Author's response to reviews

Title: A Six-generation Chinese Family in Haplogroup B4C1C Exhibits High Penetrance of 1555A>G-induced Hearing Loss

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

Thank you for your kind letter of my manuscript (MS: 1889349189388859 - A Six-generation Chinese Family in Haplogroup B4C1C Exhibits High Penetrance of 1555A>G-induced Hearing Loss) on 11 Jun 2010. We revised the manuscript in accordance with the reviewers’ comments, and carefully proof-read the manuscript to minimize typographical, grammatical, and bibliographical errors. Here below is our description on revision according to the reviewers’ comments.

Reviewer Sheikh Riazuddin’s Comment:

1) As authors mentioned and cited the literature that two nuclear genes, namely GJB2 and TRMU are known to influence the severity of hearing loss in patients with the 1555A>G mutation. Authors present data for GJB2 but not for TRMU gene. Have they sequenced TRMU in this pedigree? If not, this needs to be done and included the results. More so, author’s main conclusion from this study is that there may be nuclear factors that are responsible for variation in hearing phenotype in this family.

Reply:
We had sequenced the TRMU, We fail to find any variant in the TRMU gene. The results and related reference were added into the revised manuscript.

2) In the result section, authors mention that 21 out of 33 maternal members carrying the 1555A>G mutation exhibit bilateral and symmetrical hearing loss. Are the remaining 12 individual homoplasmic or heteroplasmic?

Reply:
The remaining 12 individual are homoplasmic.
3) In figure 1, please provide data on the status, homoplasmic or heteroplasmic, from 1555A>G mutation segregating in the family.

Reply:
We provided data in the figure 1 caption.

Answers to reviewer Regie Santos-Cortez:
Major revision:

Reply:
We had consulted a statistician. He suggested that the analysis of covariance may be more appropriate in our pedigree. So we did it, we found that 1555 A >G and aminoglycoside were the main influence factors, but no frequency specificity. The audiogram data on unaffected relatives was normal just like normal person. We had read the work of Prof. Patrick LM Huygen. We want to know whether we needed offer the whole audiogram data and analysis same as Prof. Patrick LM Huygen.

Minor revision:
Similarly the conclusion can be reworded to have a clearer message and stronger impact.

Reply:
We added the summary into the revised manuscript in the last section.

A revised manuscript with the correction sections red marked was attached as the supplemental material and for easy check/editing purpose.

We acknowledge the reviewer’s comments and suggestions very much, which are valuable in improving the quality of our manuscript. Should you have any questions, please contact us without hesitate.
Yours sincerely,

Huawei Li