Reviewer’s report

Title: A Novel ISCA2 variant responsible for an early-onset neurodegenerative mitochondrial disorder: a case report of Multiple Mitochondrial Dysfunctions Syndrome 4

Version: 0 Date: 14 Feb 2019

Reviewer: Wolfram S Kunz

Reviewer's report:

The paper reports a novel homozygous variant of ISCA2 in a consanguineous Iranian patient.

I have the following comments:

1. Supplemental table 1 can be omitted.

2. Supplemental table 2 should be extended and the alterations on protein level of the detected variants should be added. This is especially relevant for all detected homozygous variants.

3. In this line the discussion of the effect of the ISCA2 mutation in the light of other potentially disease relevant homozygous alterations (in PRICKLE1, SLC37A4, ALMS1 etc.) is completely missing and should be extended in considerable detail.

4. In this context is perhaps unclear why an apparent homozygous frameshift in SLC37A4 (glucose-6-phosphate transporter) has been considered to be not relevant.

5. Fig. 4 and 5 are redundant and should be omitted.

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.

No
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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