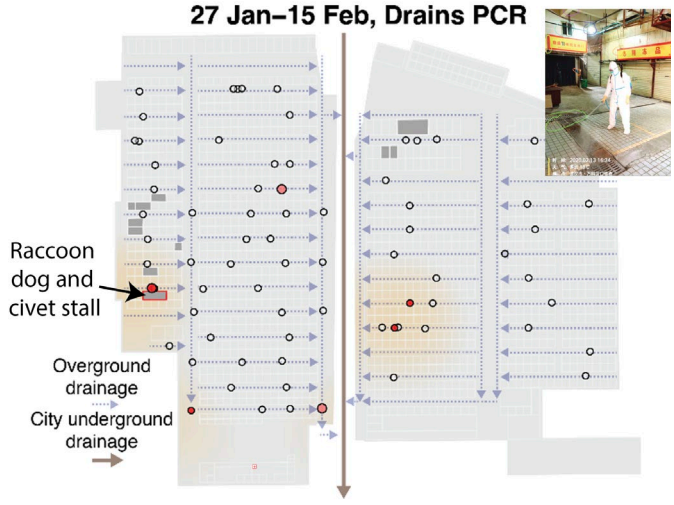

Figure 5. Testing of overground drains for SARS-CoV-2 RNA. SARS-CoV-2 contaminated run-off from live wildlife in cages is the most likely explanation for the SARS-CoV-2 positivity. The overground drains [example: inset photo] are not connected to human toilets. Ascertainment bias does not account for these results. Sampling was even across the Huanan Market (*4*).

Confirmation that this particular wildlife stall contained high levels of SARS-CoV-2 was obtained through analysis of samples taken from the overground drainage system a month or more after the market had been closed (Fig. 5). The drainage samples taken in from of this stall were among those that contained the highest amounts of SARS-CoV-2 RNA (*4*). This was also a stall that had live animals, including raccoon dogs and civets, known to be susceptible to SARS-CoV-2. It is likely that the SARS-COV-2 in this drain had come from infected animals. There were infected humans all around the market but few of the overground drains were positive.

Challenges to Crits-Christoph et al. 2024

The aforementioned Dr. Alina Chan claimed in a Medium post that more SARS-CoV-2 positive samples were found in the southwest corner because more samples were collected there (*11*). As discussed by Worobey et al. (*2*) and by Crits-Christoph et al. (*4*), this was not the case. The southwest corner of the Market was the hotspot of SARS-CoV-2 positivity in the market, even after controlling for nonrandom sampling. Indeed, most positive samples are in relatively under-sampled areas (Fig. 3A). We know the exact sampling scheme. the signal is real and not due to bias, which we directly tested for. Analysis of samples taken from the overground sewer lines provides independent confirmation that this wildlife stall contained high amounts of SARS-CoV-2 (Fig. 5). The sewers were sampled later and evenly throughout the market.

Professor Jesse Bloom from the Fred Hutchinson Cancer Center performed an analysis to determine which animal's DNA was found near SARS-CoV-2 positive samples most often (*22*). Wide-mouth bass that are not susceptible to SARS-COV-2 infection was the most prevalent animal he identified, and raccoon dogs were near the bottom of his list. In my opinion, Professor Bloom's analysis is irrelevant to understanding the origin of COVID-19 (*23*). There is no *a priori* reason to think that one infected raccoon dog would transmit SARS-CoV-2 to all or many of the

other raccoon dogs in the market. Bloom's statistical analysis simply proves that there is no meaningful correlate between the number of host reads vs the number of virus reads pointing to a specific host. His analysis does not change the fact that samples from the Market stall with the highest number of SARS-COV-2 positive samples contained DNA and RNA of susceptible animals.

