Reviewer's report

Title: Screening mutations of the Otoferlin gene (OTOF) in Chinese patients with auditory neuropathy, including a familial case of temperature-sensitive auditory neuropathy

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Reviewer: Regie Santos-Cortez

Reviewer's report:

Title: Screening mutations of the OTOF gene in Chinese patients with auditory neuropathy, including a familial case of temperature-sensitive auditory neuropathy

Authors: Wang DY et al.

The efforts placed by the authors on revising the manuscript according to the reviewers’ comments have improved the manuscript and are highly appreciated. However there are a few issues that remain unanswered.

Major revision:

From the first version of the manuscript, it was not clear that 3 of the 4 ANSD patients were heterozygous for OTOF variants. This was only made obvious when other reviewers pointed this out and when colored figures of the chromatograms were provided. Additionally Polyphen predicts p.D398E and p.E594K to be benign. On the other hand, a few articles citing ANSD patients with only a single allele copy of an OTOF variant have been published (Varga et al. 2006, Romanos et al. 2009), but these articles also presented patients that are homozygous or compound heterozygous for OTOF variants.

This issue was briefly answered in your comments but not in the manuscript. It is highly suggested (1) to clearly state in the Results section that, apart from the TSNSRAN case, the other AN patients each carry only one copy of an OTOF variant, and (2) to adequately justify in the Discussion why the AN in these 3 patients should be counted as OTOF-related despite not having a second allele and why therefore include these 3 cases in the prevalence estimate. Otherwise, only the TSNSRAN case may be considered as OTOF-related AN and, if so, the discussion/conclusion should center on the low prevalence of OTOF among Chinese AN patients rather than on mutation spectrum. Please note that this latter suggestion was already brought up previously by another reviewer. The conclusion of the abstract was revised accordingly but not the conclusion in the body of the text.

Discretionary revisions:

1. Comparison of prevalence rates between populations may be more credible if
confidence intervals are estimated.

2. Although the age distribution of the entire case group was provided, only the age/age-of-onset of the TSNSRAN patient was mentioned in the revised manuscript. Reporting the ages at disease onset (or other clinical details, for that matter) of other presumably OTOF-related AN cases might provide ideas on what indicators would lead one to differentiate OTOF cases from other AN patients and to possibly consider (if ever) genetic screening for OTOF for AN patients given that OTOF-related AN is rare in this population. This is recommended if it is clearly justified that the other 3 patients do have OTOF-related AN.

**Level of interest:** An article whose findings are important to those with closely related research interests

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

**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.