Reviewer’s report

Title: Gene-expression patterns in peripheral blood classify familial breast cancer susceptibility

Version: 2
Date: 20 July 2015
Reviewer: Logan C Walker

Reviewer’s report:

This study presents a new tool (biomarker) which has potential for estimating individual risk of breast cancer. Although important, further studies would be required to test efficacy.

Major Compulsory Revisions:

1. Tables S1 and S2 - The markers appeared to be unable to predict 1) BRCA1/2 mutation status in patients with family history, and 2) patients with (or without) family history, which limits the clinical relevance of the study in relation to improving genetic screening.

2. The mutation status is noted but not the type of mutations. Which patients had BRCA1 mutations and which had BRCA2 mutations?

3. Batch effects are significant when comparing expression profile in blood between individuals. The authors noted that the arrays had been processed at different facilities and had used a tool (ComBat) to minimise these effects. It would be beneficial to see the before and after effect of ComBat to the data. This could be presented as supplementary information.

4. The relevance of the pathway analysis is unclear. Genes/pathways that are characteristic of the familial breast cancer group are being assessed in non-breast tissue. Are the authors implying that the 250 genes used for the “biomarker” are also characteristic of asymptomatic breast tissue and/or are playing an important role in breast cancer susceptibility?

Minor Essential Revisions:

1. Abstract Methods - The training set should be referenced as the “Utah cohort”

2. Page 6 – Modify the following into 2-3 sentences for clarity “Although such aberrant expression may not manifest itself phenotypically ... carry these mutations[14–26]”

3. Suppl Data Files 1 and 2 need a key to define column headers

4. There are Supplementary Data Files 1 and 2, and Table S1 and S2, is this normal for BMC Med Genomics formatting.

Level of interest: An article of importance in its field

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