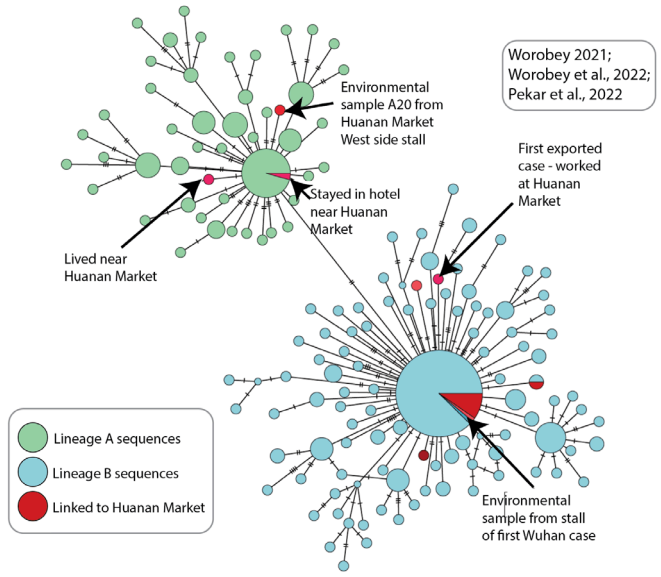

Figure 6. SARS-CoV-2 genomic diversity before February 2022 was comprised of 2 separate lineages A and B. Both lineages were associated with the Huanan Market. Lineage A is closer to the ancestral bat coronaviruses. Lineage B spilled over before lineage A. The only explanation is at least two separate cross-species transmission events into humans. Figure: courtesy of Alex Crits-Christoph (unpublished).

The molecular epidemiology of multiple zoonotic origins of SARS-CoV-2 (Pekar et al., 2022)

The existence of two distinct lineages of SARS-COV-2 also supports the two-step spillover hypothesis. Prior to February 2020, SARS-CoV-2 genomic diversity before February 2020 comprised two distinct viral lineages, denoted "A" and "B" (Fig. 6). Lineage A viruses are at least two mutations closer to bat coronaviruses, implying that they are close to the ancestor of SARS-CoV-2 than lineage B viruses. This implication is consistent with the SARS-CoV-2 genomic diversity before February 2020 comprised two distinct viral lineages, denoted "A" and "B" (Fig. 6). deep phylogenetic analysis presented in Pekar et al. (*24*). However, Lineage B viruses predominated early in the pandemic indicating earlier spread in humans. The increase in number of SARS-CoV-2 Lineage A cases followed the increase in Lineage B viruses. It is clear that Lineage B spilled over before Lineage

A, but this presents a paradox. If B evolved from A, how did it get into humans first? Only an introduction from animals of SARS-CoV-2 Lineage B followed by a separate introduction of SARS-CoV-2 Lineage A resolves the paradox. Indeed, Pekar et al. (*24*) showed that the molecular clock of SARS-CoV-2 in humans is inconsistent with a single-introduction origin of the pandemic. Most of the samples collected at the Huanan Market are Lineage B, but there was also a lineage A sample collected in the Market (*2, 4*). The detection of lineage A in the market was a major finding that confirmed the analyses of Pekar et al. (*24*). Early in the pandemic when there were a limited number of human cases virus as determined by serology (*25*) and epidemiology (*8, 12, 26*). Significantly, the entire genomic diversity of SARS-COV-2 from the very root of its phylogenic tree was present in the Huanan Market (Fig. 3).

Challenges to Pekar et al., 2022

In response to questions about the data analysis in Pekar et al., we published a formal correction to Pekar et al. (*24*) that amended one line in one computer code used in one of the analyses performed. Much has been made of the minor correction, but in reality the corrections don't change the underlying analyses or conclusions of the paper. Lineage B still spilled over before A, Lineage A is still more similar to ancestral bat coronaviruses, and lineages A and B still show massive polytomies.

Why has there been such a concerted effort to discredit this paper? You have to make a massive logical leap to discount the viability of the two-step spillover hypothesis and instead scientifically conclude that a virus that was created in a lab somehow infected the first documented patient and many of the earliest infected patients who all had links to the Huanan Market.

Significantly, this would not be the first time that a coronavirus created human infection via multiple spillovers. In fact, this was precisely the spillover pathway that the original SARS-CoV followed

not one time, but in numerous spillover events between 2002 and 2004 (*20, 27*). Thus, even if you could find a way to disregard this incongruency, you then have to believe that the coincidence that a virus allegedly created in a lab first showed up in one of the few places selling virus-susceptible animals occurred not once, but twice.

The challenges to high-profile papers are welcomed and expected. However, just because someone writes an article claiming to find an error - peer-reviewed or not – does not negate a published paper– that's not how science works.

