Reviewer’s report

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

Version: 1 Date: 19 Apr 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?

Yes - the approach is appropriate

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

Yes - experiments and analyses were performed appropriately

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

Yes - appropriate statistical analyses have been used 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 have responded to the comments but rely on their previous validation paper. This is not a true check on sensitivity. They tested 212 samples with known status but give no details about the number with known CNVs. This is a very small validation set. There were only 48 positive CNVs evaluated with no record of how many were in the really important genes. This is inadequate for any true test of sensitivity given that at most this may be 10 each for BRCA1 and BRCA2. A much larger fully blinded sample set with no 'known' number of positive CNVs should be assessed.

REQUESTED REVISIONS:

They still need to carry out a proper validation study for BRCA1 and BRCA2 CNVs.

ADDITIONAL REQUESTS/SUGGESTIONS:

No, just a proper validation.

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.

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

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