Reviewer’s report

Title: Linkage and exome analysis implicate multiple genes in non-syndromic intellectual disability in a large Swedish family

Version: 1 Date: 01 Jul 2019

Reviewer: Rolph Pfundt

Reviewer's report:

The authors have adjusted the manuscript on may points after the first round of review.

The major point of concern of both reviewer 2 and myself is not addressed in the tekst. The fact that the authors are still hanging on to a variant with a carrier frequency that is too high for a neurodevelopmental disease, is concerning. This variant may perhaps reflect a locus that is linked to the disease, but in itself shall not explain the phenotype. The authors claim that SIFT categorized this variant as intolerant, but in fact this is not the case. Upon verification SIFT predicts this change to be tolerated. This is also the case for PolyPhen prediction and the Align-GVGD classification. With both the TPR and the ACOT4 variants also likely benign the value of the manuscript in its current form is not high enough.
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.

No

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

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

Acceptable

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