Author's response to reviews

Title: Risk Factor for HIV-1 Seroconversion among Taiwanese Men Who Have Sex with Men Attending Gay Saunas

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Author's response to reviews: see over
Prof. Andrea De Luca  
Associate Editor  
Clinica delle Malatte Infettive Universitarie  
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Dear Prof. Luca,  

September 03, 2011

Thank you for your letter and reviewer’s comments on our manuscript entitled “Molecular Epidemiology of HIV-1 Infection among Men Who Have Sex with Men in Gay Saunas in Taiwan” (MS No.: 1375744107530293). Enclosed please find a copy of the revised manuscript and a point-to-point reply to the comments and questions raised by the reviewer.

If you have any further comments or questions, please feel free to contact me at the following numbers: Tel: 886-2-28267193; Fax: 886-2-28270576; email: arthur@ym.edu.tw

Best regards

Sincerely yours,

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Reply to the comments made by reviewer:

1. Comments: The title is misleading and should be changed to something like “Risk factor for HIV-1 seropositivity among Taiwanese MSM attending saunas”, because the focus is on risk factors for HIV-1 seropositivity rather than molecular epidemiology. As detailed below the phylogenetic tree analyses do not really qualify as molecular epidemiology.
   A: We have modified the title as “Risk Factor for HIV-1 Seroconversion among Taiwanese Men Who Have Sex with Men Attending Gay Saunas” (page 1).

2. Comments: The most interesting finding in this study is that circumcision was statistically associated with a higher risk of HIV-1 seropositivity. This is relevant because there is still relatively limited data on the possible effect of circumcision in MSM. The authors do not pick up on or discuss this finding, which deserves more attention including referencing to earlier studies on this topic. An analysis and discussion about possible confounders is especially relevant. Such potential confounders include differences in rate of circumcision in different ethnic groups or religions that may also track with higher or lower prevalence of HIV infection.
   A: We have discussed the effects of circumcision for HIV-1 transmission among MSM in the discussion section (page 13-14, lines 212-233).

3. Comments: Background, second paragraph: The authors are not correct when they present data on effect of ART on contagiousness. It is solidly documented that successful ART (<50 copies) strongly reduces contagiousness. The fact that HIV transmissions still occur in the ART-era indicates that transmissions occur from undiagnosed, untreated or unsuccessfully treated patients, rather than indicate that ART has no effect on risk of transmission.
   A: We have modified the sentences on effect of HAART on HIV-1 transmission according to reviewer’s comments (page 5, second paragraph).

4. Comments: It is stated that the study questionnaire was approved by the Ethics Review Board. It is vital that the entire study protocol, not just the questionnaire, was approved. Otherwise the results cannot be published.
   A: Thanks for the comments. In fact, our whole study was approved by the IRB of the university previously. Therefore, we have modified the sentence to state that the entire study protocol was approved by the Institutional Review Board of
5. **Comments:** There is too much repetition in the Results section of data that are presented in the tables. The text should bring forward the most important data in the tables, not repeat a large proportion of the tables.
A: We have condensed the ‘results section’ according to reviewer’s comments.

6. **Comments:** The phylogenetic analyses are simplistic and not properly interpreted. There are two options; either downplay the “molecular epidemiology” in the title and elsewhere or redo the analyses and interpretation. NJ and the Kimura2-parameter substitution model is OK for subtype determination, but not sufficient for detailed molecular epidemiology within subtypes. The authors need to use maximum likelihood or Bayesian methods with properly selected models of evolution (probably REV+G+I).
   The local control sequences are poorly explained (for instance, are they from MSM), not explained or indicated in the figures and probably insufficient. Furthermore, the number of sequences from the study population and other Taiwanese HIV patients is probably too small relative to all infected MSM’s in the country to find clustering patterns unless they are extremely clear. With such a small sample a star-like tree is expected and also observed. Similarly the analyses of the relationship of the study sequences to sequences from other countries is too limited to allow clear conclusions. Thus, many of the conclusions that the authors draw from the trees in the discussion are not justified by the data.
   A: We have modified our title and redone the phylogenetic analyses according to reviewer’s comments. We have tested the best fit model and used maximum likelihood method with GTR+G+I model (Methods section, page 8, lines 89-96). We have also mentioned the characteristics of our local controls (MSM or heterosexuals) in figure legend of Figure 1. (page 25, lines 414-419).

7. **Comments:** The difference between figures 1A and 1B are obscure. All study sequences were of subtype B. Using a subtype B or non-B outgroup is not interesting enough to justify the two trees. Choose a proper outgroup (such as a set of non-B reference sequences) and present just one tree.
   A: The point is well taken. We have chosen a set of non-B reference sequences as the outlier group and repeated the phylogenetic analysis as suggested by the reviewer (Fig. 1, results section, page 11, lines 167-172).
8. **Comments:** A large proportion of the discussion addresses other things than the results from this study. A better focused discussion would improve the manuscript.
   A: We have condensed the ‘discussion section’ according to reviewer’s comments.

9. **Comments:** The manuscript lacks both page and line numbers which makes reviewing difficult.
   A: Sorry for the inconvenience that we caused you. We have added both page and line numbers in the manuscript according to reviewer’s comments.