Reviewer's report

Title: Prognostic impact of Proline-, glutamic acid- and leucine-rich protein 1 tumor expression in ovarian cancer

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Reviewer: Ansgar Brüning

Reviewer's report:

The authors have analyzed the expression of PELP1 and estrogen receptors in 63 tissue samples of ovarian cancer patients and came to the conclusion that coexpression of PELP1 and ERbeta is associated with a better prognosis for ovarian cancer patients.

Data analysis and presentation:

The authors show Kaplan-Meier curves of their “positive” results only. They should also show survival data of their other calculations and factors tested, at least for comparative reasons.

The quality and resolution of the IHC shown in Fig. 1 is impressive. It appears to be that the authors achieved a strong nucleolar staining in Fig. 1A but homogeneous nuclear staining in Fig. 1B (do Figs 1A and 1B really represent the same magnification?). The Vadlamudi group recently described nucleolar localization of PELP1 (Gonugunta VK, Nair BC, Rajhans R, Sareddy GR, Nair SS, Vadlamudi RK. Regulation of rDNA transcription by proto-oncogene PELP1. PLoS One. 2011;6(6):e21095). Since intranuclear distribution of PELP1 has been reported to be cell cycle-dependent [Vadlamudi group], it might be worthwhile to perform a subgroup analysis of nucleoplasmic vs. nuleolar PELP1-expressing tissue samples in relation to patients’ survival, because higher proliferation rates (Ki67!) are known to be associated with poor prognosis. Did the authors observe any cytoplasmic staining that might be involved in the non-genomic interaction of PELP1 with ERs? This could lead to a new sub-group to be differentially analyzed. Breast cancer cells for example have been shown to express a high percentage of cytoplasmic PELP1 [Kumar group].

It could further be of interest to have a closer look at the intranuclear PELP distribution by performing immunofluorescence on cultured ovarian cancer cell lines. Because the authors stress on the relevance of PELP1/ERbeta co-expression, a co-IF of PELP1 and ERbeta at various steps of the cell cycle may lead to further insights.

What is the expression level of PELP1 in non-malignant human ovarian surface epithelial (HOSE) cells, from which most of the epithelial ovarian cancer cells arise?

Discussion:
Expression of PELP1 in ovarian cancer has previously been studied [Dimple C, Nair SS, Rajhans R, Pitcheswara PR, Liu J, Balasenthil S, Le XF, Burow ME, Auersperg N, Tekmal RR, Broaddus RR, Vadlamudi RK. Role of PELP1/MNAR signaling in ovarian tumorigenesis. Cancer Res. 2008 Jun 15;68(12):4902-9 and Chakravarty D, Roy SS, Babu CR, Dandamudi R, Curiel TJ, Vivas-Mejia P, Lopez-Berestein G, Sood AK, Vadlamudi RK. Therapeutic targeting of PELP1 prevents ovarian cancer growth and metastasis. Clin Cancer Res. 2011 Apr 15;17(8):2250-9.]. These important contributions have been cited [ref.12 and13], but not really been discussed by the authors, in particular since they report contradictory results. PELP1 has been described as a “proto-oncogene”. The authors themselves mention this in their abstract and introduction. Accordingly, but in contrast to the data presented by the authors, PELP1 expression should be associated with poor prognosis. Therefore, there are still many open questions left, which should at least be discussed.

Interestingly, Grivas et al. [Grivas PD, Tzelepi V, Sotiropoulou-Bonikou G, Kefalopoulou Z, Papavassiliou AG, Kalofonos H. Expression of ERalpha, ERbeta and co-regulator PELP1/MNAR in colorectal cancer: prognostic significance and clinicopathologic correlations. Cell Oncol. 2009;31(3):235-47] recently published data on PELP1 in colorectal cancer which are similar to those obtained by the authors of the present study. Therefore, based on the similarity and—in part-supportive nature of the data, this reference could be included and discussed.

Minor points:

Title: If possible, the authors should mention PELP1 in the title in brackets after “proline-.....”, or use PELP1 directly in its abbreviated form. Then, they will probably notice that the word “tumor” might be superfluous.

Some language mistakes should be corrected, for example:

"...accounts for more death women.."

British or American English should be used consistently and some more hyphens, if appropriate, could be used.

**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.