

24 May, 2023.

Manuscript Title: “*CCR5*Δ32, *CCR2*-64I, *SDF1*-3'A, and *IFN*λ4 rs12979860 and rs8099917 gene polymorphisms in individuals with HIV-1, HIV/HTLV-1 and HIV/HTLV-2 in São Paulo, Brazil”

Type: Original Research

Dear Kovy Arteaga-Livias,

Editor in Chief *Microbes, Infection and Chemotherapy*

First of all, we would like to thank you and the reviewers of the above manuscript for considering our manuscript for revision, and for all doubts, queries and comments, which we consider essential to improve our revised version of the manuscript. We endeavor to address and incorporate all comments, and requested information and references (highlighted in the Main Document R1). We also send apart the Authors Contribution Statement as you recommended.

We emphasize that the manuscript was sent to Editage by Cactus Communications Services Pte. Ltd. for English language editing.

In conclusion, we hope that with these changes and comments our manuscript can be considered for publication in this journal.

We look forward to hearing from you and we thank you in advance for your attention.

Sincerely yours,

Corresponding author and co-authors

Reviewers Comments and Answers:

Reviewer A

1. Relevance of the title to the content of the article

Good

2. Summary: Presents the general idea of the topic, objectives, research methods, results and conclusions, written in an objective and concise manner; and are found according to the maximum number of words per section.

Good

3. Introduction: Presentation of the subject, justification of the problem, objectives, hypotheses and methodological foundation, exposing the subject in an orderly and detailed manner

Good

4. Methodology: Describes the procedure, methods and techniques used in data collection and analysis.

Good

5. **Ethical aspects.** Does the manuscript have a paragraph on ethical aspects, where it mentions approval by the ethics committee, informed consent, and strict compliance with research ethics?

No

Answer: The ethical aspects were described in the last paragraph of the METHODS section, subsection Study Design, Population, Samples, Groups for Analysis (highlighted in Main Document R1).

6. Results: They are presented adequately and it is not redundant with tables or graphs shown.

Good

7. **Discussion:** They present a level of critical analysis in correspondence with the problem presented. Purposes of the article, scope, support theory and proposed methodological design.

Regular

Remarks

The discussion needs minor changes, like the inclusion of figure numbers, for a better understanding.

Answer: We included Table numbers for better understanding, and we have improved the discussion and added another reference as suggested by reviewer C (highlighted in Main Document R1).

8. Conclusions: Presents the author's inferences and teachings in relation to the investigated topic, it must correspond to the objectives of the study.

Good

9. **References.** Quality of bibliographic references and if they are in accordance with the Vancouver format.

Regular

Remarks

A few references are not correct

Answer: Thank you for your observation and we apologize for the wrong references 1 and 2 that were changed. In addition, we review all references in accordance with the journal's instructions and the Vancouver format (added all doi).

10. **Redaction.** Is the manuscript correctly written? Does it contain any spelling or grammar mistakes?

Needs some language corrections

Answer: We had already submitted the manuscript to Editage by Cactus Communications Services Pte. Ltd. for English editing (a company used and recommended by several prestigious international journals, see attachment), and now the R1 version has been revised by a professional residing abroad.

11. **Contributions.** What are the main weaknesses of the manuscript and how the author can do to improve it

1. Discussion needs improvement

Answer: Done

2. English improvement by a native English speaker

Answer: Done

3. References need to be changed

Answer: Done

Finally, we appreciate your comments and assistance in improving our manuscript, and we hope to have answered all of your questions and comments.

Reviewer C

1. Relevance of the title to the content of the article

Good

2. Summary: Presents the general idea of the topic, objectives, research methods, results and conclusions, written in an objective and concise manner; and are found according to the maximum number of words per section.

Good

3. Introduction: Presentation of the subject, justification of the problem, objectives, hypotheses and methodological foundation, exposing the subject in an orderly and detailed manner

Good

4. Methodology: Describes the procedure, methods and techniques used in data collection and analysis.

Good

5. Ethical aspects. Does the manuscript have a paragraph on ethical aspects, where it mentions approval by the ethics committee, informed consent, and strict compliance with research ethics?

