Reviewer's report

Title: Novel markers for differentiation of lobular and ductal invasive breast carcinomas by laser microdissection and microarray analysis

Version: 2 Date: 22 January 2007

Reviewer: José Palacios

Reviewer's report:

General

-------------------------------------------------------------------------------------------------

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

The main limitation of this study is the low number of cases analyzed, which difficult statistical comparisons and preclude general conclusions.

Regarding the tumours studied, it is not clear why the authors have selected 2 ILC (out of 5) that are ER-negative, where most ILC usually are ER-positive. In addition, IDCs are very heterogeneous and it is difficult to accept that 5 cases are representative of ductal cancer heterogeneity. It is probable that results were different if other 10 tumours were selected.

Taken into account that few breast cancers were analyzed, microarray experiment should have been done in duplicate.

The authors should have analyzed some up- and down-regulated genes by RT-PCR to validate microarray data in this series of tumours.

Validation study on TMA should have included other markers instead of E-cadherin, CK17 and CK5/6. It is obvious that ILC do not express E-cadherin, and that most lobular and ductal carcinomas are of "luminal type" and do not express basal cytokeratins, that are markers of normal myoepithelial cells, and some normal non-myoepithelial cells.

In addition, some data TMA are surprising and should be discussed. For example, absence of E-cadherin usually does not occur in IDC, even in those cases that are high grade. CK5/6 expression is frequent in medullary carcinomas, since these tumors have a basal-like phenotype, but the authors only comment about CK5/6 expression in a papillary carcinoma.

-------------------------------------------------------------------------------------------------

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

The discussion is very general and speculative. The authors do not mechanistically explore any of the suggested pathways discussed (for example TGF-beta or WNT).

Although E-cadherin loss is present in cells that undergo EMT, absence of E-cadherin is not sufficient to induce EMT. The authors do not discuss or study the expression of other luminal keratins, or other luminal markers, that are always expressed in ILC.

-------------------------------------------------------------------------------------------------

Discretionary Revisions (which the author can choose to ignore)
**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:** 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