Summary of evidence that the Huanan Market was the site where SARS-CoV-2 entered the human population and sparked the COVID-19 pandemic

Lab leak proponents point to the presence of a lab studying bat coronaviruses in Wuhan as *prima facia* evidence of a Lab Leak. They ignore or dismiss the abundant data pointing to the Huanan Market as the early epicenter of the COVID-19 pandemic. The city of Wuhan has an area of over 8500 square kilometers. By comparison, tennis court is 260 square meters - over 32 million times smaller. The significance of the fact that both SARS-CoV-2 lineage A and lineage B, as well as the DNA/RNA of raccoon dogs and civets were found within an area the size of a tennis court (i.e., the Huanan Market) cannot be overstated. Moreover, the earliest ascertained human case of COVID-19 was a vendor in the Huanan Market. Although the vendor was certainly not the first case, remarkably, her stall was also in that tennis court sized area (Fig. 3B). There is no Lab Leak scenario that can accommodate all the available scientific evidence.

SARS-CoV-2 did not spill over directly from a bat to a human

The Huanan Market papers (*2, 4, 12, 24, 26*) discussed above provide strong evidence that SARS-CoV-2 spilled over in two steps: from a bat to a non-bat animal to humans (Fig. 7). In contrast, there is no viable scientific evidence to support the bat to human spillover hypothesis

(Pathway 1). Specifically, there is no evidence that bats were sold at the Huanan Market, and no bat DNA was found in environmental samples (*4*).

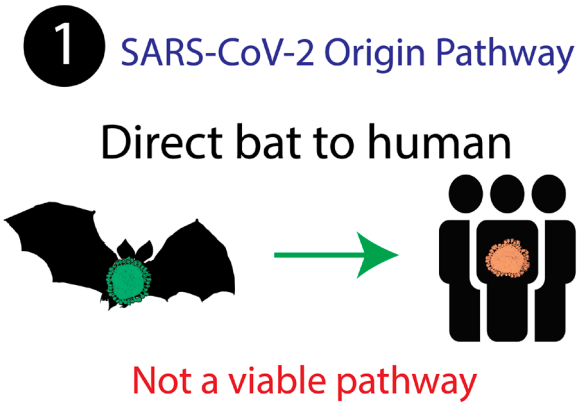

Figure 7. SARS-Cov-2 did not spillover directly from a bat to a human. Adapted from Andersen et al. (*1*).

This is not the only evidence that supports disregarding Origin Pathway 1: Direct bat to human spillover. Several coronaviruses, including BANAL-20-52 and BANAL-20-236, were found in bats in northern Laos in 2020 (*28*). The Laotian *R. malayanus* virus BANAL-20-52 has 49 of 50 amino acids in the RBD that are identical to the RBD of SARS-CoV-2. The amino acids of the BANAL-20-52 RBD are closer to the original SARS-CoV-2 viruses isolated in Wuhan than the RBD of the Omicron variants that swept the world in November 2021. Yet, the nucleotide sequence is not as close. For those versed in molecular biology and genetics, this is clear evidence that codon usage from a bat virus related to BANAL-20-52 drifted or was optimized as the virus adapted to a non-bat host. Bats are special. They can fly which means they have a highly distinct and specialized physiology. Scientific studies demonstrate that the bat immune system is different than every other mammal (*29-34*).

With the new evidence now available it is clear that adaptation from a bat to a non-bat requires a series of additional mutations to acquire the ability to spread effectively by the respiratory route and to replicate effectively in a non-bat animal (*35, 36*). No virologist would have known how to generate such mutations, and no manipulation in a lab will allow you to generate these. Replication in nature that can result in the near infinite number of permutations generated is the only way to drive the necessary evolution to create SARS-COV-2. Virologists are only just learning

about the multitude of changes in the progenitors of SARS-CoV-2 that allowed it to replicate in non-bats and spread by the respiratory route. One of these changes is in the Spike protein. The threonine at position 372 (T362) is highly conserved in bat coronaviruses (*37*). The threonine is replaced by an alanine in SARS-CoV-2 Spike, which also has the effect of eliminating one of the Spike glycosylation sites. The presence of the glycan provides a selective advantage in pH stability during fecal-oral transmission of the bat-SARS-COV-2 progenitor (*37*). This data indicates that many mutational changes to the bat coronavirus progenitor genome were needed before it could become a human pathogen.

