Author’s response to reviews

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

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MGTC-D-18-00356R1

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

Response to reviewers:

Reviewer #2:

Thank you for careful review of our manuscript, many suggestions which helped to improve this paper throughout the entire process. We highlight the comments and suggestions in yellow in the article.

Minor revisions:

-Abstract: include the p. position after the c. position
Response: c.158_159delAA (p.Gln53Arg fs*100) (Abstract section, line 31, page 1)

- Include the OMIM number for OSBPL2

Response: NM_144498.2 (Abstract section, line 32, page 1)

-Figure 2: enlarge the figures. The x- and y-axes are unclear and the x-axis does not look to be completely labelled

Response: The figures has been enlarged and attached, as shown in figure 2

-State the LOD scores in the results section

Response: Stated the LOD scores in the results section (Results section, line 138, page 5)

-Line 222: check that OSRB should be OSBP

Response: OSRB→OSBP (Discussion section, line 220, page 7)

English suggestions:

-Line 43: seriously affects

Response: seriously affect→seriously affects (Background section, line 43, page 2)

-Line 48: Based on whether…

Response: Basing on whether…

Response: Thank you very much for your advice, we have reviewed many articles in the past three years and revised the incidence rate, and replaced the original reference of 2010 with the reference of 2018.

…75%-80% is autosomal recessive, 10%-15% is autosomal dominant, and the rest are X-linked or mitochondrial [4] (Background section, line 53-54, page 2)

New references (References section, line 282-283, page 9)

-Line 54: …X-linked or mitochondrial [4].

Response: X-linked or defect in mitochondria→X-linked or mitochondrial (Background section, line 53-54, page 2)

-Line 56: Replace the word delayed with late-onset
Response: delayed → late-onset (Background section, line 55, page 2)

-Lines 148-149: instead of saying "at the end of chromosome 20," list the cytogenetic band.

Response: at the end of chromosome 20 → 20q13.33 (Results section, line 148-149, page 5)

-Line 168: … c.158_159delAA, co-segregated in the family…

Response: Removed the “was” (Results section, line 166, page 6)

-Line 176: OSBPL2 encodes a receptor

Response: OSBPL2 encodes receptor → OSBPL2 encodes a receptor (Results section, line 174, page 6)

-Line 177: To find out whether the frameshift…

Response: To find out whether frameshift → To find out whether the frameshift (Results section, line 175, page 6)

-Lines 177-178: It sounds too strong of a statement to say lipid metabolism leads to hearing loss, especially when lipid levels are normal in individuals with hearing loss?

Response: Removed the “and therefore leads to hearing loss” (Results section, line 176, page 6)

-Lines 178-179: in members of this family with the confirmed genotype…

Response: with confirmed genotype → with the confirmed genotype (Results section, line 176, page 6)

-Line 180: use the word indistinguishable instead of not distinguishable

Response: not distinguishable → indistinguishable (Results section, line 178, page 6)

-Line 196: …starting from the 53rd amino acid…

Response: from 53rd amino acid → from the 53rd amino acid (Discussion section, line 194, page 7)

-Line 204: The pathogenic variant in the OSBPL2 gene…

Response: in OSBPL2 gene → in the OSBPL2 gene (Discussion section, line 202, page 7)

-Line 208: …in the OSBPL2 gene was…

Response: in OSBPL2 gene → in the OSBPL2 gene (Discussion section, line 206, page 7)

-Line 231: …as well as by studying animal models with…
Response: model→ models  (Discussion section, line 229, page 7)

-Figure 1 legend: Modify to something like, "Members with genotypes noted were recruited for this study"

Response: It has been modified to "Members with genotypes noted were recruited for this study"  
(Figure 1 legend section, line 79-80, page 3)  

-Figure 3 legend: line 154: …around 1.5 (shorten this sentence).

Response: It has been modified to " Linkage analysis detects four loci with LOD score around 1.5,..." (Figure 3 legend section, line 153-154, page 5) 

-Figure 3 legend: line 155: B. OSBPL2 is located on chromosome 20q13.33 (red bar).

Response: B. OSBPL2 locates on the 20q13.33 chromosomal region (red bar)→OSBPL2 is located on chromosome 20q13.33 (red bar). (Figure 3 legend section, line 154-155, page 5).

-Supplementary Table 3: check the spelling of "panel", as well as "autosomal recessive" and "X-linked"

Response:In the supplementary Table 3, panal →panel; autosoma lrecessive→autosomal recessive; X-link→ X-linked

Reviewer #3

Olga L. Posukh, Ph.D. (Reviewer 3): I believe that the authors of manuscript MGTC-D-18-00356R1 "A Novel Pathogenic Variant in OSBPL2 Linked to Hereditary Late-onset Deafness in a Mongolian Family" have substantially improved the manuscript and now it is suitable for publication.

Thank you for carefully reading and accept our manuscript.