Reviewer’s report

Title: Pure exercise intolerance and ophthalmoplegia associated with the m.12,294G>A mutation in the MT-TL2 gene: a case report

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Reviewer: André Schaller

Reviewer's report:

The authors describe in their manuscript the second patient harbouring the m.12294G>A mutation in MT-TL2 gene presenting with pure exercise intolerance and ophthalmoplegia.

I have some minor and major comments on the manuscript:

Major comments :

* How was the heteroplasmy determined in patients skeletal muscle ?

* The authors claim, that the mutation is absent in other tissues than skeletal muscle. Was this determined by Sanger sequencing? If yes, Sanger sequencing has low sensitivity for very low degrees of heteroplasmy. Authors are advised to look for low heteroplasmy using a more sensitive approach (e.g. RFLP as already described for this mutation (authors reference 18). Establishing RFLP would further allow measuring heteroplasmy of COX- vs COX+ fibres, further supporting the pathogenic nature of the mutation.

* It would be interesting to include the percentage of COX- fibres from the histology.

* Please include in figure 2A control electropherogram

Minor comments :

* Please use mtDNA as abbreviation for mitochondrial DNA instead of mDNA

* Can the authors report on current treatment of the patient ?
Are the methods appropriate and well described?  
If not, please specify what is required in your comments to the authors.

No

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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