Reviewer's report

Title: Hornerin, an S100 family protein, is functional in breast cells and aberrantly expressed in breast cancer

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Reviewer: Partha Roy Roy

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In this study, Fleming et al. examines the localization of hornerin, an S100 family protein in normal mammary and breast cancer cells. The main findings of this paper are:

1) hornerin is expressed in mammary epithelial, myoepithelial and stromal cells,
2) hornerin expression goes up during involution,
3) hornerin expression is lower in less aggressive breast cancer, and
4) hornerin expression is upregulated upon induction of apoptosis.

Overall, the expression data, particularly those involving differential regulation of post-translational fragment are interesting. However, a major weakness of this paper is its descriptive nature. Altered expression of hornerin correlated with malignancy is interesting but does not provide the evidence of a causal relationship between the two. The same criticism goes for apoptosis experiments. The paper will be much stronger if the authors report additional findings on the effects of knockdown and overexpression of hornerin on invasiveness and apoptosis of some of the cell lines.

Specific Comments

1) Fig 1C: From the bar graph on the right, it is not clear whether there is any statistically significant difference in 100 kD fragment between the different MCF10A sublines.

2) Fig 4D: If lower hornerin expression is correlated with less aggressive phenotype, why do lymph-node positive and higher grade tumors have lower hornerin expression than lymph-node negative and low grade tumors, respectively?

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