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: Lorraine N. Clark

Reviewer's report:

Comments to the Author:
The study from Gao et al., describes identification of two novel nonsense pathogenic variants in the CLN8 gene in a Chinese child whose clinical phenotype was suspicious for neuronal ceroid lipofuscinosis. Targeted panel sequencing of an NCL panel with 14 disease genes (CLN1, CLN2, CLN3, CLN4, CLN5, CLN6, CLN7, CLN8, CLN10, CLN11, CLN12, CLN13 and CLN14) and an epilepsy panel with 462 genes led to the identification of the pathogenic variants in the CLN8 gene. Inheritance of the pathogenic variants in the CLN8 gene in the patient is consistent with an autosomal recessive model of inheritance with one pathogenic variant inherited from each parent. The variants were classified as pathogenic according to the guidelines of ACMG.

This is a well-conducted study, the paper is well-written and the conclusions appropriate. I have just a few comments that may help improve the manuscript:

1) On page 6 "According to the guidelines of ACMG...." It might be useful to the reader to present the evidence that was used to classify the variants as pathogenic (e.g. Table 3 Criteria for classifying pathogenic variants. Genetics in Medicine, 17 (5): 405-424, (2015)).

2) Page 3, line 9 change "frequently" to "frequent"

3) Replace use of the word "mutation" to "pathogenic variant" throughout the manuscript according to the guidelines of ACMG (e.g. see "Terminology" page 407) when referring to the CLN8 nonsense variants.
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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