Reviewer's report

Title: Impact of Y181C and/or H221Y Mutation Patterns on HIV-1 Phenotypic Resistance to Available Non-Nucleoside and Nucleoside Inhibitors in China

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Reviewer: Annapaola Callegaro

Reviewer's report:

In this work Guo et al. try to define the impact of Y181C and H221Y different resistance mutations patterns on phenotypic resistance to NNRTI and NRTI currently available in China.

Pol-gene clonal fragments with different mutations patterns, from plasma and PBMCs of HIV-1 infected patients failing a NVP regimen, were inserted into pNL4-3 backbone plasmid. Strains, containing different drug-resistance mutations profiles, were obtained. Phenotypic resistance to NNRTI and NRTI was analyze on TZM-b1- cells. The method has already been described, even by the authors, to determine the phenotypic resistance of HIV-1 virus to antiretroviral drugs.

The work, that can best be described, adds some informations in understanding the relationships between HIV-1 genotypic and phenotypic resistance to antiretroviral drugs, especially NNRTI. More understanding about novel mutations is needed to manage HIV-1 drug resistance in the clinical setting.

In my opinion, it could be considered for publication, even if some points must be clarified and more in-depth.

Background

Page 3 Line 2: “…with different combined forms…. change in ..” in different mutations patterns”… Change it also in the other parts of the manuscript.

Page 4 Line 15: “ NNRTIs have been recommended to be parts..” is more correct to change it in “ NNRTI have been used as parts…”

Methods section

Pag 6 line 16: delete “plasma”

In Patients and Samples sub-section the time intervals of samples collection during follow up should be specified

Pag 6 line 19: “ HIV-1” add subtype B

Page 7 line 1-6: viral RNA and DNA extraction and the method of cloning must be described in greater details

In Construction of recombinant virus sub-section, K101Q/Y181C, K101/H221Y and K101Q recombinant strains are reported. This contrasts with the strains
reported in the results section (page 9 and table 1): K101Q/Y181C/H221Y, K101Q/Y181C, K101/H221Y, and K101Q. Clarify this point and correct the wrong part.

Page 7 line 19-21: is not clear to me if H221Y recombinant strain was used for the experiment. Would be so from the results. Best explain this point.

Results section
Page 9 line 1-8: Plasma and PBMC sample have been collected and analyzed. Provide more details on the difference, if any, in emerging resistance mutations between plasma and PBMC.

Table 1: The EC50 of the 5 viruses: in this table EC50 and IC50 terms have been interchanged. I don’t think the two should be mixed within the same project. If the terminology such as percentage (%) of “inhibition” of virus (as reported in Figure 1) is used, then IC50 would be more appropriate.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare I have no competing interests