Reviewer’s report

Title: A heterozygous duplication variant of the HOXD13 gene caused synpolydactyly type 1 with variable expressivity in a Chinese family

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Reviewer: Sajid Malik

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BMC Medical Genetics

A 24-base pair duplication in exon one of HOXD13 gene caused synpolydactyly type 1 in a Chinese family

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Zaib et al. study a Chinese family with synpolydactyly and identify a 24 bp duplication in HOXD13. It is an interesting study, however, the manuscript would benefit from the following mandatory changes/amendments:

1. Page 2, line 15. 'were collect' should be 'were collected'.

2. Introduction: page 4, paragraph 3, 'In vertebrates HOX genes have.....' This paragraph may be omitted.

3. There should be consistency in the use of abbreviation, for instance, the authors use ExAc and ExAC.

4. The phenotype in the affected family members may be presented in a tabulated form showing major and minor symptoms in hands and feet separately.

5. The basic demographic details of the family should be provided.

6. Fig. 2. The subject IV-11 is not asymptomatic. Indeed she has camptodactyly of right 5th finger, clinodactyly of left 5th finger, camptodactyly of toes and contracture in right hallux. These changes are also reminiscent in the radiographs (though the quality of radiographs is low). Accordingly, the symbol of IV-II should be changed in Fig. 1.

7. Please remove the text mentioning lack of penetrance in the family.

8. Page 7, clinical findings. Clinical detail in the text may be omitted and can be presented in a table instead.

9. Methods: The WGS data filtration strategy is not described in adequacy. Please give detail of analyses scheme; total number of variants, how many variants were removed, how many rare variants were left in the final round, etc.

10. The genomic/UCSC coordinates of the variant should be provided.
11. All the rare variants falling in syndactyly/limb developmental genes (Shh, GLI3, LMBR1/ZRS, GJA1, LRP4, BHLHA9, APC, etc.) should be presented in a supplementary table.

12. The consequence of mutation/variant has not been reported.

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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