Author’s response to reviews

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

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Version: 2 Date: 12 May 2016

Author’s response to reviews:

Reviewer #1: In my opinion, the authors made a great effort to improve the manuscript, however there are some issues that they have to fix before the final acceptance of the paper, I made a list:

1. Response to comment: Line 65: "higer" must be changed to higher.
Response: We are very sorry for our incorrect writing, thanks for the reviewer’s reminding. We have corrected it in the article (Line 63).

2. Response to comment: The authors put in the text the name of the genotypes as "GA" or "AA", but in the tables they referred to genotypes as "G/A" or "A/A" respectively. Please ensure that the naming of the genotypes is the same in all text.
Response: Thanks for the reviewer’s kind suggestion. We are very sorry for our negligence and we have corrected the name of the genotypes as “G/A” or “A/A” in the text.

3. Response to comment: Line 170: "We adjusted the P-value by Bonferroni correction, and the results are the same as before". This is not completely correct. The statistical significance was kept after the correction procedure but the P-value changed, so is it better to indicate the exact P-value after correction.

Response: We thank the reviewer for raising this issue, and we accept the reviewer’s advice. We do have some problems in the expression of the results. We have re-written this part (Line 168-169) according to the reviewer’s suggestion.

4. Response to comment: Line 215: "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. 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." This paragraph is not clear for the readers, and I want to ask the authors to improve discussion about this. In the first reviewing process, I requested for a small discussion about statistical power in this study. I understand that carry out this type of studies is difficult in specific populations, and statistical power could be lower. However, I consider these studies are important for the scientific community, so in my opinion these works have to be published, but it is better to include one statement considering the statistical power limitation.

Response: Thank you for pointing this out. It is really true as Reviewer suggested that this paragraph is not clear for the readers. We now have a complete understanding of the reviewer’s comment. We have given a corresponding correction to the comment raised by the reviewer (Line 237-241).

Reviewer #3: Although authors have revised the manuscript substantially according to comments of reviewers, it still needs some data/clarifications.

1. Response to comment: The power analysis showed that except rs11168287, other SNPs failed to reach minimum level (80%) for a case-control genetic association study. Thus samples numbers have to be increase to have a valid association study.
Response: Thanks for the reviewer’s kind suggestion. According to the post hoc analysis, we realized that the sample size was small in our study. In this case, we could not conclude that the difference was not statistically significant, but need to increase sample size to verify. Carrying out this type of study is difficult in specific populations, and statistical power could be lower. We have added a statement considering the statistical power limitation in Discussion Section (Line 237-241). We hope that future research should pay attention to this point.

2. Response to comment: Software/programme used for power analysis should be mentioned in statistical analysis heading.

Response: Thank you for your thoughtful suggestion. We have made correction according to the reviewer’s comments. We used the software platform (http://sampsize.sourceforge.net/iface/s3.html) for evaluating the statistical power of this case-control study. We have added these contents in Statistical analysis (Line 125-126).

3. Response to comment: I believe Quantification of Vitamin D is essential for this study, not in all samples but in a decent number.

Response: We thank you for raising this issue and your suggestion is very helpful.

Carrying out this type of study is difficult in specific populations, and statistical power could be lower. In the future study of special populations, we will do our best to collect a decent sample number. We are very sorry that we can not quantify the concentrations of 25-hydroxyvitamin D3 in the serum by using HPLC-MS/MS, because the blood collected was fully used in the process of experiment. We added some contents about a low vitamin D status (Line 217-221).