Reviewer's report

Title: Targeted next generation sequencing as a tool for precision medicine

Version: 1 Date: 18 Mar 2019

Reviewer: George P. Patrinos

Reviewer's report:

This article describes a NGS-based method for analysing the coding sequences of 100 pharmacogenes.

Strong points are the ability to perform CNV analysis in the 2D6 gene and the high concordance of the findings using the new method compared to TapMan genotyping.

- The authors do not discuss the limitations of their study, in the sense that it is not able to detect pharmacogenomic variants in the introns and elsewhere.

- The authors did not compare their findings with similar studies that have been performed previously where whole genome sequencing has been used (e.g. Mizzi et al., 2014 and references therein).

- It would be useful to discuss about the feasibility and cost-effectiveness of the proposed method as compared to panel-based approaches, also deducted by the number of rare and novel variants identified using this novel method. Why someone to use this novel method and not an existing panel-based test?

Also, the authors only vaguely responded to the first round of comments, which does not allow to assess the extent of the review performed in this revision round.

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.

I am able to assess the statistics

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

Acceptable

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