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Peer Review

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

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This is a review of the manuscript "The Contentious Origins of SARS-CoV-2: A Comprehensive Review of Current Knowledge" (DOI: https://doi.org/10.32388/AZ7D1X), which was written by Jose L. Domingo (School of Medicine, Universitat Rovira i Virgili, Spain).

This manuscript provides a valuable synthesis of recent literature on the origins of SARS-CoV-2, engaging with one of the most contentious topics in virology. The author does well to emphasize the importance of phylogenetic evidence and environmental sampling data, both of which contribute to our understanding of the virus's likely zoonotic origins. The discussion of genetic relationships to bat coronaviruses is particularly relevant, as this continues to be a central piece of evidence supporting a natural spillover event. Additionally, the focus on policy-oriented recommendations, including enhanced viral surveillance and One Health approaches, adds a forward-thinking dimension to the review that could help guide future research and public health initiatives.

However, there are areas where the manuscript could be strengthened to improve its methodological clarity, logical consistency, and overall impact.

Key Areas for Improvement:

1. **Clarification of Literature Selection Criteria:** The review defines "relevant studies" based on PubMed and Scopus metrics, but it does not provide clear inclusion and exclusion criteria for selecting papers. To improve transparency and reproducibility, the author should specify:
    - How studies were deemed relevant.
    - Whether any filters (*e.g.*, study type, impact factor) were applied.
    - Summary statistics on the total number of papers screened, reviewed, and excluded.

2. **Definition of "Strong Phylogenetic Evidence:"** The manuscript states that phylogenetic evidence supports a zoonotic origin, but it does not define what qualifies as "strong evidence." Since phylogenies are hypotheses built from coded observations, it is important to distinguish between hypotheses and empirical evidence supporting them. Providing explicit criteria for evaluating phylogenetic robustness would enhance the manuscript's analytical depth.
3. **Consideration of Alternative Explanations for the Missing Intermediate Host:** The absence of a definitively identified intermediate host is presented as a lingering uncertainty, but this may not be as critical as implied. Several factors (such as insufficient investment in fundamental research or limited access to biorepositories) could explain why an intermediate host remains unidentified. Additionally, the possibility that an intermediate host was not required for zoonotic transmission should be explicitly addressed. A more balanced discussion would help contextualize this uncertainty.
4. **Timeframe Restriction and Citation Scope:** While the abstract states that only literature from December 2023 to January 2025 was analyzed, the reference list includes papers dating back to 2019. This contradiction weakens the manuscript's methodological coherence. The author should either:
    - Align the citations with the stated timeframe, or
    - Modify the methodology to reflect the broader range of sources used.
5. **Missing Key Publications on Phylogenetics:** Additionally, by restricting the review to only recent publications, key foundational studies (such as Jacob Machado *et al.*, 2021, DOI: https://doi.org/10.1111/cla.12454) are excluded, despite their significant contributions to coronavirus evolution and phylogenetics. If such omissions are intentional, they should be justified.
6. **Avoiding Speculative Reasoning in Discussions of Laboratory-Origin Theories:** The manuscript acknowledges that continued speculation about a laboratory leak persists, but it suggests that this justifies further investigation. Scientific inquiry should be driven by evidence, not speculation. The discussion would be stronger if it explicitly differentiated between scientific uncertainty (which warrants further investigation) and unsubstantiated speculation (which does not).

Declarations

Potential competing interests: No potential competing interests to declare.