

Peer Review

Review of: "The Contentious Origins of SARS-CoV-2: A Comprehensive Review of Current Knowledge"

Jonas Wolf¹

1. Hospital Moinhos de Vento, Porto Alegre, Brazil

This review provides a timely and comprehensive synthesis of scientific literature regarding the origins of SARS-CoV-2, engaging with one of the most consequential and politically sensitive topics of the COVID-19 era. A major strength of the manuscript lies in its focus on the two prevailing hypotheses—zoonotic spillover and laboratory-associated emergence—offering a balanced framework for comparison. By structuring the analysis around peer-reviewed literature published between December 2023 and January 2025, while also integrating earlier pivotal studies, the authors ensure both recency and historical continuity, which is essential for understanding the evolving discourse.

The phylogenetic evidence presented is persuasive and well-articulated, particularly in illustrating the genetic proximity of SARS-CoV-2 to known bat coronaviruses. This supports the zoonotic origin hypothesis and aligns with prevailing scientific consensus. The review effectively contextualizes these genetic findings within broader ecological dynamics, particularly through its discussion of the Huanan Seafood Market and the presence of viral RNA in animal-related environmental samples, which is a crucial and often contested piece of epidemiological evidence.

Another noteworthy contribution is the discussion of environmental sampling, which adds granularity to the narrative and shifts the focus from purely genomic to real-world virological surveillance. By integrating this data, the authors present a multi-layered evidentiary case that avoids over-reliance on any single methodology. This interdisciplinary lens aligns with the article's later advocacy for One Health frameworks, which emphasize the interconnectedness of human, animal, and environmental health.

However, while the review acknowledges the ongoing uncertainty surrounding the intermediate host, it could benefit from a more detailed discussion of the implications of this unresolved issue. For instance, how does the lack of an identified intermediate species affect current surveillance strategies? Could

alternative ecological reservoirs be playing a more complex role in viral emergence? Addressing these questions would enrich the critical discussion and nuance the current conclusion, which otherwise leans strongly toward zoonotic spillover without fully grappling with its remaining limitations.

The treatment of the laboratory-origin hypothesis, although appropriately constrained by the available evidence, appears somewhat underdeveloped. While the review rightly points out the absence of direct evidence supporting lab-based emergence, a more in-depth analysis of biosafety protocols, viral research practices in Wuhan, and metadata transparency from relevant institutions would strengthen the section's credibility. Providing a more rigorous critique of the evidence gaps and ongoing investigative limitations would help avoid the perception of dismissal and contribute to scientific openness.

Moreover, the review could be enhanced by a clearer articulation of the criteria used for evaluating the quality and reliability of included studies. For example, were particular study designs prioritized? Were preprints considered or excluded? Addressing these methodological considerations would improve reproducibility and transparency, especially given the politically charged nature of the topic.

The review's conclusion is a strong point, as it extends beyond retrospective analysis and offers constructive, evidence-based recommendations. The emphasis on viral surveillance, One Health strategies, and international cooperation reflects a forward-looking orientation and a commitment to practical public health applications. This bridges the gap between academic inquiry and global preparedness and suggests a mature understanding of the broader context in which origin debates occur.

Language clarity and scientific tone are generally well-maintained throughout the text. However, certain sections would benefit from tighter phrasing and more precise terminology. For example, terms such as "laboratory-related emergence" could be specified further—does this include accidental leaks, gain-of-function experiments, or undocumented research practices? Defining the scope of these terms would enhance interpretive clarity.

In terms of structure, the article follows a logical progression from background to evidence synthesis to conclusion. Still, the flow between sections—particularly the transition from phylogenetic evidence to environmental data—could be made smoother. The use of subheadings or visual summaries (e.g., a comparative table of supporting evidence for each hypothesis) would further enhance readability and accessibility for a diverse scientific audience.

Overall, this review makes a valuable and responsible contribution to an ongoing global discourse. Its well-supported endorsement of a zoonotic origin aligns with current data while acknowledging key

unknowns. By incorporating additional methodological rigor, expanding its treatment of alternative hypotheses, and enhancing structural clarity, the article could further solidify its role as a reliable reference point for both scientists and policymakers seeking to understand the origins of SARS-CoV-2.

Declarations

Potential competing interests: No potential competing interests to declare.