Reviewer's report

Title: Novel VPS13B Mutations in Three Large Pakistani Cohen Syndrome Families Suggests a Baloch Variant with Autistic-Like Features

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Reviewer: Wenke Seifert

Reviewer's report:

The authors present three large consanguineous Pakistani families with Cohen syndrome. The clinical assessment and the genetic studies are carried out carefully. The study identified two novel homozygous mutations causing the Cohen syndrome phenotype. Moreover, in two separate Baloch families a founder mutation was identified, indicating that Cohen syndrome may be a more common diagnosis for individuals with intellectual disability in this Pakistani subpopulation.

Major comments

1. Please provide the MR Images as Supplemental file. This would improve the quality of the manuscript.

2. The autism phenotype in the ATM02 family is interesting, however, similar observations have been made in context of Cohen syndrome (Ionita-Laza I. et al. 2014 Plos Genetics and Yu TW et al. 2013 Neuron). Those results from the literature should be implemented in the discussion of the manuscript.

3. In general, please remove the statements about the transmembrane domains in VPS13B. It has been shown biochemically that VPS13B is a soluble protein without any transmembrane domains. Therefore, any predictions about mutations affecting those are not helpful.

Minor comments

Overall, please check again carefully for minor grammatics and spelling errors: e.g. line 72 “IDdisorder”.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests