Reviewer’s report

Title: The p.Phe174Ser mutation is associated with mild forms of Smith Lemli Opitz Syndrome

Version: 0 Date: 20 Nov 2015

Reviewer: Filippo M. Santorelli

Reviewer's report:

Major changes:

1. With hindsight the clinical case satisfies at large a diagnosis of SLOS and it is unclear why biochemical screening for elevated 7-dehydrocholesterol and 8-dehydrocholesterol was not considered as a low-priced, first-tier diagnostic testing. This is also considering a recent work (Anal Bioanal Chem 2015; 407:5227-5233) offering rapid and cheap LC-MS/MS-based quantification of cholesterol and related metabolites in DBS from patients.

2. The authors discuss their findings properly but refer to literature too much updated. Please refer to more recent works on SLOS and DHCR7. I have noticed that a special issue on SLOS can be found in the supplements of the American Journal of Medical Genetics Part C (Seminars in Medical Genetics). Even more recent work on SLOS can be cited properly. The authors might consider "rejuvenating" the bibliography of this manuscript.

Minor changes:

1. Please, cite the present age of this boy (page 8, ln 1).

2. Please, indicate the genotype of the patient' s sib

3. Please, mitigate your conclusion. Page 11, ln 23 say: "This study offers further clinical significance to the p.Phe174Ser variant ...." and not "This study confirms the pathogenicity of the p.Phe174Ser variant ..." since no functional studies to address directly the pathogenetic consequences of the gene change were adopted.
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.

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.

Not relevant to this manuscript

Quality of written English 
Please indicate the quality of language in the manuscript:

Acceptable

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