Manuscript NO.: 59042, Case Report

Title: A novel de novo mutation in the *ASXL3* gene in a Chinese boy with microcephaly and speech impairment: The Bainbridge-Ropers syndrome

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Dear editor and reviewers,

Thanks for your time and efforts in evaluating our work, and we are very grateful for the constructive feedback. According to your suggestions, **we have carefully amended the relevant part in manuscript and showed changes using track changes**. We hope the correction will meet your requirements and the publication standard.

Major revisions we made include:

1. We have improved the title according to the reviewer's comment and the guidelines for writing and formatting high quality case reports.
2. We have updated the format of our manuscript according to the guidelines and requirements for manuscript revision and the format for manuscript revision.
3. We have removed Figure 2 to the "Supplementary Materials" and renamed it as Supplementary Figure 1. Then Figure 3 of our original manuscript have been renamed as Figure 2 in the revised manuscript. A new Figure 3 has been added to summarize the *ASXL3* mutations identified in patients with Bainbridge-Ropers syndrome (BRPS) to date (including the novel variants of this study). A new Supplementary Table 1 have been added to provide clinical summaries of BRPS patients in the reported cases and our patient. The corresponding parts have been rewritten in the revised article.
4. We verified the reported cases of BRPS available in the literature (searched on http://www.ncbi.nlm.nih.gov/pubmed and http://www.cnki.net/) and found a total of 49 relevant patients had been reported previously, so we have corrected the total number of reported cases and the positive characters in the "DISCUSSION" and added relative references (a total of 18 references are cited, including 11 references published in the last 3 years) in the "References" of the revised manuscript.
5. We have normalized the mutation nomenclature based on Human Genome Variation Society (HGVS) recommendations (http://varnomen.hgvs.org/), and corrected the confused sentences in the

revised manuscript.

Other revisions:

Please see point-to-point response below for details. We hope this revised manuscript addressed the concerns of reviewers and sincerely appreciate your consideration of our work.

Best regards,

Mingyan Jiang

Reviewer Comments:

Reviewer #1:

In the manuscript the authors present a case report of a novel mutation in the The Bainbridge-Ropers syndrome, these are my comments:

1) Title should be modified "A novel de novo"?, please correct it.

- We appreciate the reviewer's comment. We used the phrase "a novel *de novo*" to describe an unreported *ASXL3* variant detected in our patient but not in his parents, and we were also worried that the usage was improper. We have corrected the title to "Novel mutation in the ASXL3 gene in a Chinese boy with microcephaly and speech impairment: A case report of Bainbridge-Ropers syndrome" in the revised manuscript.

2) Summary, please correct nomenclature (p.E599X).

- We thank the reviewer's correction. We have corrected the mutation nomenclature to p.E599* according to the online software HGVS nomenclature version 2.0 (Mutalyzer 2.0, https:mutalyzer.nl/) in the revised manuscript.

3) Specify if parents were young.

- We appreciate the reviewer's suggestion. We have confirmed the parents were young when the proband was born and added the description "mother and father both born in 1990" in the "CASE PRESENTATION" of the revised manuscript.

4) *Correct the text and the nomenclature "…the deletion of one base pair (G>T) and resulted in the replacement of the amino acid (histidine) (c.1795 G>T; p. E599X, 1650)….," it was not a replacement of histidine, it was the substitution for a stop codon. Please describe properly the pedigree and electropherograms (codon and patient and parents).*

- We appreciate the reviewer's correction and we apologize for the confusion. The confused sentences have been corrected in the revised manuscript.

5) *Figure 2 is unnecessary.*

- We appreciate the reviewer's comment. We have removed Figure 2 to the "Supplementary Materials" and renamed it as Supplementary Figure 1.

6) *Please include a couple of phrases about characteristics of the gene.*

- We thank the reviewer's suggestion. We have added some sentences about *ASXL3* gene and the reported mutations in the "INTRODUCTION" and "DISCUSSION" sections, and adjusted the references accordingly in the revised manuscript.

Reviewer #2:

This is an important case report. Figure 2 may be revised to indicate more detailed information about each line.

- We appreciate the reviewer's comment. We have indicated the median±standard deviation of each lines on the right side of this figure. Further, we have removed Figure 2 to the "Supplementary Materials" and renamed it as Supplementary Figure 1, combined with another reviewer's comment.