Reviewer’s report

Title: Identification of candidate breast cancer predisposing variants by performing whole exome sequencing on index patients from BRCA1 and BRCA2-negative breast cancer families

Version: 2 Date: 25 Feb 2019

Reviewer: Melissa Southey

Reviewer's report:

The authors have satisfactorily attended to the vast majority of this reviewer's comments.

4) Perhaps "...over-represented in BC patients. These over-represented genes were especially functional in the DNA double strand break repair process" would read better as "over-represented in women with breast cancer and commonly involved in DNA double-strand break repair".

9) I think the breast cancer penetrance estimates for pathogenic variants in PALB2 are now well established - I would cite Antoniou et al NEJM. Note: These are penetrance estimates - I do not think that "exact penetrance" figures are realistic.

Page 12, line 27. I suggest "more frequently tackle genes functionally" would read better as "more frequently identified in genes functionally".

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

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Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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