Reviewer’s report

Title: Detection of Large Rearrangements in a Hereditary Pan-Cancer Panel using Next-Generation Sequencing

Version: 2 Date: 26 Jun 2019

Reviewer: Reviewer 2

Reviewer's report:

"PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses one or several testable research questions? (Brief or other article types: is there a clear objective?)

Yes - there is a clear objective

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?

No - there are major issues

EXECUTION - Are the experiments and analyses performed with sufficient technical rigor to allow confidence in the results?

No - there are minor issues

STATISTICS - Is the use of statistics in the manuscript appropriate?

No - there are issues with the statistics in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?

No - there are minor issues
OVERALL MANUSCRIPT POTENTIAL - Has the author addressed your concerns sufficiently for you to now recommend the work as a technically sound contribution? If not, can further revisions be made to make the work technically sound?

Maybe - with major revisions

PEER REVIEWER COMMENTS:

GENERAL COMMENTS: The authors maintain that they have carried out a validation of sensitivity that meets current guidelines. They have not however, carried out a sufficient validation of large rearrangements. How can a single LR in BRCA2 be a statistically significant validation of LRs in BRCA2? Their numbers may be sufficient in a large-scale validation assessment that includes point mutations but has no level of statistical significance for LRs for BRCA2 and many of the other genes with one or two LRs assessed.

REQUESTED REVISIONS:

They still need to carry out a full scale validation of LRs in BRCA1 and BRCA2.

ADDITIONAL REQUESTS/SUGGESTIONS:

No, just the bigger LR validation."

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.

I am able to assess the statistics

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

Acceptable

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

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