> "Circumstantial evidence is a very tricky thing. It may seem to point very straight to one thing, but if you shift your own point of view a little, you may find it pointing in an equally uncompromising manner to something entirely different."
>
> **— Sir Arthur Conan Doyle, The Adventures of Sherlock Holmes**

SARS-CoV-2 is the only sarbecovirus with a furin cleavage site – time to shift your point of view

One of the most common pieces of circumstantial evidence mentioned by those that favor the Lab Leak hypothesis is that no close relative of SARS-COV-2—meaning a bat coronavirus in the subgenus sarbecovirus—has ever been found with a furin cleavage site ("FCS"). Those favoring the Lab Leak hypothesis rely on this lack of FCS to imply that the FCS of SARS-COV-2 was inserted in a laboratory. Following the advice of Sherlock Holmes to look at circumstantial evidence from different viewpoints the fact that no bat sarbecovirus has a FCS indicates that a FCS is not selected for in coronaviruses replicating in bats. FCS's are very common in non-bat coronaviruses. Thus, the lack of a FCS in any bat sarbecovirus is also evidence that SARS-COV-2 did not spill over directly from a bat to a human. It is possible that one might find a bat

sarbecovirus with a FCS, but based on the available evidence, it's much more likely that the FCS in SARS-CoV-2 arose during replication in a non-bat animal.

More importantly, if you put a FCS in a bat sarbecovirus you it is very unlikely you will get a pandemic pathogen. You would simply have a bat coronavirus with a FCS that remains dozens of mutations distant from such a pandemic pathogen. The available evidence strongly suggests that the transition of a bat coronavirus to a virus highly transmissible by the respiratory route and adaptation to non-bat physiology/ immunity would have required many more changes than simply inserting a FCS.

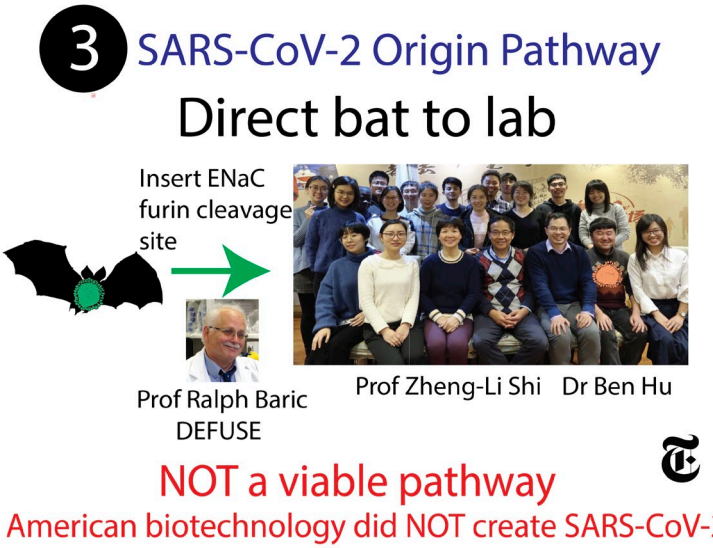

Figure 8. SARS-CoV-2 did not spillover directly from a bat to a lab.

American biotechnology did not create SARS-CoV-2

This brings us to the specific lab origin hypotheses based on the DEFUSE proposal submitted in March 2018 to the Defense Advanced Research Projects Agency (DARPA) by scientists from EHA, UNC and the WIV (*38*) (Fig. 8). In one frequently analyzed paragraph the DEFUSE applicants proposed to add proteolytic cleavage sites to spike sequences of novel bat sarbecoviruses and to insert novel cleavage sites found in bat coronaviruses into lab constructs of other coronaviruses. Prominent Lab Leak advocate Dr. Alina Chan, author of the recent Op-Ed in the New York Times on SARS-CoV-2 origins (*7*) is fond of saying that SARS-CoV-2 is a

unicorn and the FCS is its horn (*39, 40*). In Chan's analogy a bat coronavirus is a horse. Chan frames DEFUSE as a proposal to put a horn on a horse, which was followed by a unicorn showing up in Wuhan. Just putting a horn on a horse, however, does not make it a unicorn, which is a magical creature. It would just be a mundane horse with a horn, with no special properties and likely one that would replicate no better, if not worse, than the bat coronavirus before you put in the FCS. There are just simply too many other mutations needed to change a bat coronavirus into a pandemic pathogen capable of respiratory spread in non-bat animals. When you realize that SARS-COV-2 did not spill over directly from a bat to a human you can see that the DEFUSE proposal is actually evidence that WIV, UNC and EHA did not engineer SARS-COV-2, or even accidentally release it.

