Author’s response to reviews

Title: Vitamin D Receptor Gene Associations with Pulmonary Tuberculosis in a Tibetan Chinese population

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Author’s response to reviews:

Dear Hilary Logan:

On behalf of my co-authors, we thank you very much for giving us an opportunity to revise our manuscript, we appreciate you and reviewers very much for your positive and constructive comments and suggestions on our manuscript entitled “Vitamin D Receptor Gene: Association with Pulmonary Tuberculosis in the Tibetan Chinese population”. (Manuscript ID: INFD-D-15-00216).

Not long ago, Tibet University for Nationalities was renamed to Xizang Minzu University, and we built two new laboratories in School of Medicine of Xizang Minzu University, Key Laboratory for Basic life science Research of Tibet autonomous region and Key laboratory for molecular genetic mechanisms and intervention research on high altitude disease
of Tibet autonomous region. All of the changes are marked using the track changes mode in MS Word in revised Title page. We are very sorry we missed a supported founder in our original manuscript and we added the funder, the Major science and technology research projects of Xizang (Tibet) Autonomous Region (2015), in the revised Acknowledgement section.

We have carefully evaluated the reviewers’ critical comments and thoughtful suggestions, responded to these suggestions point-by-point, and revised the manuscript accordingly. After entering your website at http://infq.edmgr.com/l.asp?i=29655&l=KRAWFSZ8 for any additional comments, we also performed some language corrections in revised manuscript according to the advice of reviewer 3. Revised portion are marked using the track changes mode in MS Word. The main corrections in the paper and the responds to the reviewer’s comments are as follows:

Responds to the reviewer’s comments:

Reviewer #1:

1. Response to comment: Could the authors include a table which contains the information about age and gender of the analyzed groups, cases and controls?
Response: We thank the reviewer for raising this issue. In the process of collecting samples, we ignored the patient's age and gender, we will pay attention to these aspects in the future research.

2. Response to comment: Authors established a threshold of statistical significance of P=<0.05. However in none of the analysis they include a correction of P-values by using Bonferroni or Benjamini & Hochberg step-up false discovery rate correction. Could the authors include a correction procedure and include the corrected P-values in the analysis?
Response: Thanks for the reviewer's kind suggestion. We agree with the reviewer’s viewpoint. We had adjusted the P value in our study by Bonferroni correction. The Bonferroni correction is based on the idea that if an experimenter is testing n dependent or independent hypotheses on a set of data, the probability of type I error is offset by testing each hypothesis at a statistical significance level 1/n times what it would be if only one hypothesis were tested. We had added the corrected P-value in Table 2, Table 3 and Table 4. We are really sorry for our negligence of these details in our manuscript. All the changes were marked clearly in the revised manuscript.

3. Response to comment: Is it possible to include a short discussion about statistical power of the study?
Response: We thank the reviewer for raising this issue, this point is very important for supporting our study results. Power analysis can be used to calculate the minimum sample size required so that one can be reasonably likely to detect an effect of a given size. If the power
value less than 75%, we could not conclude that the difference was not statistically significant, but need to increase the sample size to verify. Conversely, we can conclude that the difference was statistically significant. We have performed a short discussion about statistical power of our revised study in discussion section. All the changes were marked clearly in our revised manuscript.

4. Response to comment: For all document, <<Mycobacterium tuberculosis>> or <<M. tuberculosis>> should be typed in italic font.

Response: Thanks for the reviewer’s kind suggestion. <<Mycobacterium tuberculosis>> or <<M. tuberculosis>> had been typed in italic font and all the changes were marked clearly in the revised manuscript.

In all, the reviewer’s comments are quite helpful, and we revised our paper point-by-point. Thank you again for your help!

Reviewer #3:

1. Response to comment: an important component is missing: the power analysis. Authors should performed a post hoc power calculation to demonstrate that they have taken adequate number of patients and controls for this study.

Response: We agree with the reviewer’s viewpoint. Post-hoc power analysis is conducted after a study has been completed, and uses the obtained sample size and effect size to determine what the power was in the study, assuming the effect size in the sample is equal to the effect size in the population. We have performed a post hoc power calculation in our revised manuscript. Post-hoc power value we calculated of rs11574143, rs7975232, rs11574079, rs3819545, rs11168287 were 77.59%, 45.41%, 62.96%, 4.13%, 100%, respectively. If the power value less than 75%, we could not conclude that the difference was not statistically significant, but need to increase the sample size to verify. Conversely, we can conclude that the difference was statistically significant. All the changes were marked clearly in our revised manuscript.

2. Response to comment: in this study authors have observed association of three SNPs (rs11574143, rs11168287 &rs11574079) with risk to PTB and no association of other two (rs7975232 & rs3819545). However in the discussion section link between rs7975232 & rs3819545 with PTB was not properly discussed, these may be enlighten.
Response: We are really sorry for our unclear presentation in our manuscript and thanks for the reviewer’s careful review. We have corrected our mistakes in the statement. All the changes were marked clearly in our revised manuscript.

3. Response to comment: function of vit D gene polymorphism is solely depend on levels of vit D. authors should quantify Plasma/serum levels of vitD3 and correlate these with polymorphism in association with susceptibility/resistance to PTB.

Response: Thank you for pointing this out. We are very sorry to quantify Plasma/serum levels of vitD3, we just conducted a preliminary study and simply describe the mechanism of vitamin D action. Most importantly, our experimental conditions are not up to the requirements. We will continue to focus on the development of this topic in the future.

We acknowledge the reviewer’s comments and suggestions very much, which are valuable in improving the quality of our manuscript.

Editorial Requests

1. Response to comment: Ethics: If your study involves humans, human data or animals, then your article should contain an ethics statement which includes the name of the committee that approved your study. If ethics was not required for your study, then this should be clearly stated and a rationale provided.

Response: Thank you very much for your reminder. The Human Research Committee of the Tangdu Hospital for Approval of Research Involving Human Subjects approved the use of human tissue in this study. These contents were contained in our manuscript.

2. Response to comment: Consent: If your article is a prospective study involving human participants then your article should include a statement detailing consent for participation. If individual clinical data is presented in your article, then you must clarify whether consent for publication of these data was obtained.

Response: Thanks for your kind suggestion. We obtained signed informed consent from each study participant, and our article included a statement consent for participation.
3. Response to comment: Availability of supporting data: Bio Med Central strongly encourages all data sets on which the conclusions of the paper rely be either deposited in publicly available repositories (where available and appropriate) or presented in the main papers or additional supporting files, in machine-readable format whenever possible. Authors must include an Availability of Data and Materials section in their article detailing where the data supporting their findings can be found. The Accession Numbers of any nucleic acid sequences, protein sequences or atomic coordinates cited in the manuscript must be provided and include the corresponding database name.

Response: We thank you for raising this issue and your suggestion is very helpful. We added Availability of data and materials section in our article.

4. Response to comment: Authors Contributions: Your Authors Contributions’ section must detail the individual contribution for each individual author listed on your manuscript.

Response: Thank you for your thoughtful suggestion. Our manuscript had listed the detailed contribution for each individual author in Authors Contributions’ section.

In all, the reviewer’s comments are quite helpful, and we revised our paper point-by-point. Thank you again for your help!

We appreciate for editor and reviewer’s warm work earnestly, and hope that the revised manuscript has addressed all the criticisms raised by the reviewers and that the manuscript is now suitable for publication in your journal. Should you have any questions, please contact us without hesitate.

Best regards!

Yours sincerely,

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