Reviewer's report

Title: Association of PALB2 sequence variants with the risk of familial and early-onset breast cancer in a South-American population.

Version: 3 Date: 8 October 2014

Reviewer: Lauren G Aoude

Reviewer's report:

The authors sought to determine the contribution of PALB2 mutations to Breast cancer predisposition in a Chilean population. Though there was a negative outcome, the study is none the less interesting to the scientific community as this population is currently unreported on in terms of PALB2 contribution to breast cancer.

Minor essential revisions:
1. The term “OC” needs to be defined at first use (Methods, paragraph 2).
2. Transcript ID and amino acid change should be annotated at first mention of the 3 variants detected (Results, paragraph 1).
3. Discussion point stating that rs45551636 is not reported in African-American BC cases (ref 53 in the manuscript) is incorrect. The study reported this variant in a small proportion of their cases and controls. NHBLI ESP6500 also reports this variant in 26/3424 African-American individuals. Authors should discuss both the European American and African-American population data from the ESP6500 for the 2 SNPs.
4. Where possible be consistent with number of decimal points when quoting population-frequencies.
5. Last sentence of the Discussion is rather over stated given the evidence present is obtained from predictive software. The authors should not state that this is a “probably pathogenic”. They do not provide strong enough evidence to make such a statement.
6. Table 3: The data under each BC group does not match the headings- please revise carefully.

Discretionary Revisions:
1. Background: Could a proportion of families be explained by mutations occurring as yet unidentified high-risk genes. Please comment.
2. Given that PALB2 also predisposes to pancreatic cancer (Jones et al. 2009), the authors might consider looking at families with a combination of BC and pancreatic cancer. Do any of the families with the variants described in this manuscript have a history of pancreatic cancer?

Reference
1. Jones, S., et al., Exomic sequencing identifies PALB2 as a pancreatic cancer

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.