Author's response to reviews

Title: HIV-1 subtype and viral tropism determination for evaluating antiretroviral therapy options: An analysis of archived Kenyan blood samples.

Authors:

Raphael W Lihana (lihanaraphael@gmail.com)
Samoel A Khamadi (skhamadi@gmail.com)
Raphael M Lwembe (rlwembe@yahoo.com)
Joyceline G Kinyua (kinyuajoyceline@yahoo.com)
Joseph K Muriuki (jmuriuki@kemri.org)
Nancy J Lagat (Nlagat@kemri.org)
Fredrick A Okoth (Fokoth@kemri.org)
Ernest P Makokha (epmakokha@yahoo.com)
Elijah M Songok (Esongok@kemri.org)

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Author's response to reviews:

Comment 1

The authors have superficially addressed all of the specific concerns in the prior review, but they have not addressed the general concern about evidence-based conclusions. The revised conclusions (from the abstract) are as follows (my numbering):

"i. Prevalence of recombination among this population was low.

ii. Dual co-receptor usage was observed in minor viral populations in two patients.

iii. In evaluating treatment options with novel targets, determination of HIV subtypes and viral tropism would be recommended before commencement of therapy for better clinical outcomes."

Statement (i) is supported by the data, except that the word "population" should be replaced with "sample".

Statement (ii) is weak, since co-receptor usage was not formally tested; it was only inferred from sequence data (as noted in prior review).

Statement (iii) is not supported by the current manuscript at all. How were subtypes or tropism shown to be relevant for therapeutic decision-making?

Response (i):

As recommended, the statement in the conclusion of the abstract (page 2) has now been replaced with: “….prevalence of recombination in this sample was low”.

Response (ii):
The statement of our conclusion (Abstract, page 2) has been changed to reflect the objectives of the study and now reads,

“HIV-1 subtype A accounted for majority of the infections. Though perceived to be a high risk population, the prevalence of recombination in this sample was low with no dual infections detected. Genotypic co-receptor analysis showed that most patients harbored viruses that are predicted to use chemokine co-receptor 5 (CCR5).”

Response (iii):
Thank you very much for pointing out this misplaced statement. Since the sentence has not been supported by the manuscript, it has been removed from the conclusion so that the outcome of the study reflects its initial objectives.

Comment 2
On page 8, paragraph 2 ends with: The scale-up of ART "will eventually change evolutionary lineages among prevalent HIV-1 subtypes." This statement is confusing, but could be replaced with "This is likely to resulting in increasing prevalence of resistance."

Response:
Thank you for your suggestion. The statement has been changed according to your recommendations and now reads,

“This is likely to result in increased prevalence of resistance” (page 8, 2nd paragraph).

Comment 3
On page 9, paragraph 2 ends with: "More clones and use of more sensitive methods such as allele-specific PCR and single-genome amplification, would be ideal." This is untrue. The problem is not an issue of sensitivity, but of the relevance of the assay. For example, allele-specific PCR is useless for testing tropism, because tropism is a phenotype based on multiple dispersed amino acids in Env. Rather, a biological assay would be needed.

Response:
This statement has been reviewed to give a better conclusion on viral tropism. It now reads,

“A more sensitive and reliable phenotyping assay would be ideal to elucidate this.”(Page 9, 2nd paragraph).