A particularly unsound variant of the Lab Leak theory espoused in the recent NYT Op-Ed is that it is evident that SARS-CoV-2 was engineered based the FCS of human amiloride-sensitive epithelial sodium channel a subunit (ENaC). SARS-CoV-2 shares an eight amino acid identity (RRARSVAS) with one of the FCS present in human ENaC. ENaC cleavage by furin has been studied at UNC (*41, 42*). The DEFUSE proposal highlighted the collaboration between EHA, UNC and WIV. Based on these coincidences Professors Jeffrey Sachs and Neil Harrison wrote a paper (*5*) insinuating that that Professor Zheng-li Shi, Head of the bat coronavirus research program at WIV, and Professor Ralph Baric, a leading coronavirologist at UNC, had collaborated to design the FCS of SARS-CoV-2 based on ENaC. Professor Ebright is credited as a contributor on this paper. Sachs subsequently proclaimed that he was convinced that American biotechnology was likely responsible for the COVID-19 pandemic (*43-45*). For the ENaC hypothesis to be true, UNC or WIV researchers would have had to possess the direct SARS-CoV-2 progenitor isolated from another animal—not a bat (*6, 46*). WIV collected SARS-like coronaviruses from bats, but there is no evidence that WIV ever possessed the direct SARS-COV-2 progenitor. I have exhaustively reviewed the available literature and evidence regarding the origin of COVID-19 and have seen

no credible evidence to support this outlandish and dangerous hypothesis that American biotechnology is responsible for the COVID-19 pandemic.

Conclusion

I support the efforts of the HSGAC to better understand the origins of SARS-CoV-2 pandemic. I also encourage the Committee to empower the scientific enterprise to address the certainly of that viral threats will emerge from nature in the future. Such studies will require extensive international cooperation and careful attention to biosecurity and biosafety concerns for handling potential pandemic pathogens in the field. As a member of NIAID's Centers for Research in Emerging Infectious Disease (CREID) network I know that such work can be done responsibly and safely. We also know that serious viruses can get into large commercial animal farming industries as happened in the case of the spillover of SARS-COV-2 in Wuhan in 2019 from the Chinese wildlife trade. The wildlife trade in China was formerly the only enterprise in the world comparable in size to the United States cattle industry. A stark and timely reminder is the current serious threat from bird flu to the United States cattle industry (*47*).

A small, but vocal, group of scientists appear to be advocating for the SARS-CoV-2 Lab Leak hypothesis to help advance their own decades long opposition to virology research that they consider to be risky, and to criticize Dr. Anthony Fauci and other NIH administrators that have overseen virology funding (*48, 49*). The new guidance from the Biden White House Office of Science and Technology Policy shows that research with high-risk pathogens and types of experiments that require review can be clearly defined in a way that does not obstruct vitally-important low-risk research (*50*). It's important that all stakeholders, including virologists, can contribute expertise without enduring defamation, harassment, or retaliation.

