

Review of: "Protection against COVID-19 in African population: Immunology, genetics, and malaria clues for therapeutic targets"

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Potential competing interests: No potential competing interests to declare.

This paper provides an innovative and thorough examination of the potential immunological and genetic factors influencing COVID-19 outcomes in African populations. While some hypotheses remain speculative, the integration of evolutionary, immunological, and genetic insights makes it a valuable resource for understanding the unique epidemiological patterns observed in Africa. However, further empirical validation and a more balanced consideration of non-genetic factors are essential to substantiate the proposed mechanisms and broaden their applicability.

Suggestions for Improvement of the Paper

- 1. The role of LAIR-1 and glycophorins in SARS-CoV-2 infection is speculative and would benefit from experimental validation.
- 2. While the genetic explanations are compelling, the paper does not fully address non-genetic factors such as demographic structures (e.g., a younger population), underreporting, or differences in health systems, which may also contribute significantly to the observed discrepancies.
- 3. Africa is a genetically and epidemiologically diverse continent. The paper does not sufficiently address regional differences in COVID-19 outcomes or genetic diversity.
- 4. Potential confounding factors, such as the impact of climate, socioeconomic disparities, and access to healthcare, are not deeply analyzed.
- 5. While the association between malaria and a reduced inflammatory response is well-documented, the causative link to reduced COVID-19 severity in African populations remains speculative and indirect.

Furthermore, the paper would benefit from the inclusion of more updated references to strengthen its relevance and reliability. Integrating recent studies and findings related to the topic will demonstrate the author's awareness of current developments in the field and ensure that the paper remains up-to-date.

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These enhancements will contribute to the overall quality and impact of the paper, enhancing its value to the academic community and readers interested in the subject matter.

