Reviewer's report

**Title:** Evaluation of the need for routine clinical testing of PALB2 c.1592delT mutation in BRCA negative Northern Finnish breast cancer families

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**Reviewer:** Sanna Pakkanen

**Reviewer's report:**

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Article reviewed:
"Evaluation of the need for routine clinical testing of PALB2 c.1592 del T mutation in BRCA negative Northern Finnish breast cancer families"

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This is a nice straight forward study with well-defined study question suggesting that PALB2 c.1592delT should be a routine part of the genetic counseling protocol for Finnish high-risk breast cancer cases tested negative for mutations in BRCA1/BRA2. However there are some concerns needed to answer before this manuscript is recommended for publication.

Major Compulsory Revisions

Question 1:

The authors found that in the Northern Finnish 1997-2011 study cohort 4,8% of the 62 female index individuals tested negative for germline mutations in BRCA1/BRA2 were PALB2 c.1592delT mutation carriers. The authors suggest that PALB2 c.1592delT testing should be a routine part of national counseling protocol.

However in a study by Kuusisto et al. (2011) (http://breast-cancer-research.com/content/13/1/R20) with very similar patient material from Tampere University Hospital District, 82 BRCA1/BRA2 mutation negative index females were tested for PALB2 c.1592delT mutation and no mutation carriers were found. The authors have not discussed this contradictory finding. Could there be regional differences in the frequency of this mutation in
Finland? Is it possible to confirm the finding in a nationwide breast cancer family data?

Question 2:
How is the pedigree data collected? Are family histories registry based confirmed?

Question 3:
In Abstract the authors state that given the potential benefits versus harms of this testing, this PALB2 c.1592delT should be a routine part of the genetic counseling protocol. The benefits are well discussed later in text, but the harms have not been addressed. Here the possibly found mutation carriers may have a risk to other cancers too (pancreatic cancer).

Minor Essential revisions

Question 4:
In Materials and Methods, Patient material first paragraph, when defining the Lund criteria number four criteria is “four or more relatives”. Should it be “four or more first degree relatives”?

Question 5:
In Figure 2 FAM A on female is marked as “Cancer ?” If that cancer is not confirmed is it better left out from the pedigree?

Question 6:
The information on family pedigrees on Figure 2 and in supplementary data Table 1 are different. Has the family ids been mixed? (For example FAM A in figure 2 does not have a breast cancer female whose age at diagnosis is 43).

Discretionary revisions

Question 7:
In Figure 2, how is the index person selected?

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests.