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

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Reviewer: Drakoulis – Yannoukakos

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The manuscript "Identification of candidate breast cancer predisposing variants in a virtual panel of 492 cancer-associated genes by performing WES on breast cancer cases from BRCA1/2-negative families with elevated breast cancer risk" by Bahadur Shahi et al describes the whole exome sequencing analysis of 54 patients with breast cancer, negative for mutations in BRCA1-2 genes. As a second step they analyzed bioinformatically a set of 492 genes in order to identify mutations and genes that may me associated with breast cancer.

They propose some known to predispose to breast cancer genes such as PALB2, BARD1, CHEK2, RAD51C, FANCA and RINT1 and others known to predispose to other cancer types but not well-studied in the context of familial BC (EXO1, RECQL4, CCNH, MUS81, TDP1, DCLRE1A, DCLRE1C and PDE11A). They also identified mutations in genes associated with different hereditary syndromes but vaguely related with familial cancer syndromes (ABCC11, BBS10, CD96, CYP1A1, DHCR7, DNAH11, ESCO2, FLT4, HPS6, MYH8, NME8 and TTC8).

This type of work is preliminary in terms of finding new cancer predisposing allele. These results needs to be confirmed from larger studies.

In any case they indicate some potentially breast cancer predisposing genes but they have to be confirmed.

However this manuscript merits the publication in BMC Cancer as it is well written and documented.
Ae 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?
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Yes

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