Author's response to reviews

Title: Evaluation of a microcolony growth monitoring method for the rapid determination of ethambutol resistance in Mycobacterium tuberculosis.

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Author's response to reviews:

Dear Editor,

We would like to thank you and reviewers for the feedback.

Below are our responses to the points made by the reviewers.

Looking forward to your response.

Yours sincerely, Alice den Hertog

Reviewer 1: Materials and methods is not clear, it is confusion. If it should be rewritten and added any photo for explanation, it would be better understood. In addition it should added other important antituberculose agents including rifampicin and isoniazid to the study.

>To add Rifampicin and isoniazid is a study on its own and, although interesting, in our opinion not required to support the results for Ethambutol drug susceptibility testing.

>Reviewer 2 specifically mentions the method section is clear, and we have published the microcolony culture method earlier so if questions remain, a detailed description can be found in the reference.

Dear Authors;

I have read and analysed the manuscript entitled “Evaluation of a microcolony growth monitoring method for the rapid determination of ethambutol resistance in
Mycobacterium tuberculosis”.
The methodology of the study is good designed and well described in the text.
Discussion and conclusion sections are well balanced and adequately supported by the data.
Results of this study is promising for possible future studies with more number of strains.

>Thank you, also for the detailed corrections of the text.

Minor Essential Revisions:
Some minor revisions are needed.
- Words should be abbreviated in their first usage through the text (such as RIF [3rd line of 1st paragraph instead of 1st line 3rd paragraph in Background], TB [1st line of 2nd paragraph in Background instead of 1st line 1st paragraph in Methods], PAO [2nd line of 1st paragraph instead of 4th line of 1st paragraph in “Microcolony growth monitoring” section], etc.).
> Thank you, we have adapted this

- The abbreviations of EMB (in the Background section of Abstract), MIC (in the 3rd paragraph of Background), MODS (in the 4th paragraph of Background), OADC (in the 2nd paragraph of “Strains” section of Methods), MLPA (in the 3rd paragraph of “Strains” section of Methods), PAO (in the 1st paragraph of “Microcolony growth monitoring” section of Methods), etc. should be clarified in their first usage.
> Thank you, we have adapted this, except for MODS, which is the name of the assay and OADC which is the trade name of the enrichment

- Because embCAB is a gene name, it should be written as italic form in text (in 6th paragraph of Background and in 4th paragraph of Discussion).
- Because embB is a gene name, it should be written as italic form in text (in 4th
paragraph of Discussion and in reference 22).
> We have italicized the gene names
- In the last paragraph of Background, “… 20 tuberculosis strains …” should be written as “… 20 TB strains …”.
> Done
- Extra information about MLPA procedure should be given.
> We have added the type of markers detected by this method, namely “resistance associated markers and lineage type markers”. Further technical description of the method is in our opinion not necessary as a very detailed description of the method is given in the cited reference, and as we do not show the resulting data in detail.
- In title of 2nd section of Methods, “DST …” should be used instead of “Drug susceptibility testing ....
> Done
- In the 4th paragraph of Background, “… 8 mg/L ethambutol …” should be written as “… 8 mg/L EMB …”.
> Done
- In the 6th paragraph of Background, “… BACTEC MGIT …” should be written as “… Bactec MGIT …” for standard usage.
> BD uses BACTEC spelled in capitals
- In “Image and data analysis section” of Methods, after “… den Hertog et al. 2010 …” should be added reference number (“… den Hertog et al. 2010 [3] …”).
> Done
- “… was seen …” should be written instead of “… was see …” (5th line of 2nd paragraph in “Effects of EMB on the growth of reference strains” section).
> Done
- In title of 4th section of Discussion, “… such as RIF and …” should be used instead of “… such as rifampicin and ...”.
> Done
- TB, MODS, SMI, OADC, MLPA, GU, DPA abbreviations should be included to list of abbreviations.
> We have added the abbreviations that are used more than once to the list

References should be given according to the writing rules of the journal.
- “Mycobacterium tuberculosis” should be written as italic in References.
> Done

- Doi number should be deleted from reference 4.
> Done

- In reference 5, “Antimicrobial susceptibility testing of Mycobacterium tuberculosis (EUCAST document E.DEF 8.1) –“ should be written as bold.
> Done

- “, i” should be deleted from the end of reference 6.
> Done

- In reference 7, the first letters of title words of the manuscript should not be written as capital letter and Plos ONE should be written as Plos One (as reference 3 and 23).
> We adhere to the spelling of PLOS ONE

- From reference 12 to reference 24, the names of journals shoud be written as italic.
> Done

- Quotation marks should be removed from manuscript titles of reference 17 and 18.
> Done

- The author name of reference 18 should be written as Lowe DG instead of Lowe D. In reference 18, the name of journal should be shortened.
> Done

- In reference 21, the names of authors should be written as Plinke C, Rüsch-Gerdes S, Niemann S and the name of gene (embB) should be written as
italic.

>Done