Reviewer’s report

Title: Lessons learned from Whole Exome Sequencing reanalysis: Our experience on 200 Lebanese exomes

Version: 0 Date: 01 Oct 2018

Reviewer: Reviewer 2

Reviewer's report:

PEER REVIEWER COMMENTS: To view the full report from the academic peer reviewer, please see the attached file.

REVIEWER COMMENTS FROM REPORT: The authors of this manuscript apply whole exome sequencing (WES) to identify the genetic causes of a series of diseases presented in a total of 200 Lebanese patients previously referred to the Medical Genetics Unit of the Saint Joseph University.

This is an interesting piece of work, the methods are quite well described, and the results are clearly summarized in three tables. However, I would strongly suggest the authors to rewrite parts of the abstract and the main text in order to improve the overall clarity and soundness of their work. Specific comments are highlighted in the "suggested revisions" section

REQUESTED REVISIONS:

Abstract:

"connecting a rare variation". Should be "connecting a rare genetic variation"

"a clear phenotype with a detailed family history and ending, in some cases, with functional assays that are crucial for the validation of the pathogenicity of a mutation". From the abstract and this part in particular, it is not very clear that the authors are actually aiming to identify the genetic cause of specific diseases. I would suggest rewriting the first part of the abstract accordingly.

"a wide spectrum of genetic disorders". I would recommend listing at least some of them for clarity.

"49.5% overall success rate". The meaning of "success rate" should be explained/described (i.e. the specific genetic mutation causing the phenotype/disease)
"diagnostic yield", not clear what this really means (sensitivity ?)

" were reanalyzed", how? Please briefly described what was changed.

Main text

"An initial analysis was performed, followed by data re-analysis", should be described in more detail.

The introduction should be expanded by describing the importance of having a genetic test for the certain diseases, methods currently available and the relevance of their study within the context.

"All types of mutations (small frameshift, nonsense, splice sites, and missense mutations) were identified." Suggest rewriting.

"all "private" Lebanese polymorphisms". Not clear.

The list of "lessons learned" in the discussion is mix of a bit of everything. I would rather move the description of the specific mutations identified to the results. The discussion should include the overall outcome of the study, positive results or difficulties and future directions.

"of low-cost molecular diagnostics". Is WES low cost? I believe the authors refer to other tools, this therefore should be clarified.

A few English grammar/typos to be corrected along the text.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

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.

No
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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