REFERENCES

1. K. G. Andersen, A. Rambaut, W. I. Lipkin, E. C. Holmes, R. F. Garry, The proximal origin of SARS-CoV-2. *Nat Med* **26**, 450-452 (2020).
2. M. Worobey *et al.*, The Huanan Seafood Wholesale Market in Wuhan was the early epicenter of the COVID-19 pandemic. *Science* **377**, 951-959 (2022).
3. E. Holmes., Novel 2019 coronavirus genome. https://virological.org/t/novel-2019-coronavirus-genome/319. 2020.
4. A. Crits-Christoph *et al.*, Genetic tracing of market wildlife and viruses at the epicenter of the COVID-19 pandemic. *bioRxiv : the preprint server for biology*, 2023.2009.2013.557637 (2023).
5. N. L. Harrison, J. D. Sachs, A call for an independent inquiry into the origin of the SARS-CoV-2 virus. *Proc Natl Acad Sci U S A* **119**, e2202769119 (2022).
6. R. F. Garry, The evidence remains clear: SARS-CoV-2 emerged via the wildlife trade. *Proc Natl Acad Sci U S A* **119**, e2214427119 (2022).
7. A. Chan, Why the Pandemic Probably Started in a Lab, in 5 Key Points. https://www.nytimes.com/interactive/2024/06/03/opinion/covid-lab-leak.html. (2024).
8. M. Worobey, Dissecting the early COVID-19 cases in Wuhan. *Science* **374**, 1202-1204 (2021).
9. C. Huang *et al.*, Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* **395**, 497-506 (2020).
10. WHO, WHO-Convened Global Study of Origins of SARS-CoV-2: China Part: Joint WHO-China Study, 14 January-10 February 2021 : Joint Report. (2021).
11. A. Chan, Evidence for a natural origin of Covid-19 no longer dispositive after scientific peer review. (2022).
12. E. C. Holmes *et al.*, The origins of SARS-CoV-2: A critical review. *Cell* **184**, 4848-4856 (2021).
13. D. Stoyan, S. N. Chiu, Statistics did not prove that the Huanan Seafood Wholesale Market was the early epicentre of the COVID-19 pandemic. *Journal of the Royal Statistical Society Series A: Statistics in Society*, qnad139 (2024).
14. F. Debarre, M. Worobey, Confirmation of the centrality of the Huanan market among early COVID-19 cases. arXiv:2403.05859v1. (2024).
15. M. Weissman, Proximity ascertainment bias in early covid case locations. Journal of the Royal Statistical Society Series A: Statistics in Society. p. qnae021. (2024).
16. F. Debarre, M. Worobey, No evidence of systematic proximity ascertainment bias in early COVID-19 cases in Wuhan Reply to Weissman. arxiv.org/html/2405.08040v1. (2024).
17. X. Xiao, C. Newman, C. D. Buesching, D. W. Macdonald, Z. M. Zhou, Animal sales from Wuhan wet markets immediately prior to the COVID-19 pandemic. *Scientific reports* **11**, 11898 (2021).
18. W. J. Liu *et al.*, Surveillance of SARS-CoV-2 at the Huanan Seafood Market. *Nature*, (2023).
19. B. Kan *et al.*, Molecular evolution analysis and geographic investigation of severe acute respiratory syndrome coronavirus-like virus in palm civets at an animal market and on farms. *J Virol* **79**, 11892-11900 (2005).

