Author’s response to reviews

Title: Association of 4p14 and 6q27 Variation with Graves Disease: a Case-control Study and a Meta-analysis of Available Evidence

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Author’s response to reviews:

Feb 28, 2017

Dear Editor,

Thank you very much for your support and appreciation of our manuscript. Now we are sending you a newly revised manuscript entitled: “Association of 4p14 and 6q27 Variation with Graves Disease: a Case-control Study and a Meta-analysis of Available Evidence” (MGTC-D-16-00094R1).

We really appreciate the valuable comments and suggestions from the two reviewers. After carefully reading those important comments, we have made a great effort to improve the quality of the manuscript. A number of modifications have been made in the revised manuscript as required. Now we’d like to present all the amendments in a point-to-point way. We hope that all these revisions can meet the comments and suggestions of the reviewers. If more information is needed about the manuscript, please don’t hesitate to contact us.

Sincerely,
Reviewer reports:

Reviewer 1: Minor revisions:

1. The authors should review the text in order to correct typographical and grammatical errors; i.e. page 6, line 25: "All GD patients with GD..."

We thank the suggestions of the reviewer. We carefully reviewed the text and did a big effort to improve the English.

2. On page 10, lines 11-12, the authors should exclude the word "strong", since a OR of 1.27 (1.22-1.32) does not indicate a strong effect.

We really thank the reviewer’s scrutiny and revised the statement.

3. In Discussion section, from page 11 on, the authors explained some process that the two SNPs could be involved. I would suggest that the authors include a brief paragraph of this information in Introduction section.

As suggested, we included a brief paragraph of this information in Introduction section and shortened the discussion. The new paragraph was printed in blue in the revised text.

4. On page 11, lines 34-35, gene names should be written in italic format.

Corrected.

5. On page 12, lines 54-58, the phrase should be rewritten for better understanding.

We rewrote the sentence.

Reviewer 2: The authors in this article replicated association to two SNPs, rs6832151 at 4p14 and rs9355610 at 6q27, discovered in GWAS in Chinese population. To elucidate discrepancies between studies trying to replicate the same finding the authors also conducted a meta analysis of
all published studies. The meta analysis confirmed the association. The paper is focused and well written, with the major novelty being the meta analysis.

Major comments

In discussion, a lot of focus is on the function of genes in close proximity to the studied polymorphisms. Interesting as it is to speculate on disease causing mechanisms, maybe this section could be shortened and instead more focus should be on the discrepancies in the genetic signals.

We appreciate reviewer’s remarks. As suggested, we shortened the discussion and gave a brief statement. A discussion of the discrepancies in the genetic signals was presented. The revised text was printed in blue in the new manuscript.

Minor comments

Inconsistencies in reference writing space/no space before ref number.

We carefully checked the manuscript and added a space before every ref number.

In table 1, write out the numbers instead of ratios.

We wrote out the numbers as suggested.

In methods section, in the paragraph about meta analysis, the last two sentences feel like repetition stated just before and should be removed.

The last two sentences were removed.

In next paragraph you describe a random effect model, but has it been used? If not, maybe it is not necessary to mention.

The random effect model was not used in our analysis. We removed the description about the random effect model.

In discussion, on page 1, the last to sentences are unclear and need to be clarified.

We rewrote the sentence and made it easy to read.