Author's response to reviews

Title: Combined examination of sequence and copy number variations in human deafness genes improves diagnosis for cases of genetic deafness

Authors:

Haiting Ji (haiting123456@163.com)
Jingqiao Lu (jlu30@emory.edu)
Jianjun Wang (jwang33@emory.edu)
Huawei Li (hwli@shmu.edu.cn)
Xi Lin (xlin2@emory.edu)

Version: 5 Date: 20 August 2014

Author's response to reviews:

Editorial Comments

Abstract

Please ensure that your abstracts are identical on the 'Manuscript Details' page of the submission system and in the main body of the manuscript. These are currently different.

_____ Answer: We have resubmitted the “Manuscript Details” page of the submission system, and ensured that this is identical to the abstract in the main body of the manuscript.

**********************************************************************

Editorial requests

We recommend that you copyedit the paper to improve the style of written English. ……

_____ Answer: Two native-English speakers have read the manuscript and made numerous corrections in the revised manuscript.

Answers to Reviewers’ comments/questions:

Referee 1: Reviewer's report:

The authors satisfactorily completed all suggested edits and have greatly improved their manuscript.

Minor essential revision:

The authors indicate that this is the first study examining CNVs in hearing loss genes. However, two papers have recently been published on this same topic. Please change the manuscript to reflect that this is not the first CNV study in hearing loss and perhaps at least reference these manuscripts, or ideally add a
sentence to the discussion. The references are: ……

Answer: We have removed the mention of “first study or first paper” throughout the manuscript. The sentence (starting from page12 line288) “……To our knowledge, this is the first study that evaluated the impact of CNVs in certain targeted deafness genes (supplemental Table 1) on genetic hearing loss.” has been changed to “……The contribution of CNVs to genetic deafness only begins to be revealed recently in a few papers that have addressed this specific topic [15-16]. We have evaluated the impact of CNVs in 80 targeted deafness genes (supplemental Table 1) on genetic hearing loss. …… “.

The two suggested references are both cited in the revised manuscript.

Quality of written English: Needs some language corrections before being published

Answer: Two native-English speakers have read the manuscript and made numerous corrections in the revised manuscript.

Referee 2: Reviewer’s report:
Major Compulsory Revisions: None
Minor Essential Revisions:
1. Under Patient History and physical/laboratory examination under "Methods", fourth line from the top in the first paragraph, patients with history of meningitis (particularly Haemophilus influenza type b or Hib) and maternal CMV, if they are known, should be added in the exclusion criteria.

Answer: We added following sentence (starting from page3 line82): "……Patients with history of meningitis and maternal Cytomegalovirus (CMV), if they are known, were also excluded. …… “

2. Under NGS protocol and data analysis, in page 7, line 159, the statement "Information in this database was collected from Human Genome Mutation Database (HGMD), data on unpublished mutation and normal hearing control NGS data the authors, and consensus predications....". This sentence is incomprensible as written. It needs to rewritten or rephrase it to be clearly understood.

Answer: We have changed the sentence (starting from page7 line159) to: "……Information in this database was collected from the following sources: (1) Human Genome Mutation Database (HGMD); (2) data from unpublished mutation and normal hearing control results obtained in the authors' lab; (3) data made from consensus predications of both PolyPhen and Shift bioinformatic algorithms [10].”

"Minor Issues":


1. Under "NGS protocol and data analysis, in third paragraph (line 156, page 7), (coverage#20..., need a space after coverage.
   Answer: Correction was made as suggested.

2. Under the same paragraph as above, highly-likely (page 7, line 165). I don't think hyphon is needed here.
   Answer: Correction was made as suggested.

3. "highlylikely" in page 15, line 344, add a space between highly and likely.
   Answer: Correction was made as suggested.

4. In page 7, line 167, please check (#0.005).
   Answer: We checked this. Our criteria were indeed set at #0.005 (less than 5 in every 1,000). Change was not made.

5. In page 13, line 297, "The highincidence..", add space between two words.
   Answer: Correction was made as suggested.