Reviewer's report

Title: CD44 isoforms are heterogeneously expressed in breast cancer and correlate with tumor subtypes and cancer stem cell markers

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Reviewer: Dalil Hannani

Reviewer's report:

The objective with this article was to determine if the expression of alternatively spliced isoforms of CD44 correlates to breast tumor subtypes and patient overall survival.

In order to do that, Olsson and colleagues analyzed the expression of 4 alternatively spliced CD44 isoforms by qRT-PCR and exon-exon spanning assays in 187 breast tumors and 13 cell lines. This study revealed that each isoform is associated to a particular tumor cell type. Indeed, CD44s is predominant in both cancer stem cells (ALDH1+) and basal-like tumors, but not in CD44hiCD24low/-cells. Importantly, the isoforms studied in this paper are associated to the expression of hormone receptors and Her2. Patients can be clustered in 4 groups that have different clinical outcome.

This study is in line with previous reports showing that CD44s is associated with epithelial-to-mesenchymal transition and breast tumor progression (Brown et al, J Clin Invest 2011).

Minor Essential revision:

1- In the first paragraph of results, authors conclude that the concordance of CD44 expression (determined by Flow Cytometry) and mRNA expression (determined by qRT-PCR) is very good. However, in table1, Flow Cytometry results are expressed as % of positive cells instead of MFI. Also, some results are not in concordance since 79.6% MDA-MB-361 are positive for CD44 expression and the relative mRNA expression is 0.95 while 65.8% of HCC1428 are CD44+ with a relative mRNA expression of 8.96. Authors have to clarify this point.

2- Figure 2B illustrate the CD44 variants appearance under non-adherent conditions in JIMT-1. Did you perform the same experiment using the other cell lines? If yes, please clearly detail it in the text.

3- Authors must justify why they focused on the 3 isoforms described in this study, in addition of CD44s.

Discretionary revisions:

1- Paragraph titles can be improved by making sentences that summarize the data presented in each paragraph.
Level of interest: An article of importance in its field

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