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How science demolishes the right-wing fiction of a Wuhan “lab leak” as the source of coronavirus

Conclusion of a three-part series

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22 June 2021

This is the conclusion of a three-part series. Part one can be viewed here , and part two here.

Glossary

In the interests of clarity, since much of the following discussion includes scientific terminology, further obscured by the shorthand of Twitter threads and other online exchanges, a glossary of key terms and abbreviations may be helpful to the reader.

- ACE2: Angiotensin-converting enzyme II, an enzyme on the surface of many human cells, targeted by the spike protein of SARS-CoV-2
- FCS: Furin cleavage site, a point on the spike protein of SARS-CoV-2 where the protein is easily cut by a protease called furin, helping it invade cells in the host human
- nCoV2019: An early acronym referring to the virus now called SARS-CoV-2
- RaTG-13: A bat virus found in caves in Yunnan province in China, genetically similar to SARS-CoV-2, but not a precursor, despite the claims of the conspiracy theorists
- RBD: Receptor-binding domain, a portion of the spike protein of SARS-CoV-2 which attaches to a human host cell
- S1/S2 boundary: The point on the spike protein of SARS-CoV-2 where the furin cleavage site is located in order to split the protein most efficiently
- SARS-CoV-1: The virus that caused the SARS pandemic in 2002, which was largely contained
- SARS-CoV-2: The virus that causes COVID-19
- WIV: Wuhan Institute of Virology, the lab where Dr. Shi Zhengli conducted research on bat coronaviruses

Ralph Baric and Edward Holmes

There are three main centers for CoV studies globally, including the Wuhan Institute of Virology (WIV), the University of North Carolina (UNC), led by Dr. Ralph Baric, and the University of Texas Medical Branch (UTMB) Health Galveston, Texas.

The enormous and collaborative scientific discourse that existed between UNC and WIV, as Dr. Kristian Andersen mentioned (see part two), provides an understanding of what forms of viral experiments were feasible.

Dr. Shi and Dr. Baric published a 2015 report demonstrating the feasibility of attaching a SARS-like spike protein to the backbone of a SARS virus, creating a chimeric virus (so-called after the Chimera of Greek mythology, because it combines two separate microorganisms), that proved pathogenic in mouse models. The designed virus was created in Dr. Baric’s lab at UNC.) But, as previously stated, the RaTG13 genome found in Yunnan Province did not produce a live virus, nor was it sufficiently close in its genetic makeup to the SARS-CoV-2 virus to allow bioengineering to create the hitherto unknown SARS-CoV-2.

According to an account published in the *New Yorker*, Dr. Baric, who was one of the signatories calling for more investigation into the origin of the SARS-CoV-2 virus, said, “I really believe that the genetic sequence for sars-CoV-2 really points to a natural-origin event from wildlife.” Perhaps the most renowned and leading expert on coronaviruses in the world, Dr. Baric carefully explained that the repository of viruses in nature is magnitudes higher than what would be found in the library of the Wuhan lab.

Dr. Baric also noted that the SARS-CoV-2 virus is so different than any other known virus, to engineer it “from an ancestral strain” would have been a truly unprecedented feat of molecular biology. “And of course, you don’t know what you’re engineering, because SARS-CoV-2 would not have existed,” Baric said.

Counterfactually, he stated he had seen no evidence that the virus had been collected from the wild, unknown to the lab, and somehow escaped the containment of the WIV. The *New Yorker* report concluded, “All that is known for sure is that a pathogen that likely originated in bats had transferred species and caused a global pandemic in human beings, perhaps in a way that had only happened a few times in modern medical history or in a way—through a lab—that may never have happened before. Baric’s preference was for the theory that resembled previous outbreaks.”

