Reviewer's report

Title: The prognostic significance of Proline, glutamic acid, leucine rich protein 1 in triple-negative breast cancer: a retrospective study on 129 cases

Version: 2
Date: 14 April 2015
Reviewer: Julie Ostrander

Reviewer's report:

This study describes the analysis of 129 triple-negative breast cancers for PELP1 expression and clinicopathological variables. The authors found that PELP1 was expressed at moderate and high levels in all tissues, and that high PELP1 expression correlated with lymph node stage. Combining PELP1 expression with Ki-67 LI, the authors found that the double high population had reduced disease free survival and overall survival. This study adds to the body of work on PELP1 expression in breast cancer, specifically in the TNBC population and is suggestive that PELP1 expression in combination with Ki-67 could be used as a biomarker of aggressive TNBC.

Minor essential revisions.

1. The explanation for a lack of cytoplasmic PELP1 staining in the current study and the study by Habashy et al should be more comprehensive. The authors suggest that the studies of cytoplasmic functions of PELP1 are flawed because a cell line model expressing an NLS mutant of PELP1 has been utilized to study cytoplasmic functions. This explanation does not accurately represent the published data. There are a number of papers that show PELP1 IHC staining in the cytoplasm. It was the IHC results that lead to the in vitro studies. The PELP1 NLS mutant is a tool to study the signaling, not evidence that cytoplasmic PELP1 occurs in vivo. Alternatively, both the Bethyl laboratory and Novus Biologicals PELP1 IHC antibodies were raised to PELP1 amino acids 1000-1050, thus an alternate explanation could be that this epitope is masked when the protein is in the cytoplasm. It is recommended that the authors modify this section of the discussion to include alternate explanations for the discrepancy in the literature. Of note, most of the PELP1 interacting proteins that have a role in metastasis are cytoplasmic proteins (page 12, line 19).

2. The authors note that the limitation of the study is the small sample size. But is this study powered to observe differences in DFS and OS comparing PELP1 low vs. high groups?

3. There should be more about the similarities/differences between the Habashy et al study in the discussion.

4. page 4, line 6. "lacks" should be "lack"

5. page 6, line 5-7. Alternative version... "Twelve patients were excluded from the
study cohort due to gender (male), or acceptance of neo-adjuvant chemotherapy. The pathological slides of the remaining 147 patients were reviewed... 18 were excluded for discordance between the reviewers, leaving 129 patients in the study.

6. sliders should be slides.

7. Instead of writing "Habashy’s paper", in the manuscript by Habashy et al.

8. page 8, line 10. 38 of 129 is 29.4%

9. define Ki-67 LI.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**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'