Reviewer's report

Title: Women with familial risk for breast cancer have an increased frequency of aldehyde dehydrogenase expressing cells in breast ductules

Version: 2 Date: 17 June 2013

Reviewer: Margaret Currie

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The paper by Isfoss et al. examined ALDH+ cells in breast ductules in patient sub-groups and in different levels of the ductular epithelium within patient subgroups. Although this paper will contribute to the field by showing a number of associations between ALDH+ expression in non-tumour ductule cells and known breast cancer risk factors, the manuscript requires work before it is suitable for publication.

Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

1) Define very clearly what is meant by ‘ALDH+ cells’ (ductules only) and use this term consistently throughout the text.

2) Abstract 1st Para. The background paragraph is vague; clarify ‘patient hormonal factors’ and ‘various risk factors for breast cancer’. Define the question posed by this research.

3) Abstract last Para. Describe the potential implications of the study in the conclusion.

4) Background 3rd Para, last sentence. There are several recent papers that have shown ALDH+ cells in histologically normal breast tissue are related to risk factors and outcome in breast cancer, and these should be acknowledged.

5) Methods 1st Para. Be consistent with the patient group names in the abstract, methods, results and Tables. List how many patients are in each group (A-F).

6) The archived tissue samples were collected from 1984-2010. Over this time, major changes occurred in surgical techniques and in tissue collection, preservation and storage techniques. Such factors may all impact on the quality of immunohistochemical analysis, and these issues should be addressed. Similarly, discuss and/or clarify what type of oral contraceptive was used by patients.

7) Results, Discussion, Conclusion. These sections were weakest and need work; there was very little discussion about how these results add to current knowledge, the biological implications of the results, or the strengths and limitations of the study. The conclusion did not give a clear explanation of the importance and relevance of the results.
Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

8) Abstract 2nd Para. BRCA1/2 mutation carriers (n=22?).

9) Background 1st Para. Only one reference cited (7) for ‘recent studies’.

10) Background 4th Para. Clarify ‘might be related to hormonal status’.


13) Results and Discussion. ALDH+ cells in relation to HRT and contraceptive pills. 2nd Para. Replace ‘induces a risk’ with ‘increases the risk’.

Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

14) Consider removing the key words ‘epidemiology’ and ‘progenitor cells’ and replacing them with ‘breast ductules’.

15) A measure of adiposity (e.g. BMI) would have been interesting, particularly in the post-menopausal women. Is this data available for inclusion?

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

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.