Reviewer’s report

Title: Clinical and genetic analysis of two wolfram syndrome families with high occurrence of wolfram syndrome and Diabetes type II: a case report

Version: 0 Date: 19 Sep 2019

Reviewer: Anlu Chen

Reviewer's report:

Sobhani and colleagues studied extended consanguineous families and identified a novel mutation in a highly disease-associated gene, WFS1. This manuscript would be interested to researchers in this rare disease field and in general overlaps with the journal's interest. I only have some minor suggestions below.

1. In general, high-resolution images are required. Some contexts are unreadable, especially in Figure 1.
2. On page 3, the authors mentioned 'a second locus containing a gene designated as WFS2'. It might be reasonable to specify the WFS1 locus first.
3. On page 3, WFS2 is an alias for CISD2.
4. Please add a table to compare the clinic presentations among all patients.
5. Please confirm that if 'DM' mentioned in the clinic presentations all referred to 'T2DM'?
6. Is there any special reasons to keep the family name as 'Family IR-WS-18' and 'Family IR_WS_25'? If not, change to Family I and Family II, respectively.
7. It's confusing when referring to family members. For example, please use I-III-8 to represent case 1.
8. In Figure 1, please double check if all consanguineous marriages have been marked as double lines.
9. In Figure 1, male partner can be put to left of female partner on relationship line. (Bennett RL. et al., J Genet Counsel, 2008)
10. In Figure 1, please double check the color indications.
11. In Figure 2, there's no V-9 in Family I. I assumed it's III-9 in Family I.
12. In Figure 4, there's no VI-1 or V-1 in Family I. I would assume it's IV-1 and III-1, respectively.
13. In Figures 5 and 6, please add reference genome sequence and fully mark the chromat of the patients. For example, C/G indicates heterozygous at certain position. Please align the panels A and B if possible.
14. In Figures 5 and 6, please specify the ID of individuals represented in these figures.
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.

Yes

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:

Acceptable

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