Reviewer's report

Title: Elevated cyclin B2 expression in invasive breast carcinoma is associated with unfavorable clinical outcome

Version: 1 Date: 29 August 2012

Reviewer: Fernando Schmitt

Reviewer's report:

The authors analyzed the expression of five biomarkers – CCNB2, ASPM, CDCA7, KIAA0101, and SLC27A2 – in a cohort of 80 patients with breast carcinoma. In a previous study, the gene expression of these five biomarkers was significantly deregulated in aggressive breast tumors. In the present study, the authors showed that the immunohistochemistry expression of CCNB2 was associated with short disease specific survival (DSS) in patients with breast cancer. By multivariate regression analysis, the protein expression of CCNB2 was found as an independent prognostic marker of DSS. They also tested the predictive power of CCNB2 and showed that the association of this biomarker with clinicopathological parameters achieved the higher index (C-index) for predicting breast cancer specific-survival. Furthermore, the immunohistochemical expression of CCNB2 was validated by quantitative RT-PCR: a positive association between the mRNA and protein levels of CCNB2 was observed. On the other hand, the immunohistochemical expression of ASPM, CDCA7, KIAA0101, and SLC27A2 did not correlate with clinicopathological parameters and DSS in this series of breast cancer.

Major compulsory revisions:

1. Methods, section Tumor specimens. On page 5, the authors stated that “the tumors were stratified according to disease-specific survival (DSS) with 8-year censoring, axillary lymph node status, and stratified histological grade (BRE grade I and II versus III)”. According to the data in Table 1, the tumors were stratified only by DSS (with 8-year censoring) and histological grade, not including the axillary lymph node status;

2. Results. The increased cytoplasmic expression of CCNB2 was associated with unfavourable prognosis, as was demonstrated by Kaplan-Meier analysis (figure 1). In table 2, which was the P-value for CCNB2 expression according DSS: P < 0.001? On page 9, “The univariate Cox proportional hazards regression analysis…with DSS (HR, 6143; 95% CI: 1.872-20.161; P =0.003; Table 2)” is not correct. Probably, the correct is HR, 6.1; 95% CI: 2.0-20;

3. Result. On page 9, I suggest to change the order of the results: first, the description of the immunohistochemical findings (corresponding to figure 2); followed by the data contained in table 2 regarding the expression of CCNB2; and finally the Kaplan-Meyer analysis (corresponding to figure 1). I suggest the same for the others biomarkers;
4. Discussion. On page 14, “We have shown a slightly significant interaction of CCNB2 protein expression with breast tumor type (P = 0.04).” This statement should be included in the Results, and the authors would try to explain this interaction. According to table 2, lobular carcinoma is preponderantly positive for CCNB2 (87.5% positivity) against ductal carcinoma (71.0% positive for CCNB2);

5. Discussion. This section is too long. I suggest the authors to begin the discussion with the main results of the study, namely the correlation of CCNB2 expression and the clinical outcome of this cohort of breast cancer patients. The authors would focus the discussion on cell cycle and breast cancer, comparing this study with others that studied the role, or the expression, of other cell cycle factors or biomarkers in breast tumors. Some topics are exhaustive and not relevant for the discussion (example: the “topic” about the heterogeneity of breast tumors on page 13).

Minor Essential Revisions:
1. Some abbreviations are not usual. On page 5 (line 10), the phrase “stratified histological grade (BRE grade I and II versus III)” should be replaced by: stratified according to the histological grade as defined by Bloom, Richardson, and Elston/Ellis (BRE) grading system (with appropriate reference). It is the same with some abbreviations that appear for the first time in the manuscript: HER2/neu on page 4 (third line) and ER/PR on page 8 (ninth line).

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

Quality of written English: Acceptable

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