Yes

6. Results: They are presented adequately and it is not redundant with tables or graphs shown.

Good

7. **Discussion:** They present a level of critical analysis in correspondence with the problem presented. Purposes of the article, scope, support theory and proposed methodological design.

Regular

Remarks

The discussion is very extensive and descriptive, it would be interesting to explore some hypotheses related to the inference of polymorphisms on the course of coinfection.

Answer: We appreciate your comments. We agree that the discussion is extensive, but we intended to compare the frequencies of polymorphisms in the genes analyzed in the

present study with those described in others populations from Brazil. We also improved and discussed hypotheses related to the inference of these polymorphisms in HIV infection and HIV/HTLV co-infections, and added the reference you suggested (highlighted).

8. Conclusions: Presents the author's inferences and teachings in relation to the investigated topic, it must correspond to the objectives of the study.

Poor

Answer: We agree that the conclusions are poor, but the only thing we can say is that all polymorphism profiles described in the literature were found in the present study, and in percentages that resemble descriptions of mixed-race populations. Also, we concluded that the search for $\Delta 32$ polymorphism can be used as a predictive marker for ART introduction (as well documented in previous studies worldwide). The other findings of polymorphisms, mainly in HIV/HTLV-2 co-infections, led us to raise hypotheses that need to be evaluated and confirmed in well-designed studies in the future.

9. References. Quality of bibliographic references and if they are in accordance with the Vancouver format.

Regular

Remarks

I suggest including an additional reference : da Silva Prates G, Malta FM, de Toledo Gonçalves F, Monteiro MA, Fonseca LAM, R Veiga AP, M C Magri M, Duarte AJS, Casseb J, Assone T; ADEE 3002 GROUP. AIDS incidence and survival in a hospital-based cohort of HIV-positive patients from São Paulo, Brazil: The role of IFN- $\lambda 4$ polymorphisms. J Med Virol. 2021 Jun;93(6):3601-3606. doi: 10.1002/jmv.26054. Epub 2020 Oct 10. PMID: 32449798.

Answer: The reference was included

10. Redaction. Is the manuscript correctly written? Does it contain any spelling or grammar mistakes?

Acceptable

11. Contributions. What are the main weaknesses of the manuscript and how the author can do to improve it

In fact, the Brazilian population is of mixed race, and the data obtained in this study do not support this discussion, since specific tests to determine genetic ancestry should have been carried out to support such a conclusion. Thus, the conclusion only reflects the prevalence of the polymorphisms studied in this population, without predicting any hypotheses related to both population and clinical outcomes.

I suggest that the author explore some common outcome among the individuals studied, or that he proposes only to present the prevalence of polymorphisms.

Answer: We agree with the reviewer that specific tests are needed to determine genetic ancestry, and add this information in the text (highlighted). We tried to explore some common outcome of the individuals studied.

Finally, we appreciate your concerns, suggestions, and assistance in improving our manuscript, and we hope to have answered all of your questions and concerns.



Editing Certificate

This document certifies that the manuscript listed below has been edited to ensure language and grammar accuracy and is error free in these aspects. The edit was performed by professional editors at Editage, a division of Cactus Communications. The author's core research ideas were not altered in any way during the editing process. The quality of the edit has been guaranteed, with the assumption that our suggested changes have been accepted and the text has not been further altered without the knowledge of our editors.

MANUSCRIPT TITLE

CCR5^{Δ32}, CCR2-64I, SDF1-3'A, and IFNλ4 rs12979860 and rs8099917 gene polymorphisms in individuals with HIV-1, HIV/HTLV-1 and HIV/HTLV-2 in São Paulo, Brazil

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April 08, 2023

JOB CODE

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Vikas Narang

Vikas Narang
Chief Operating Officer - Editage



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