Reviewer’s report

Title: A novel compound heterozygous variant of the SLC12A3 gene in Gitelman syndrome pedigree

Version: 0 Date: 08 Oct 2017

Reviewer: Chao Xu

Reviewer's report:

In this article, the authors reported a case of GS pedigree and identified two novel missense mutations (Asn640Ser and Asp841Gly) in SLC12A3 gene. They predicted that these two novel mutations might cause impairment or loss of NCC protein function by building the three-dimensional structure model.

Overall, the study design is clear. However, the experiment data were rather rare and the identified SLC12A3 mutation is suspected in this case since initial presentation. So, it is not suitable for acceptance of BMC Medical Genetics in its current version. Maybe Case Report or Letter to the Editor is acceptable.

There are several major points:

1) The conservation among species of the mutant amino acid residue shoud be analyzed.

2) The credibility of the three-dimensional structure model is ambiguous. The authors should confirm the feasibility of the model through several protein model evaluation website.

3) The authors didn't specify what the fork stands for in Figure 4 Pedigree Chart.

4) The patient suffered from metabolic complications such as impaired glucose tolerance and hyperuricaemia. The authors only explained the correlation between hypokalemia and impaired glucose tolerance. Is there any relationship between hypokalemia and hyperuricaemia?

5) Some grammar errors.
Are the methods appropriate and well described?  
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?  
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?  
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?  
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

Quality of written English  
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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