Reviewer's report

Title: Identification of two novel null variants of CLN8 by targeted next-generation sequencing: first report of a Chinese patient with neuronal ceroid lipofuscinosis due to CLN8 variants

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Reviewer: Manoj Menezes

Reviewer's report:
Gao Z et al. report a Chinese patient with a phenotype consistent with NCL who was identified using next-generation sequencing to have compound heterozygous null variants in the CLN8 gene. The authors state that this is the first Chinese patient to be reported with CLN8 and describe the benefit of rapid diagnosis in a phenotype with multiple candidate genes using next-generation sequencing.

1. The manuscript requires extensive review of sentence construction and grammar.

2. The authors refer to this being the first Chinese patient 'affected' (abstract line 29), first Chinese patient 'presenting' (page 9 line 2) and first NCL patient 'confirmed' to carry CLN8 mutation in China (page 3 line 58). The authors refer to the mutations listed on the NCL Mutation Database (http://www.ucl.ac.uk/ncl/). Unless the authors have access to a comprehensive database of all identified NCL mutations in Chinese patients, it would be more prudent to say that this is the first Chinese patient 'reported' to have CLN8 mutations.

3. In the abstract (line 31) and in the conclusion (page 9 line 5), the authors state that their findings expanded the 'genetic' and ethnical diversity of pediatric NCL. This is not correct as no new genes or disease mechanism has been identified.

4. At a number of points in the manuscript the authors refer to the 'phenotypic' 'genetic' and 'allelic' heterogeneity of human disease, but the use is confusing. It may be straight forward
to say that the severity and phenotypic heterogeneity of NCL could be attributed to the different genes and different mutations in the same gene reported to cause the disease.

**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

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Not suitable for publication unless extensively edited

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