Reviewer’s report

Title: Expression of estrogen receptor beta in the breast cancer cells of BRCA1 mutation carriers

Version: 1 Date: 12 December 2007

Reviewer: Anna deFazio

Reviewer’s report:

The aim of this study was clear: to determine the expression of ERβ in BRCA1-associated breast cancer and to compare with the pattern of expression of other hormone receptors. However, the specific hypothesis being addressed by determination of HER-2 receptor expression was not clearly defined.

There is one previous study describing the expression of ERβ in breast tumors in BRCA1 carriers, as referenced in this manuscript (Daidone et al 2007). It is noteworthy that this previous publication was a Letter to the Editor. A more detailed section in the Discussion comparing the results of the current manuscript with this previous study is warranted. Comparison of expression of ER±, β and progesterone receptor in BRCA-associated breast cancers as presented in this manuscript is new information.

Major Compulsory Revisions

1. Given variable results in the literature with different ERβ antibodies, the authors should consider inclusion of photomicrographs (with appropriate staining controls) to confirm specificity of staining, or at least reference published validation of this particular antibody.

Minor Essential Revisions

2. In general, the Title and Abstract accurately reflected the main findings, although the aim would be better moved from the Methods to the Introduction of the Abstract. Also the antibody to ERβ is suggested to be a monoclonal antibody in the Abstract but polyclonal in the body of the manuscript. In the Abstract the p-value for ER-positive BRCA1-related cancers compared with the control group was P<0.0001 whereas in Table 2, this was P<0.001.

3. It would be appropriate for the authors to indicate from the literature whether the antibody used to detect progesterone receptor is able to detect both PR-A and PR-B (see Mote et al Endocrinology 147: 5503–5512, 2006)

4. In the methods section the authors state: In cases of 2+ results achieved for confirmation of overexpression of HER-2 protein, the amplification of crbB2 (sic) gene was checked with the use of fluorescent hybridisation in situ (FISH) (sic), however there was no indication as to how this information was used, eg were 2+ cases without amplification, not considered to over-express HER2?
This should be specified in the methods.

5. Addresses of reagent suppliers are not specified.

6. The level of significance and specific tests used were not described in the narrative of the results nor were the specific statistical tests indicated in the legend to tables.

7. Figure 1 and the legend to Figure 1 are not publication quality. The legend lacks detail, the axis titles are missing, unclear and/or misspelt.

8. The column titles in the Tables are inconsistent and in Table 2 and 3 are not clear ie in Table 1: Patients with mutated BRCA1 gene in Table 2 and 3: BRCA1 positive BC (this terminology is ambiguous).

9. In the main, the discussion is supported by the data, however the discussion related to cDNA microarray studies could be shortened as it is peripheral to this study.

10. The abbreviation of breast cancer to BC is unnecessary and inconsistently applied.

11. There are a large number of typographical and grammatical errors, a selection of which are listed below:

Abstract
Line 2: frequently estrogen receptor negative than the nonhereditary BC.
Line 14: ad Fisher's Exact Test; the statistical significance was considered when p<0.05.

Introduction
Paragraph 1: The finding of Hall at al, in 1990, that familial breast cancer is associated with the pathology of one of the genes located in 17q21 chromosome, began a new era in the heredity breast cancer research, and has consequently led to the identification of BRCA1 and BRCA2 suppressor genes in 1994 and 1995.

Paragraph 1: They are responsible for the proper course of the cell cycle, DNA damages reparation, and are also instrumental in the process of cell differentiation. (also not referenced).

Paragraph 3: Their tumors rarely present the expression of receptors for the sex hormones.

Paragraph 4: When dimerisated,
This selective estrogen receptor moderator

Methods
Paragraph 1: The patients were operated either
Paragraph 4 of crbB2 gene

Results

Abbreviation of estrogen receptor is inconsistently applied

is that most hereditary cancers have been found triple-negative

Discussion

Title

Out of the hereditary cancer patients in our study group, 75% were found triple-negative, lacking ERÎ±, PgR and overexpressing HER-2.

Abbreviations

estrogen receptor alfa (alpha)
selective estrogen receptor moderator (modulator)
EGFR epithelial growth factor (epidermal growth factor receptor)

Discretionary Revisions

The BRCA1 mutation positive cohort was restricted to carriers of three common Polish mutations and was dominated by one particular mutation. It would be useful if the authors could discuss what proportion of Polish BRCA1 mutation carriers carry these mutations ie how representative is this cohort of Polish population, and whether these mutations are found in other ethnic groups.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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

Quality of written English: Not suitable for publication unless extensively edited

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.