Reviewers report

Title: A Novel Pathogenic Variant in OSBPL2 Linked to Hereditary Late-onset Deafness in a Mongolian Family

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Reviewer: Elodie Richard

Reviewers report:

Wu et al studied a large Mongolian family with dominant late-onset hearing loss. Using whole genome sequencing and Sanger sequencing, the authors identified and validated a new mutation in OSBPL2, a reported gene for late-onset hearing loss. This new variant is a 2bp deletion, which leads to the same abnormal protein than a mutation that has been previously reported in a Chinese family by Xing et al (2015).

The study is well planned and the conclusions are strong. However, I have one important revision:

- The authors need to state in the discussion (at least) that the new mutation they identified is leading to the same abnormal protein than a previously reported mutation (Xing et al, 2015). This is an important fact, which is strengthening the pathogenicity of their own mutation, and needs to be discussed. One or two sentences about the impact of the mutation on the protein (abnormal sequence for one specific domain for example) will also beneficiate to the discussion.

I also have some minor revisions/changes suggestions for the authors:

- Figure 1: it would be more informative to add the segregation data to the pedigree. Consider adding a legend to the figure where the arrow would be explained.

- The authors stated that they have performed whole genome sequencing to identify the mutation however there is no details about the reason why they used whole genome sequencing vs. whole exome sequencing. In addition, the authors may consider adding more details about the whole genome sequencing protocol.

- Figure 2: the authors may consider adding a legend on the audiograms with the units (thresholds dB, frequency Hz). They may want to add the age of the individuals on the panel or adding it to the legend. Symbols used (O, <, > and X) are not explained neither in the figure nor the legend. "Severe" is misspelled in the legend.
In section 2.2 of the text (Whole genome sequencing results), the authors stated that they have used "a variety of databases". It would be more informative to give some examples with their appropriate reference/website.

Figure 3: it may help the reader to point the OSBPL2 locus with an arrow.

Table 1: I would suggest to revise the title of the different cells of the table (nucleotide change, amino acid change for example)

Figure 4 is missing a negative control.

Figure 5: I would suggest to replace "normal" to "non affected" or "control" in (a) and "c.158_159delAA" with "affected" or "carrier"

Table 2: the authors may consider adding the units for the different measures.

In the discussion, the authors stated that OSBP/ORP family members have been shown to cause diseases. Even if the references are noted, the authors might consider adding the name of some of the disease in parenthesis in the main text.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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Not relevant to this manuscript

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