Reviewer’s report

Title: Xp11.22 Duplications in Four Unrelated Chinese Families: Delineating the Genotype-phenotype Relationship for HSD17B10 and FGD1

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Reviewer: Aleksander Jamsheer

Reviewer's report:

Wang et al. present a report of four patients carrying Xp11.22 duplications of different sizes. All affected male individuals manifested intellectual disability (ID), including delayed speech and also some additional features depending on size of the duplication and its gene content. The authors suggest two dosage-sensitive genes, HSD17B10 and FGD1, which - once duplicated - are responsible for ID/psychomotor retardation and hypogonadism, respectively.

Hypogonadism, including cryptorchidism, small testes, and micropenis was not linked to FGD1 duplications, and indeed FGD1 seems to be a perfect candidate gene for this phenotype.

With their study, the authors expand the phenotypic spectrum of Xp11.22 duplications and provide useful genotype-phenotype correlations helpful in the prognosis and genetic counseling of patients carrying duplications spanning the different portions of Xp11.22 region.

However, several minor remarks should be addressed prior to publication.
1) Page 3, lines 4-5, sentence starting with "He presented with mild ID…" If the patient was examined at the age of 4 years, why was mild intellectual disability recognized? Was the patient psychologically assessed? What was the IQ and which test was used?
2) Page 4, line 21, please correct "electroencephalographic" to "electroencephalography".
3) Page 4, lines 35-36, please correct "7 moths" to "7 months".
4) Page 5, line 50 and page 7 lines 6-7, "duplication was direct". What does this mean? Do you mean that the duplication was in tandem orientation? Please be precise.
5) Page 7, line 2-4, "…duplication at Xp11.22 was a disease-causing effect". Please correct the sentence.
6) Page 8, lines 4-5, abstract, list of abbreviations "Aarskoh-Scott syndrome" should be corrected to "Aarskog-Scott syndrome" throughout the manuscript.

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:

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