Author's response to reviews

Title: Do the mutations of C1GALT1C1 gene play important roles in the genetic susceptibility to Chinese IgA nephropathy?

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Author's response to reviews: see over
Dear Marshall,

Re: “Do the mutations of C1GALT1C1 gene play important roles in the genetic susceptibility to Chinese IgA nephropathy?” (MS: 4437889032345027).

We have revised the above paper according to the reviewers’ comments and recommendation. The answers for these questions were listed in the attached pages. We thank the Reviewers and yourself for the valuable comments. All the page numbers refer to the revised manuscript in which all changes are underlined. And we have revised the style of our manuscript according to the guideline of the journal. We hope the revised form will be suitable for publication in your journal.

Thank you for your consideration.

Yours sincerely

Hong Zhang
Associate Editor
1. The assistant editor commented that the duration of follow up in this study was too short to analyze the outcome of IgAN. We agree with the comment. In our study, the relationship between the polymorphisms and the progression of IgAN was not the core item which we mainly concerned. We added more appropriate discussion.

Revised manuscript: See changes in section of Results (Page 8 Line 19) and in section Conclusions (Page 10 Line 16).

2. The assistant editor suggested that we should revise the manuscript to address several editorial points. We changed it according to the guideline of BMC medical genetics.

Revised manuscript: See main changes in sections of Conclusions, Competing interests and Authors' contributions (Page 11 Line 15-Page 12 Line 1).

Reviewer: 1
1. The reviewer commented that we report a minor allele frequency of 48.48% of the rs3810744 SNP and wondered whether this number relates to IgAN cases or controls. In fact, we have screened SNP in all of the 46 individuals, including 27 unrelated patients with IgAN (6 females) and 19 unrelated healthy controls (6 females). In the subsample and the total sample, the SNP wasn’t associated with the susceptibility to IgAN. So it relate to neither cases nor controls. We have illustrated more clearly in the manuscript.

Revised manuscript: See changes in section of Methods (Page 6 Line 7-8).

2. The reviewer pointed out that there were some inconsistencies of the figures. Because the genotypings were unsuccessful for three controls and one patient in this study, we were afraid that the information could not be transferred exactly by table 1 so we deleted table 1 and described these information in the revised section of method.

Revised manuscript: See changes in Methods (Page 4 Line 27-28, Page 5 Line 1-2)
3. The reviewer thought that we should specify whether the rs17261572 SNP’s were identified in B lymphocytes from IgAN cases or controls. We agreed with the suggestion completely and added these data in the revised manuscript.

Revised manuscript: See changes in Results (Page 8 Line 28-29, Page 9 Line 1).

Reviewer: 2

1. The reviewer commented that there was considerable interest in genetic factors predisposing to IgAN and study of this gene was of interest despite this essentially being a "negative" study. We completely agreed with the comment.

Revised manuscript: No changes.

Reviewer: 3

2. The reviewer commented that we did not detect any somatic mutation of the gene, but performed simple association analysis of SNP in the present study. Therefore the title does not adequately represent the substance of the study. In fact, in this study, we have detected the somatic mutation (or mosaic mutation) in B lymphocyte. This kind of mutation could be proved in different clones derived from one patient, especially in a male patient. But we haven’t found any somatic mutations in these patients.

Revised manuscript: See changes in Methods (Page 7 Line 4 and Line 13).

3. The reviewer pointed out that the duration of follow up in this study was too short to analyze the outcome of IgAN and only 16% of patients reached the endpoint in our study. We agree with the comment. In our study, the relationship between the polymorphisms and the progression of IgAN was not the core item which we mainly concerned. We added more appropriate discussion.

Revised manuscript: See change in Results (Page 8 Line 19) and Discussion (Page 10 and Page 6 Line 14).
4. The reviewer asked how the authors selected individuals, 15 patients and 7 controls among 661 and 277, for sequencing analysis of the whole coding region? We added the relative information in the section of methods.

Revised manuscript: See change in Methods (Page 5 Line 2-3).