Reviewer's report

Title: Identification of a novel nonsense mutation in SH2D1A gene from a patient with X-linked lymphoproliferative syndrom type 1: a case report

Version: 1 Date: 08 Jan 2018

Reviewer: Laura S. Schmidt

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Lyu and colleagues describe a case of an 18 month old male patient with a novel nonsense mutation in SH2D1A and a diagnosis of XLP1. They show that the mutation results in a truncated mRNA and suggest this causes the production of a non-functional protein. They demonstrate that the mutation was inherited from the patient’s mother.

1) pg 7, line 29-30: use of "might be pathogenic" suggests that pathogenicity is not confirmed. However, nonsense mutations typically are considered "likely pathogenic" since they truncate the protein, so this would be a better choice of wording here.

2) Fig 3: patient is hemizygous not homozygous for mutation.

   Also symbols on pedigree need to be defined in legend (white symbol with dot, arrow indicates proband, etc.)

3) A truncated SH2D1A mRNA may still produce a truncated protein that could have partial function. It would be informative to perform Western analysis of the mutant SAP protein to determine if it is produced and stable or unstable. In addition, if a stable truncated protein is produced, the authors should discuss the potential consequence of a c-terminally truncated SAP protein based on knowledge of its function and the importance of the c-terminus to function, if this is known.
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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