Author’s response to reviews

Title: New PCNT Candidate Missense Variant in a Patient with Oral and Maxillofacial Osteodysplasia: A Case Report

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Author’s response to reviews:

April 30, 2019

Doctor Helena Kuivaniemi

Editor

BMC Medical Genetics
Dear Editor:

I along with my coauthors wish to re-submit a revised manuscript to BMC Medical Genetics, titled “New PCNT Candidate Missense Variant in a Patient with Oral and Maxillofacial Osteodysplasia: A Case Report” (manuscript ID: MGTC-D-18-00515). Please note the revised title.

The manuscript has been carefully rechecked and appropriate changes have been made in accordance with the reviewers’ suggestions. The responses to their comments have been prepared and attached herewith.

Based on the comments, we have further discussed and described the candidate gene approach and gene annotation procedures in the Case presentation and Discussion sections. This approach is summarized below:

1. We attempted to diagnose the patient using clinical features. The features did not correspond to a typical disorder, as described in the Case presentation and Discussion sections.

2. We performed whole exome sequencing, which was described in the Case presentation.

3. We detected 83 heterozygous variants in this patient, which were not detected in the negative control (her mother), as described in the Case presentation.

4. We evaluated the effects of the variants on the corresponding proteins using PolyPhen-2 and CADD, which revealed 12 SNVs in 11 genes that were probably damaging; this is described in the Case presentation.

5. Among these 11 genes, only PCNT is expressed in skeletal organs. PCNT is also the only gene with reported mutations that are clinically related to a skeletal disorder (microcephalic osteodysplastic primordial dwarfism type II), which has been described in the Case presentation and Discussion. The phenotype of microcephalic osteodysplastic primordial dwarfism type II is similar to the facial abnormally seen in this patient.

6. We identified the new PCNT variant as a candidate gene mutation, which is described in the Discussion.

And we apologized our missubmission and followed your comments below.
1. Provide a detailed response to each comment by each reviewer and state where the changes were made (page number and line number). Copy and paste your revised text into your response so that reviewers can easily see what you have changed.: The responses to their comments have been prepared and attached herewith.

2. Provide a tracked version of the manuscript: The tracked version of the manuscript has been prepared with red letters and attached herewith.

3. Deposit the sequence data to a public database and provide the accession number. E.g. European Nucleotide Archive (ENA): We have modified manuscript.

As the reviewer suggested that the candidate gene approach could be more clearly stated, we hope that our revisions have clarified this process.

We thank you and the reviewer for your decision and insights, which have enriched the manuscript and produced a more balanced and better account of the research. We hope that the revised manuscript is now suitable for publication in your journal.

I look forward to hearing from you.

Sincerely,

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