Reviewer’s report

Title: Molecular diagnosis in recessive pediatric neurogenetic disease can help reduce disease recurrence in families

Version: 0 Date: 26 Aug 2019

Reviewer: Research Square Reviewer 2

Reviewer's report:

"PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses one or several testable research questions? (Brief or other article types: is there a clear objective?)
Yes - there is a clear objective

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?
Yes - the approach is appropriate

EXECUTION - Are the experiments and analyses performed with sufficient technical rigor to allow confidence in the results?
Yes - experiments and analyses were performed appropriately

STATISTICS - Is the use of statistics in the manuscript appropriate?
Yes - appropriate statistical analyses have been used in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?
Yes - the author's interpretation is reasonable

OVERALL MANUSCRIPT POTENTIAL - Has the author addressed your concerns sufficiently for you to now recommend the work as a technically sound contribution? If not, can further revisions be made to make the work technically sound?
Yes - current version is technically sound

PEER REVIEWER COMMENTS:

GENERAL COMMENTS: My overall impression is that the manuscript is sound and that the revision was done well, and took into account all the suggestions of the initial reviewers. I think the manuscript improved in the process.

ADDITIONAL REQUESTS/SUGGESTIONS:
I agree with the suggestion to merge table 1 with sup table 1, they provide very similar information, and presenting it twice is overkill. I would consider it typical (important) supplemental information
The authors speak about genes/variants that were re-interpreted as pathogenic, and as a consequence families were re-enrolled in the study p12 lines 5-7. In figure 1 they give the amount of families that concerns this. This is important information and should be provided in the text on p12 with a reference to figure 1 for clarity.

I found it interesting that in 7% of the cases WGS led to identification of the disease that was missed by exome. This is actually results material and could be expanded upon if needed. Now its buried in the methods section.

The study design section is quite long and could do with a bit of trimming as it re-states some information present in the introduction.

p4, early fetal ultrasound. What is exactly early? The authors should give numbers here, as this varies by country. The sentence on p4 line 13 about brain development needs a reference.

One important point that is unclear at the moment is what happened to the remaining 417 families. In the results section on p13 line 1-2 I read that these were followed-up but didn't have any pregnancies. However in the discussion on p17 line 17-18 it says ""we were not able to follow-up and determine if they were pregnant"". The authors need to sort this out as its important information.

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.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

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