Placing Dr. Baric’s comment in context, a recent article accepted to the journal *Cell* by Edward Holmes and colleagues, “Identification of novel bat coronaviruses,” sheds light on the evolutionary origins of SARS-CoV-2 and related viruses. The discussion section includes the following passage:

> In total, we assembled 24 novel coronavirus genomes from different bat species, including four SARS-CoV-2 like coronaviruses. Additional PCR-based tests revealed the presence

> of these four viruses in nine individual samples collected in Yunnan province between May and July 2020. Together with the SARS-CoV-2 related virus collected from Thailand in June 2020, these results clearly demonstrate that viruses closely related to SARS-CoV-2 continue to circulate in bat populations, and in some regions might occur at a relatively high frequency.

The authors state that the "Rhinolophus pusillus virus RpYN06 was the closest relative of SARS-CoV-2 in most of the genome, although it possessed a more divergent spike gene." The other three related SARS-CoV-2 viruses had genetically distinct spike genes that were capable of binding to the human ACE2 receptor, though lacking a furin cleavage site. The study acknowledges that the direct progenitor of SARS-CoV-2 remains unclear. However, the study provides strong circumstantial evidence that implicates a natural origin for the SARS-CoV-2 virus.

Holmes, an evolutionary biologist and virologist at the University of Sydney, Australia, calculates that "the level of genome sequence divergence between SARS-CoV-2 and RaTG13 is equivalent to an average of 50 years (and at least 20 years) of evolutionary change."

"Hence, SARS-CoV-2 was not derived from RaTG13," Holmes has written, adding that "the abundance, diversity and evolution of coronaviruses in wildlife strongly suggests that this virus is of natural origin."

Benhur Lee and Stephen Goldstein

Dr. Benhur Lee is the Ward-Coleman Chair in microbiology at the Icahn School of Medicine at Mount Sinai Hospital in New York City. His lab focuses on explaining how viruses co-opt basic cell biological processes to complete their life cycles and the numerous strategies used by viruses to propagate themselves.

In response to the claim by Nicholas Wade in his attack on Andersen's "proximal origin" study that the Wuhan lab used an unpublished coronavirus DNA backbone derived from RaTG13 as the basis for engineering a new and deadly virus, the Benhur Lee Lab offers a pointed reply, arguing the inherent improbability of such a course of action:

> To reiterate, most of SARS-CoV-2 comes from a bat coronavirus closely related to RaTG13. This virus is not known to cause disease in humans. If we were virus engineers (and this actually happens to be my job in the Benhur Lee lab), we would need to: Make a virus backbone from a never-before-seen virus that looks like, but isn't, RaTG13, without having any reason to believe it would be a better starting place than a previously characterized virus (like the original SARS-CoV). [Then] spend months to years building a system that is easy to engineer (reverse-genetics system) when there are other virus backbones readily available. [Afterwards], choose the RBD region from an unknown pangolin coronavirus even though all computer models show it should be suboptimal at binding ACE2, and show that it binds well in spite of the models. All of these steps sound like bad ideas from a scientist's perspective. There were easier ways to engineer a coronavirus, and no one would have rationally chosen either the bat virus backbone or the pangolin portion of the spike protein. Therefore, *SARS-CoV-2 is unlikely to be man-made from pieces of other viruses* —we have zero evidence that any person or lab has attempted even one part of this process.

In other words, no virus engineer would have proceeded in the fashion alleged by the promoters of the "lab leak" theory. The random variation of natural selection provides a far superior explanation of the actual course of development of the virus, and given that we are only 18 months into the pandemic, the "gaps" in this explanation simply reflect the actual development of scientific knowledge, not some nefarious conspiracy.

According to the lab's hypothesis

> The available data suggests a two-step process that may have given rise to SARS-CoV-2. 1) A bat coronavirus likely infected an intermediary animal (potentially a Malayan pangolin) where it recombined with a non-bat coronavirus. Then, 2) over time, either in the intermediary animal or while in humans, SARS-CoV-2 developed additional mutations—a polybasic cleavage site and a nearby O-linked glycan addition site. [More on this below]

The Benhur Lee Lab adds that SARS-CoV-2 either acquired these gains before spillover into humans or acquired them while developing in humans. These hypotheses are in agreement with Kristian Andersen's conclusions.

