Reviewer's report

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

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Reviewer: Sheikh Riazuddin

Reviewer's report:

The manuscript by Huawei Li and co-authors describes a six-generation Chinese Han pedigree suffering with maternally transmitted hearing impairment. Authors found 1555A>G mutation segregating in a homoplasmic fashion in all the affected individuals except one. Sequencing of a candidate modifier gene GJB2 did not reveal any mutation segregating in all the affected individuals.

Specific comments:

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.

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?

3) In figure 1, please provide data on the status, homoplasmic or heteroplasmic, from 1555A>G mutation segregating in the family.

Recommendation:

The paper is recommended for publication with the above revisions.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests