Reviewer’s report

Title: Novel Loss-of-Function Variants of TRAPPC2 Manifesting X-linked Spondyloepiphyseal Dysplasia Tarda: Report of Two Cases

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Reviewer: George Tiller

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The manuscript by Won et al. describes two novel TRAPPC2 mutations (one of which was reported previously by the authors; see reference 9) in two individuals with SED tarda. The authors studied the effect of the mutations on the expression of the TRAPPC2 gene product in a simple in vitro system. As expected from the nature of the mutations, no protein product was demonstrated on Western blot, although the mutant gene constructs appeared to have been transcribed. The latter conclusion relies on one experiment (RT-PCR on RNA from transfected cells), but a critical control experiment (omitting the RT step) was not performed. Contamination of the RNA samples with plasmid DNA could have produced the same result. Contrary to the authors' conclusion, this manuscript does not "significantly contribute to the understanding of the clinical spectrum and genotype correlation of the TRAPPC2 gene," as they admit in their introduction that "neither types nor sizes of mutations seem to have any correlation with severity of the disorder."

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.

No

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:

Needs some language corrections before being published

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