Author's response to reviews

Title: HIV-1 transmitted drug resistance-associated mutations and Mutation Co-variation in HIV-1 Treatment-Naive MSM from 2011 to 2013 in Beijing, China

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Author's response to reviews: see over
Response to reviewer’s report -1:

In this manuscript, the authors studied HIV-1 transmitted drug resistance (TDR)-associated mutations and mutation co-variation in HIV-1 treatment-naive MSM from 2011 to 2013 in Beijing, China. They found Among 223 samples sequenced and analyzed, HIV-1 CRF01_AE, CRF07_BC, and subtype B were accounted for 60.53%, 27.80%, and 9.86%, and 57 MSM had at least one TDR-associated mutation, with different distribution of TDR-associated mutations among different HIV-1 subtypes/each year. This study revealed a very comprehensive genetic characterization of HIV-1 strains prevalent in MSM group and provided important information to understand the TDR and evolution of HIV-1 among MSM population in China, suggesting that high-risk behavior for HIV-1 transmission might cause an increased rise of HIV TDR-associated mutations.

Overall, this is a well designed study providing interesting and significant findings. Most of the conclusions are justified by the data provided. A few issues need to be addressed.

Major comments

1. In the 2nd paragraph of the result, the authors mentioned “(1065 bp total, encoding the protease gene and part of the reverse transcriptase gene region)”. However, they stated it differently in the 2nd paragraph of Materials and Methods section “The HIV-1 pol gene (1,197 bp length) containing the full-length protease gene and the first 300 codons of the reverse transcriptase gene were amplified and sequenced”. Was the length of amplified fragment 1065bp or 1197bp? Please clarify it.

Response: Thanks! We made a mistake here, the length of amplified fragment is 1197bp. We have corrected it in line 190.

2. In the 5th paragraph of the discussion, the authors mentioned “Subtype B has higher rate (54.54 %) of TDR-associated mutations than subtype B and CRF01_AE among HIV-1 infected MSM.” Please explain why there are two “subtype B” compared here.

Response: Thanks! The sentence “Subtype B has higher rate (54.54 %) of TDR-associated mutations than subtype B and CRF01_AE among HIV-1 infected MSM.” in line 269 should be changed to “Subtype B has higher rate (54.54 %) of TDR-associated mutations than CRF07_BC and CRF01_AE among HIV-1 infected MSM.”

3. The co-variation analysis provided very useful information. The Jaccard similarity coefficient was used to measure the co-variation between TDR mutations and positive
selected mutations. Please provide the criteria that the authors used to judge whether the co-variation is statistical significance or not.

Response: Thanks! The Jaccard similarity coefficient was used to measure the co-variation between TDR mutations and positive selected mutations. Fisher’s exact test was used to check the significance of co-variation. If the P adjusted value < 0.2, co-variation was considered statistical significance. We add the description in line 180.

Minor points

The authors should very carefully edit the manuscript and they should get help from a native English speaker to critically read and revise this manuscript since there are too many typos and errors, such as:

Response: Thanks! We have revised this manuscript according to the help of a native English speaker.

1. The title: “HIV-1 transmitted drug resistance-associated mutations and Mutation Co-variation in HIV-1 Treatment-Naïve MSM from 2011 to 2013 in Beijing, China” should be “HIV-1 transmitted drug resistance-associated mutations and mutation co-variation in HIV-1 treatment-naïve MSM from 2011 to 2013 in Beijing, China” Page 2, line 3, “Although transmitted drug resistant were report” should be “Although transmitted drug resistance was reported”

Response: Thanks! We revised the title. Because we modified the background of the abstract, we delete “Although transmitted drug resistant were report”

2. Page 2, line 4, “HIVtransmitted” should be “HIV transmitted”. Page 2, line 7, “therapy(ART)-naïve” should be “therapy (ART)-naïve”.

Response: Thanks! We revised it in line 64.

3. Page 4, line 4, “might cause HIV drug resistance transmission increase among MSM or not” changed to “might cause the increase of HIV drug resistance transmission among MSM”.

Response: Thanks! According to the suggestions from the native English speaker, we modified the description in background section. In the revised background, we deleted the sentence “might cause the increase of HIV drug resistance transmission among MSM”.

4. Page 6, line , “The detailed procedure was: first, positive selected mutations were selected using selection pressure” should be changed to “Briefly, positive mutations were selected using selection pressure”.
Response: Thanks! We revised it in line 171.

5. The subtitles of Results, “Patient Characteristics” should be “Patient characteristics”, and “HIV-1 Genetic Characteristics” should be “HIV-1 genetic characteristics”.

Response: Thanks! We revised the subtitles of Results.

6. In the 2nd paragraph of Results, the statement of “Two hundred and twenty-three pol sequences (85.11%, 223/262) were successfully amplified.” was repeat of the similar statement in the 1st paragraph of Results “Among them, the pol genes of 223 samples (85.11%, 223/262) were amplified and sequenced”. One of these two statements should be deleted.

Response: Thanks! We deleted it in line 190.

7. In the 3rd paragraph of Results, “….protease inhibitor (PI), nucleoside/nucleotide reverse transcriptase inhibitor (NRTI), or non-nucleoside reverse transcriptase inhibitor (NNRTI)...”, the authors can use the abbreviations directly, because they are used in the above.

Response: Thanks! We revised it in line 200.

8. Page 10, line 4, In the 4th paragraph of Discussion, “However, the proportion of subtype CRF01_AE was 56.0%, B was 30.8%, and CRF07_BC was 12.6% in the study performed by Li et al from 2007 to 2010 [21]” should be changed to “In the study performed by Li et al from 2007 to 2010 [21], the proportion of subtype CRF01_AE, B, and CRF07_BC were 56.0%, 30.8%, and 12.6%, respectively.”

Response: Thanks! We revised it in line 260.
Response to reviewer’s report -2

This is an interesting and analysing paper on TDR and Mutation Co-variation. Some modifications are required before publishing:

1. Abstract: Although transmitted drug resistant were report

It should be restated

Response: Thanks! We modified the background of the abstract and restated transmitted drug resistance in line 58-60.

2. Introduction, 2nd paragraph: TDR has the potential to compromise first-line etc.


Response: Thanks! According to the suggestions from the native English speaker, we modified the description in background section. In the revised background, we deleted the sentence “TDR has the potential to compromise first-line etc”.


It should be specified if the CALIBRATED POPULATION RESISTANCE TOOL (http://hivdb.stanford.edu) was used to analyse sequences for TDR.

Response: Thanks! We used HIV db software (Stanford HIV Drug Resistance Database, http://hivdb.stanford.edu, version 7.0) instead of CALIBRATED POPULATION RESISTANCE TOOL (http://hivdb.stanford.edu) to analyze sequences for TDR. Because the CPR tool is closely linked to HIVDB( Gifford RJ, Liu TF, Rhee SY, et al. The calibrated population resistance tool: standardized genotypic estimation of transmitted HIV-1 drug resistance. Bioinformatics. 2009 May 1;25(9):1197-8), the HIVDB could be used to analyze the TDR-associated mutation either.

4. Results

The two criteria regarding the population should be described in material and methods, study patients

Response: Thanks! We described the criteria in material and methods, study patients in line 125-128.
5. The authors rather curiously listed no study limitations, such as time of infection (some TDR could have been missed in those patient initial infections, population sequencing (minority variants))

Response: Thanks for your advice about the limitation of this research. According to your suggestion, we added the study limitations in line 289-297.