Reviewer’s report

Title: A novel GLI3 Mutation Affecting the Zinc Finger Domain Leads to Isolated Polydactyly

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Reviewer: Yiping Shen

Reviewer’s report:

Volodarsky et al., reported a novel missense variant in the zinc finger domain of GLI3 in a large Moroccan kindred. The variant was found to co-segregate with the isolated polydactyly in the pedigree, demonstrating the linkage and complete penetrance of the gene/variant with the clinical phenotype. The data are convincing and results are clearly stated in this short report.

While GLI3 mutations are uncommonly reported as a cause of isolated polydactyly, recent publications such as [Wang et al., Novel frame-shift mutations of GLI3 gene in non-syndromic postaxial polydactyly patients. Clin Chim Acta. 2014 Mar 22;433C:195-199.] added new evidence, suggesting the role of GLI3 in patients with isolated bilateral polydactyly affecting both hands and feet. It is recommended that the authors discuss the possible reasons/mechanisms that a variant located in the domain that often leads to syndromic polydactyly could cause isolated polydactyly and the extensive phenotypic heterogeneity among individuals within the kindred.

The author should have reference for “page 3 line 61-62” after “, and that mutations affecting the zinc finger domain (ZFD) of GLI3 specifically cause GCPS”.

Level of interest: An article whose findings are important to those with closely related research interests

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 interest