Reviewer's report

Title: Identification of a region required for TSC1 stability by functional analysis of TSC1 missense mutations found in individuals with tuberous sclerosis complex

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Reviewer: Teguh Haryo Sasongko

Reviewer's report:

The authors, Mozaffari M et al., reported their work in studying the protein functional analysis of hamartin affected by missense mutations. This study is very much similar to their previous publication, Nellist M et al. Eur J Hum Genet 2009;17:319-28. However, in this study they used totally different set of mutations as study material in which they added a few mutations (L50P, E51D, L61P, L93R) representing more upstream region of their previous report.

This paper lacks of novelty since it just added to database of missense mutation with pathogenic effect to hamartin.

The conclusion was inappropriately drawn. It is apparent from their results that while L50P have pathogenic effect, E51D does not seem to give pathogenic effect. It is therefore not appropriate to make such a generalized conclusion about role of a protein region by only analysing the protein function after a missense mutation occured.

Level of interest: An article of limited interest

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 interests