Reviewer’s report

**Title:** PHENOTYPIC AND GENOTYPIC ASPECTS OF TOWNES-BROCK SYNDROME: CASE REPORT OF PATIENT IN SOUTHERN BRAZIL WITH A NEW SALL1 HOTSPOT REGION NONSENSE MUTATION

**Version:** 0  **Date:** 17 Aug 2016

**Reviewer:** Dylan Sweetman

**Reviewer's report:**

The manuscript describes a novel case of TBS and identifies a mutation in the SALL1 gene, known to be causative in cases of this syndrome. The manuscript is clearly written and the case clearly fits the clinical presentation and molecular biology of TBS.

One area that could be made clearer is how the mutation identified in this case compares to those seen in other TBS patients. In general the mutations associated with TBS are nonsense mutations in the 5' region of the gene found between the glutamine rich region and the first set of paired zinc fingers. These seem to escape NMD and act as dominant negatives, probably by sequestering full length proteins in the cytoplasm. Other mutations in SALL1 are normally associated with less severe malformations. However this case seems to involve a missense mutation but still has a severe range of abnormalities. If the authors described in more detail how this mutation is likely to affect the protein and how this relates to other SALL1 mutations in TBS it would provide additional valuable detail to help put this case into context.


**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.

Unable to assess

**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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