Reviewer’s report

Title: Novel NOG (p.P42S) mutation causes proximal symphalangism in a four-generation Chinese family

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Reviewer: Sajid Malik

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BMC Medical Genetics

Identification of a novel NOG mutation (P42S) in a four generation Chinese family with proximal symphalangism

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Yanwei Sha

Sha et al. recruit a Chinese family with proximal symphalangism and identify a mutation in NOG which segregates with the phenotypes. This is an interesting study, however, the manuscript would benefit from the following mandatory changes/amendments:

1. It is not clear how many subjects were subjected to whole genome sequencing.

2. The subjects who were blood sampled should be mentioned on the pedigree

3. Please mention the UCSC genomic coordinates of the variant.

4. It is not clear how the variant in NOG was detected. Please mention the filtration strategy in detail.

5. The list of all variants observed in brachydactyly/sympalangism genes should be presented in a separate table.

6. Please mention that it is not an isolated type of symphalangism. Slight hearing loss is observed in two subjects. Therefore, the authors should not present this case as an isolated entity. The hearing loss in two subjects should be mentioned in the Abstract.
7. The association of symphalangism and hearing loss should be discussed. Detailed differential diagnosis of a combination of symptoms (symphalangism and hearing loss) should be presented. There are several disorders which exhibit both features, like MULTIPLE SYNOSTOSES SYNDROME 1; X-LINKED DEAFNESS 2; DFNX2; TEMTAMY PREAXIAL BRACHYDACTYLY SYNDROME; etc.


9. It would be worthwhile to present hand photographs of a couple of subjects, in order to observe dermatoglyphics.

10. Genotypic assignment of the analyzed subjects should be mentioned on the pedigree.

11. The picture quality of Fig. 2 and 3 is poor. I am not able to assess the phenotype and chromatograms.

12. There are several mutations already reported in NOG which cause symphalangism. It would be worthwhile to present a summary table showing all such known mutations in NOG.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**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:

Needs some language corrections before being published

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