Reviewer's report

Title: Elevated MED28 expression predicts poor outcome in women with breast cancer

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Reviewer: Gulisa Turashvili

Reviewer's report:

Major Compulsory Revisions

Abstract
1. This paper describes the immunohistochemical expression of MED28 in breast cancer rather than the association of MED28 expression with human breast cancer progression.

Methods
1. 242 tissue samples from 210 patients were used for TMA. What was the reason for including more than one tissue sample for some patients?
2. How many cores were taken from each case?
3. Of 210 patients, 179 had invasive carcinoma. Were the remaining cases metastatic tumors, DCIS and normal tissues? How many in each group? How were DCIS and normal tissues obtained?
4. Was survival information only available for 88 patients?
5. Was immunohistochemistry done without antigen retrieval?
6. Which anti-HER2 antibody was used?
7. The scoring system used is unclear: a) if MED28 shows both nuclear and cytoplasmic expression, why was only cytoplasmic expression used for analysis? b) what was the difference between 1 and 2 staining intensities? c) was 0 negative or weakly positive? d) By the percentage of glandular cells, do the authors mean tumor cells?

Results
1. The TMA consisted pf 242 surgical cases but survival analysis was only done on 88 patients and table 1 also shows the clinical and demographical charateristics for 88 patients. This should be specified in the text.
2. The expression pattern in the nuclear and cytoplasmic components was highly correlated - do the authors mean staining intensity? Did they score cytoplasmic and nuclear staining separately? Figure 1c, DCIS shows only cytoplasmic staining in some cells and both nuclear and cytoplasmic staining in other. Figure 1d, IDC is mostly nuclear-cytoplasmic, and the staining could have been scored as such.
3. Fig. 1 - What are the numbers on Fig. 1E - Normal (n = 136), DH(n = 39), DCIS (n = 92), IDC (n = 440), Metastasis (n = 110)? Fig. 1B appears to be columnar cell lesion.

4. Show MED28 expression in metastatic cancer.

5. MED28 expression in DCIS and IDC was app. 3-fold higher than either normal or DH levels - is this the comparison of staining intensity or the integrated value?

6. Was MED28 expression different between normal tissue and DH, between primary and metastatic carcinoma or between IDC and DCIS?

7. Did the authors have survival info for the 66 patients with recurrence data and vice versa?

8. Fig. 2A - sample size is 51 for MED28 expression <1.34 but Kaplan-Mayer plot only shows a few events.

9. Define early stage and late stage tumors.

10. Sample size is very small for late stage cases - 8 and 11, Fig. 3b.

11. Table 1 - it is unclear how low and high MED28 expression was defined.

12. How many cases were MED28 positive and how many were unscorable on the TMA?

Minor Essential Revisions

Abstract

1. The association of MED28 expression with clinicopathological variables rather than with histopathological subtypes was assessed.

Results

1. ’a significant predictor of death due to disease’ - may be better to use more specific term Disease-specific survival (DSS).

Discretionary Revisions

1. Lobular epithelium may be better term than glandular epithelium.

**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