Reviewer’s report

Title: Prevalence of CCR5delta32 in Northeastern Iran

Version: 0 Date: 04 Aug 2019

Reviewer: Daniela Zanetti

Reviewer's report:

Comments to the Authors

The authors present an interesting study about a 32-base pair deletion (Δ32) in the open reading frame (ORF) of C-C motif chemokine receptor 5 (CCR5). The CCR5Δ32/Δ32 seems to be protective against the HIV infection, while the CCR5Δ32 heterozygote genotype (CCR5Wild/Δ32) considerably hinders the onset of AIDS but is not quite protected against it. The authors aim to assess the frequency of CCR5Δ32 in the healthy Iranian population.

The analysis is generally well-conceived and executed, and the paper is easy to follow. However, the study needs additional analysis and a deeper discussion in order to be suitable for publication.

Major comments:

1. The authors assessed that the frequency of CCR5Δ32 allele in the general population of North East of Iran has not been investigated, and that the low prevalence of CCR5Δ32 allele in the Iranian population may result in the increased susceptibility to HIV-1. Has the prevalence of HIV-1 in Iran been investigated before? Is the prevalence of HIV-1 in Iran higher than in Europe and in East Asia? The authors should analyze the allele frequency of the CCR5 locus in relation to the HIV-1 prevalence in Iran and in other countries.

2. The authors affirmed that the samples are not in HWE (P-value = 0.0199) without discussing the possible reason of this result. This point needs further explanations.

3. The Δ32 mutation at the CCR5 locus is a well-studied example of natural selection acting in humans. It would be interesting for the manuscript to perform some type of selection analyses (spatial ancestry analysis or maybe a geographical distribution of the minor allele frequency of the CCR5 locus) using the Iranian population together with the 1000 Genome Populations, if no other populations are available. In addition to this, it would be interesting to compare the geographical allele frequency distribution of the CCR5 locus with the prevalence of HIV-1 in different countries. The two maps (allele frequency of CCR5 and prevalence of HIV-1) will be useful to discuss about the origin of CCR5 in Iran compared to other countries.

4. Page 7: Some studies have shown the relation between CCR5Δ32 allele and MS disease.
Can the authors discuss the possible links between CCR5Δ32, MS and HIV-1?

5. Can the authors explain this sentence?
An application of this research can be identified the most appropriate individuals to work with HIV-1 in the laboratories, in which we could enroll personnel having this mutation to reduce the risk of HIV-1 infection in the laboratories.
What does it mean "to work with HIV-1 in the laboratories"? Is there perhaps an high risk of HIV-1 infection in the laboratories? Could the authors contextualize this affirmation?

Minor comments:
1. What does the term Caucasian mean in this context? Europeans? The reference 17 did not use the term Caucasian.
2. Page 5 discuss the origin of these genotypes
3. Page 6: In addition, the bioinformatics analysis indicated that mutated proteins lost three alpha helices, as the results of this changes degraded in the cells.

Nevertheless, modeling indicated that the truncated protein also have the required domains for virus attachment and these domains did not show major conformational alterations with the wild type ones, so we can conclude that displaying the truncated protein on the cell surface may be a possible way of virus entry.

4. Page 6 and 7: In addition, the bioinformatics……………… which may be considered as research area to the prevention of HIV infection
Please, add some references for all this section.

5. Page 8: whereas some side effects such as drug-drug interactions, substantial toxicity, difficulties in adherence, and increased costs remain.

6. Page 8: an higher susceptibility should be taken to prevent
Moreover, these findings provide a vision (what does the term "vision" mean for the authors?) for scientists to define future research in the field of immunobiology of HIV-1 in Iranian population.

7. The authors should revise the language of all the manuscript, especially the discussion.

8. Availability of data and materials
Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

What about the 400 samples genotyped? I think that the authors generated and analyzed new data in the current study.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published
Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal