Author’s response to reviews

Title: Case reports: three Novel variants in PCCA and PCCB Genes in Chinese Patients with propionic acidemia

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Author’s response to reviews:

Dear Editor and Reviewers:

We greatly appreciate this opportunity to revise our manuscript. We would like to thank the reviewers for their kind comments regarding our work and for their efforts in reviewing this paper. We have carefully read the editor’s and the two reviewers’ comments regarding our submission (MGTC-D-19-00561R2), and have responded point by point to each of the reviewers’ comments as listed below, and the revised portions in the paper. We feel that the editor and reviewers’ comments have greatly helped us to strengthen our manuscript and we hope that the revised version will be acceptable for publication in BMC Medical Genetics.

Sincerely yours,

QI Yang.

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The Maternal and Child Health Hospital of Guangxi Zhuang Autonomous Region
Editor Comments:

1 - Any manuscript submitted to a BioMed Central journal must be original and the manuscript, or substantial parts of it, must not be under consideration by any other journal. We note that the current submission contains some textual overlap with other previously published works. Please re-write these sentences and phrases in your own words to ensure no overlap. If there is overlap in the Methods section, please ensure that you summarize the methods and cite the source.

We recommend the authors use an anti-plagiarism software, such as turnitin or other freely available ones, to assess any overlap and reduce it.

There is considerable overlap with:

https://tessera.spandidos-publications.com/mmr/17/3/4433 and

Response: Thanks for the excellent suggestion. We have revised this manuscript accordingly as follow: Peripheral blood was obtained from the patients and their parents. DNA was isolated from peripheral blood using the Lab-Aid DNA kit (Zeesan Biotech Co., Ltd., Xiamen, China) according to the manufacturer’s protocol. NanoDrop ND-2000 spectrophotometer and software (NanoDrop 2000; NanoDrop Technologies; Thermo Fisher Scientific, Inc., Waltham, MA, USA) were used for DNA quality detection. Primer version 3 (frodo.wi.mit.edu) was used to design PCR primers for PCR amplification of all exons and and flanking introns of the PCCA (NM_000282.3) and PCCB genes (NM_000532.4) (Tables 3 and 4). Each 50 μl primary PCR mixture contained 200 ng genomic DNA, 2.5μl 10X buffer, 8 μl of a dNTP mixture (2.5 mmol/L), 2 U Taq DNA polymerase (Takara Biotechnology Co., Ltd., Dalian, China), 1.5 μl (10 μmol/L) of each prime. PCR amplification including the following steps: (1) denaturing initial: 95 °C for 5 min. (2) 35 cycles of 95 °C for 30 s, 56–60°C for 30 s, 72 ºC for 60 s, (3) final extension: 72 ºC for 10min. The PCR products were sequenced directly in an ABI 3500 genetic analyzer. (Thermo Fisher Scientific, Inc.).

To evaluate whether novel variants were disease-causing mutations or polymorphisms, PolyPhen 2.0 and Mutation Taster tools were performed to analyze the functional effects of novel variants. Variants were further evaluated according to the ACMG and AMP standards and guidelines.

2 - Please revise your ‘Declaration’ section to be in the following order with a heading:
Declarations

- Ethics approval and consent to participate
- Consent for publication
- Availability of data and materials
- Competing interests
- Funding
- Authors' Contributions
- Acknowledgements
- Authors' Information (optional)

Response: We appreciate with editor and have revised this manuscript according to the Submission Guidelines.

3 - The 'Consent for publication' section covers manuscripts that contain any individual person’s data in any form (including individual details, images or videos), for which consent to publish must be obtained from that person, or in the case of children, their parent or legal guardian. It is a requirement for Case Reports. This is separate from the consent to participate approval. Your manuscript includes three cases where age, gender, sequence data and medical details are present. For this consent to publish is a requirement.

Response: We appreciate with editor and have revised this part accordingly as follow:

Consent for publication

The parents of the three children (under 18) has signed written informed consent for publication of clinical and genetic data. This study was approved by the Institutional Review Boards and Ethics Committees of Guangxi Maternal and Child Health Hospital.

4 - Please use one set of unique initials per author in the Authors' contributions section. Are YQ and QY one individual?

Response: Thanks for the excellent suggestion. We have revised it:

Author contributions
QY and XF designed the study and drafted the manuscript; HX, QY, JSL, MTL and SY extracted, analyzed, interpreted the data, and collected the clinical data; QLZ, XH, GXG and SHF performed the targeted sequencing, analyzed and interpreted the data; XH and QY participated in the study coordination and revised the manuscript. All authors read and approved the final version of the manuscript.

5 - At this stage, please upload your proofread manuscript as a single, final, clean version that does not contain any tracked changes, comments, highlights, strikethrough or text in different colours. All relevant tables/figures/additional files should also be clean versions. Figures (and additional files) should remain uploaded as separate files. Please ensure that all figures, tables and additional/supplementary files are cited within the text. Should you wish to respond to these revision requests, please include the information in the designated input box only.

Response: Thanks for the excellent suggestion. We have upload our manuscript as necessary.

Reviewer reports:

Nani Maharani (Reviewer 1): Dear Authors,
Thank you for your reply and improvement on the manuscript. A little more re-check on the typos will make it perfect.

Response: Thanks for the excellent suggestion. We have carefully checked the article and modified the corresponding position.

Dwi Aris Agung Nugrananingsih, M.D., M.Sc., Ph.D (Reviewer 2): all the issues raised by the reviewer have been addressed properly.

Response: Thanks.