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: 20 June 2013

Reviewer: Joana Paredes

Reviewer's report:

Dear Authors,

The aim of this article was to address possible associations between breast cancer risk factors and the cellular expression of the breast cancer stem cell marker ALDH in ductules of benign human breast tissue. Due to this study, the authors have demonstrated that, in benign breast tissue, there is a positive and strong association between the frequency of ductular ALDH+ cells and breast cancer family history.

Although the objective and results of the paper are very interesting, there are some important points that need to be improved or clarified, which are detailed below:

Major Compulsory Revisions

1) The Background section needs to be highly improved. The authors need to describe an increased number of findings concerning ALDH expression in breast cancer, including the one previous published by the group. The text is too much fragmented, and the aim needs to be better explained.

2) Page 6 and Table 1. The authors need to correct the text concerning the data that is presented in Table 1, in order to have coherency between both. Additionally, there is also the need of some corrections within Table 1: there is one missing case in the parity part, there are also an increased number of missing cases in the Hormonal use at time of surgery... Please correct this table according with the data described in the manuscript text.

3) Figure 1. The authors should include pictures showing the differences between ALDH+ positive cells located adluminally, intermediately and basally in the TDLUs. Please discuss in the “Results and Discussion section”, why the expression location can influence the risk.

4) Table 2: It is very difficult to understand the 37 patients included in the arm “pre-menopausal patients with familial history of breast cancer (without BRCA1/2 mutations)”, based in table 1. In fact, it is difficult to understand the numbers of these patients based in the previous cohort of 106 patients. Please clarify this issue.

5) Please describe, as a Table, the numbers and statistic associations found. It is
my feeling that the number of cases is too small to take some conclusions. This table should be included to complement the figures presented.

6) Please improve the Discussion of the results found in the context of this work.

**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'