20. Molecular evolution of the SARS coronavirus during the course of the SARS epidemic in China. *Science* **303**, 1666-1669 (2004).
21. Z. Shi, Z. Hu, A review of studies on animal reservoirs of the SARS coronavirus. *Virus Res* **133**, 74-87 (2008).
22. J. D. Bloom, Association between SARS-CoV-2 and metagenomic content of samples from the Huanan Seafood Market. *Virus evolution* **9**, (2023).
23. F. Débarre, What we can and cannot learn from SARS-CoV-2 and animals in metagenomic samples from the Huanan market. *Virus evolution* **10**, vead077 (2024).
24. J. E. Pekar *et al.*, The molecular epidemiology of multiple zoonotic origins of SARS-CoV-2. *Science* **377**, 960-966 (2022).
25. L. Chang *et al.*, Serosurvey for SARS-CoV-2 among blood donors in Wuhan, China from September to December 2019. *Protein & cell* **14**, 28-36 (2023).
26. E. C. Holmes, The Emergence and Evolution of SARS-CoV-2. *Annual review of virology*, (2024).
27. L. F. Wang, B. T. Eaton, Bats, civets and the emergence of SARS. *Curr Top Microbiol Immunol* **315**, 325-344 (2007).
28. S. Temmam *et al.*, Bat coronaviruses related to SARS-CoV-2 and infectious for human cells. *Nature* **604**, 330-336 (2022).
29. M. Ahn *et al.*, Bat ASC2 suppresses inflammasomes and ameliorates inflammatory diseases. *Cell* **186**, 2144-2159.e2122 (2023).
30. A. T. Irving, M. Ahn, G. Goh, D. E. Anderson, L. F. Wang, Lessons from the host defences of bats, a unique viral reservoir. *Nature* **589**, 363-370 (2021).
31. E. D. Laing *et al.*, Enhanced Autophagy Contributes to Reduced Viral Infection in Black Flying Fox Cells. *Viruses* **11**, (2019).
32. L. F. Wang, D. E. Anderson, Viruses in bats and potential spillover to animals and humans. *Current opinion in virology* **34**, 79-89 (2019).
33. L. F. Wang, A. M. Gamage, W. O. Y. Chan, M. Hiller, E. C. Teeling, Decoding bat immunity: the need for a coordinated research approach. *Nature reviews. Immunology* **21**, 269-271 (2021).
34. K. S. M. Yong *et al.*, Bat-mouse bone marrow chimera: a novel animal model for dissecting the uniqueness of the bat immune system. *Scientific reports* **8**, 4726 (2018).
35. S. Temmam *et al.*, SARS-CoV-2-related bat virus behavior in human-relevant models sheds light on the origin of COVID-19. *EMBO Rep* **24**, e56055 (2023).
36. S. Fujita *et al.*, Virological characteristics of a SARS-CoV-2-related bat coronavirus, BANAL-20-236. *EBioMedicine* **104**, 105181 (2024).
37. X. Ou *et al.*, Host susceptibility and structural and immunological insight of S proteins of two SARS-CoV-2 closely related bat coronaviruses. *Cell discovery* **9**, 78 (2023).
38. S. Lerner, M. Hibbet, Leaked grant proposal details high-risk coronavirus research. https://theintercept.com/2021/09/23/coronavirus-research-grant-darpa/. (2021).
39. M. Kaplan, After death threats, Dr. Alina Chan doubles down on COVID-19 origin theory. https://nypost.com/2021/12/22/dr-alina-chan-doubles-down-on-covid-19-origin-theory/. (2021).

40. S. Knapton, Wuhan lab leak 'now the most likely origin of Covid', MPs told. https://www.telegraph.co.uk/news/2021/12/15/wuhan-lab-leak-now-likely-origin-covid-mps-told/. (2021).
41. A. García-Caballero, Y. Dang, H. He, M. J. Stutts, ENaC proteolytic regulation by channel-activating protease 2. *The Journal of general physiology* **132**, 521-535 (2008).
42. P. Kota, M. Gentzsch, Y. L. Dang, R. C. Boucher, M. J. Stutts, The N terminus of α-ENaC mediates ENaC cleavage and activation by furin. *The Journal of general physiology* **150**, 1179-1187 (2018).
43. C. Boyd, Covid leaked from an AMERICAN lab and not the notorious Chinese facility at centre of pandemic cover-up, claims top US professor described as 'Xi propagandist' https://www.dailymail.co.uk/health/article-10980715/Covid-leaked-AMERICAN-lab-claims-professor-Jeffrey-Sachs.html. (2022).
44. R. J. Kennedy, J. Sachs. (2022).
45. T. Carlson, Jeffrey Sachs explains the cover-up of the COVID origins. https://www.instagram.com/tuckercarlson/reel/C7h5g12P52N/. (2024).
46. R. F. Garry, SARS-CoV-2 furin cleavage site was not engineered. *Proc Natl Acad Sci U S A* **119**, e2211107119 (2022).
47. CDC, Current H5N1 Bird Flu Situation in Dairy Cows. https://www.cdc.gov/bird-flu/situation-summary/mammals.html?CDC_AAref_Val=https://www.cdc.gov/flu/avianflu/mammals.htm. (2024).
48. D. A. Relman, Opinion: To stop the next pandemic, we need to unravel the origins of COVID-19. *Proc Natl Acad Sci U S A*, (2020).
49. R. Ebright, For the hearing Revisiting Gain of Function Research. https://www.hsgac.senate.gov/imo/media/doc/Ebright. (2022).
50. OSTP, United States Government Policy for Oversight of Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential. https://www.whitehouse.gov/ostp/news-updates/2024/05/06/united-states-government-policy-for-oversight-of-dual-use-research-of-concern-and-pathogens-with-enhanced-pandemic-potential/. (2024).