As previously stated, the RaTG13 virus lacks the furin cleavage site. The Benhur Lee Lab noted

> a hypothetical generation of SARS-CoV-2 by cell culture or animal passage would have required prior isolation of a progenitor virus with very high genetic similarity, which has not been described. The subsequent generation of a *polybasic cleavage site* would have then required repeated passage in cell culture or animals with ACE2 receptors like those of humans, but such work has also not previously been described.

In other words, the Wuhan lab has not reported any of the intermediate steps that would be required to facilitate the creation of SARS-CoV-2, steps that would have been routinely reported in previous publications, because no one, either at the Wuhan lab or in its international professional audience, would have recognized this as creating precursors of a deadly virus. The trajectory from RaTG13 to SARS-CoV-2 is so complicated and unlikely, involving, by Holmes' estimate, nearly 1,200 separate edits to the genome, that not even natural selection, with billions upon billions of such "edits," can account for it.

A similar assessment of the natural origins of SARS-CoV-2 appeared last week in *Foreign Policy* magazine, hardly a bastion of hostility to American imperialism or sympathy to the Chinese government. The article by contributor Justin Ling carries the headline, "The Lab Leak Theory Doesn't Hold Up."

Ling points out that the apparent geographical path of SARS-CoV-2, from bat caves in southern Yunnan province to animals sold at a wet market in central China (Wuhan) to human beings, far from being improbable, as claimed by Nicholas Wade and other "lab leak" advocates, is nearly identical to that followed by the original SARS outbreak in 2002.

He cites the views of Stephen Goldstein, who studies evolutionary virology at the University of Utah, and denies that there is "growing evidence" to support the lab leak hypothesis.

Commenting on the findings of Edward Holmes, Goldstein regards the number of changes required to transform RaTG13 into SARS-CoV-2 as an insurmountable hurdle. "Cramming 50 years of evolution into eight is impossible," Goldstein said. "Forcing 1,000 nucleotide changes—just, no."

Goldstein also rejects the argument that the furin cleavage site on SARS-

CoV2 demonstrates its artificial or engineered character, one of the main pseudo-scientific claims of Wade & Co. “You cannot, in a normal cell culture, maintain the furin cleavage site,” he told Ling. Instead of the furin cleavage site being particularly well adapted for humans, the opposite is true.

“No virologist would use that cleavage site,” he told Ling, adding that in the lab, the cleavage site has a tendency to delete itself, and to employ it would “require doing things differently than everyone does them,” and would actually slow down replication of the virus. “We’re not good enough, in virology, to make the perfect virus,” Goldstein concludes.

Finally, it is worth briefly discussing the O-linked glycan modifications necessary for the function of SARS-CoV-2 virus, mentioned by the Benhur Lee Lab. In the “Proximal origins” paper, Dr. Andersen’s team had noted that the O-linked glycan sites on the SARS-CoV-2 virus aid it to evade the host’s immune system by masking the virus. Other functions include helping the virus to bind to the host cell and enter and leave the cell after replicating itself.

A July 2020 article published in *Science*, analyzing the spike protein of the SARS-CoV-2 virus for vaccine development, notes that these “O-linked glycan sites” develop under the pressure of natural selection. In order to acquire them the SARS-CoV-2 virus needed the selective pressure of being exposed to a living organism with an intact immune system. The generation of the “O-linked glycans” is unlikely to have occurred from cell-culture passage in a laboratory. The virus would have to be passed through animals to enhance these particular functions.

As Ling noted in the *Foreign Policy* article, paraphrasing Dr. Goldstein, if the scientists at Wuhan had attempted a serial animal passage experiment, meaning to have the virus replicate and mutate in animals until an efficient and suitable virus was created, “The lab would need to run a veritable petting zoo of different animals to perfect this kind of zoonotic transmission. And it still doesn’t account for the decades of necessary evolution. Prior to the outbreak in December 2019, nothing closely resembling the COVID-19 virus was reported in any lab. Since it has emerged, it has taken hundreds of millions of infections to net just a handful of serious mutations and variants.”

