Reviewer's report

Title: Suppression of the Epithelial-Mesenchymal Transition by SHARP1 Is Linked to the NOTCH1 Signaling Pathway in Metastasis of Endometrial Cancer

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Reviewer: Ivan Casaburi

Reviewer's report:

The study by Yun Liao et al. investigated the inhibitor role of SHARP1 on invasion, migration and metastasis processes in endometrial cancer EC by using two EC cell models such as Ishikawa and HEC-1B cell lines. In addition, the authors showed also that overexpression of SHARP1 affects NOTCH1 signaling interfering with Epithelial-Mesenchymal Transition in endometrial cancer cells. The in vitro findings are borne out also in IHC experiments performed in primary tumors and metastatic lymph-nods where the authors show a negative correlation between the expression of SHARP1 and E-Cadherin, a known membrane protein associated with an epithelial cell phenotype underlying SHARP1 as new biomarker to define the metastatic potential of EC.

Despite the experimental design is accurate and the results well-structured, there are some concerns regarding some of the results shown by the authors.

Major comments:

1. Fig 1B: it seems that after 24h, the cell density is greater in overexpressing SHARP1 samples compared to each controls and that cells of the migratory front edge do not show a spindle phenotype. Could the authors perform the same experiment using specific mitotic inhibitor or reducing the observation time right before the cell division?

2. Fig.2A. The picture illustrated by the author in the right panel does represent a real Ishikawa cells shape? or did the authors use some unreported experimental condition? Moreover, cell in this picture are quite different from that reported in Fig1 B (Ishikawa control).

3. The western blotting reported in Fig 1A (SHARP1 and beta-actin expression) are the same blots reported in Fig.2B. This is not scientifically fair. Please provide a new wb and specify in figure legends or methods section if membranes are stripped and reprobed with the reported antibodies.

4. Fig.3C IF for E-cadherin and Vimentin are not convincing. Please provide a better experimental results since from the illustrated pictures it is not possible to distinguished protein expression from the natural IF background, at least for E-Cadherin. For Vimentin pictures it seem that SHARP1 overexpressing cells are less than control but no survival analysis were performed. Moreover, why the IF does not reveal the presence of SHARP-1 protein since the plasmid does contain GFP.

Minor comment:
1. Please provide, if any, the protocol number of the approved animal study.
2. Please specify how the clones selection for SHARP1 overexpressing cells has been done?
3. Does SD come from one experiment or from all the experiment?
4. Please substitute “capacities” (results section: SHARP1 inhibits EC-cell migration………) with “capabilities”. English language should be improved all over the paper.
5. Please check your cell lines for mycoplasma contamination since DAPI staining it is not so clear.

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

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

**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