Author’s response to reviews

Title: A Novel Small Deletion of LMX1B in a Large Chinese Family with Nail–Patella Syndrome

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Cover Letter for Revised Manuscript MGTC-D-18-00540R1

To: Dr. Victor Faundes, Editor

    BMC Medical Genetics

Dear Dr. Victor Faundes,

We thank you very much for giving us an opportunity to revise our manuscript entitled "A Novel Small Deletion of LMX1B in a Large Chinese Family with Nail–Patella Syndrome" (reference ID: MGTC-D-18-00540R1). We express our sincere gratitude to the reviewers for their prompt, thorough scrutiny and positive recommendations towards improving the manuscript. We have undertaken a thorough revision on the manuscript taking into account every comment, suggestion and questions raised by the reviewers. A point-by-point response to your comments and the details of changes are shown in the below.
We are pleased to submit our revised manuscript to BMC Medical Genetics for your publication consideration.

Thank you so much!

Best regards,

Faithfully,

JIN Fan, MD

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Editor Comments:

Thank you very much for addressing all the concerns and suggestions raised by reviewers and me. However, two little improvements can be still done, especially about the interpretation of the variant. The ACMG 2015 guidelines are the main standard now for interpretation of variants, not just the use of in-silico predictions. Therefore, in the "Bioinformatic analysis" subsection, this must be clearly stated. Also, in the 'in-silico functional annotation of the variant" subsection, all ACMG 2015 criteria that this variant meets must be detailed, giving as a final conclusion the type of interpretation, which is actually "Likely Pathogenic" using those guidelines.

Response: Thank you so much for your comments. We have clearly described interpretation of the variant in our newly revised manuscript, (Bioinformatic analysis subsection, page 7, highlighted with red). We have also given a final conclusion about the variant depending on the ACMG 2015 guidelines. We agree with you and believe it is a "likely pathogenic" variant. All the criteria that this variant met were described detailed base on the ACMG 2015 (in-silico
functional annotation of the variant subsection, page 9 and page 10, highlighted with red). To consist with the whole article, we have replaced "pathogenic" with "likely pathogenic" in other sections of the manuscript (Discussion section and conclusion section, page 11, highlighted with red), and we have displaced "pathogenic mutation" with "mutation" in two places (abstract section, results subsection and conclusion subsection, page 2, highlighted with red). In addition, we have cited the article of the ACMG 2015 guidelines, so the references were rearranged (Bioinformatic analysis subsection, page 7, and the references section, page 15 and page 16, highlighted with red).

Reviewer reports:

Ralph Witzgall (Reviewer 1): None.

Takuya Takeichi (Reviewer 2): I have no comments.