Conclusion

In five years of extensive work at the Wuhan lab, Dr. Shi Zhengli explained that her team discovered only 11 full-length genomes of SARS-related CoV. This speaks to the complexity of such research. Only three live viruses have been collected in the nearly 20 years since the SARS-CoV-1 epidemic.

It also took more than 15 years after SARS-CoV-1 was discovered for the animal origin to be identified. There is nothing unusual in this. For instance, Ebola is thought to have a zoonotic origin (derived from nature), but its natural reservoir remains unknown 40 years later. The argument that the pool for SARS-CoV-2 has yet to be uncovered and, therefore, by Wade’s troubled logic, it must have been manufactured in a Chinese lab, is a false one generated for political purposes.

As to the three WIV workers who allegedly fell ill with respiratory illnesses in November, the WHO-convened global study of the origins of SARS-CoV-2 offers a critical glimpse into the months leading into the pandemic in Wuhan. Using surveillance data on influenza-like illnesses and severe respiratory illnesses, they showed that laboratory cases of influenza began to climb quickly in early November.

It was only in early to the middle of December when unusual respiratory illnesses began to rise in the city. Corroborating this was the finding that excess deaths (deaths compared to previous years’ averages) did not start to climb sharply until the second week in January of 2020, centered in the area around the Hunan seafood market before expanding into the wider region. Additionally, the report comments that several international conferences were held in Wuhan from September to December 2019 without confirmation that any superspreading events had occurred as a byproduct of these gatherings.

Aside from Dr. Shi’s claim that all employees at WIV had tested negative and there were no infections reported at the institute, given the asymptomatic nature of COVID-19 infections, if in November three WIV workers were infected with SARS-CoV-2, it would most likely have led to a cluster of outbreaks at the institute, necessitating the closure of the facility for infection control and monitoring, well before the epidemic in Wuhan. The foreign press would have immediately reported such an event. These facts would have also come to the attention of the US intelligence community, the World Health Organization, and leaked by dissidents.

This review of the science demonstrates that the hypothesis identified as most likely in March-April 2020—a natural origin of SARS-CoV-2—remains after more than a year the most plausible. No evidence has been brought forward to undermine it. The campaign in support of the “lab leak” theory has no significant scientific basis.

As the *World Socialist Web Site* has explained:

> The promotion of the lab-origin theory is driven by political conditions and social interests, motivated by two interrelated purposes. First, it aims to divert attention from the actions of the US and other governments in implementing policies that led to deaths on a massive scale. As the public begins to recover from the overwhelming shock of the pandemic, there will be demands for explanations for why so many people died, along with accountability for those responsible. ... Second, the Wuhan lab lie seeks to drum up nationalist hatred to support the Biden administration’s central strategic aim: the preparation for economic and potentially military conflict with China.

Efforts to assist the scientists in their collaboration to identify the source of the virus and prepare for future pandemic pathogens are of vital global interest. The bourgeois press campaign maligning the Chinese scientists and their colleagues in the United States and elsewhere sabotages such collaboration and undermines both science and public health all over the world for the most nefarious purposes.

As the WSWS stated early in this malignant campaign,

> The structure and methods of the “Wuhan lab” conspiracy theory are highly similar to other conspiracy theories promoted for political purposes, with which the propagandists in Washington and other world capitals are very familiar. ... The Chinese government, for its part, cannot but interpret the promotion of this lie as preparation for war, responding in a way that will make escalation more likely, creating a deadly cycle of militarization. A military conflict between the United States and China—the largest economies and militaries in the world—would have catastrophic consequences for all of humanity.

This warning is entirely vindicated by this review of the scientific literature on the origins of SARS-CoV-2, the virus that causes COVID-19.

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