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: Pellegrino Michele

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Minor Essential revisions

In this work the authors evidence that the overexpression of SHARP1, is able to inhibit the migration, invasion and metastasis of human endometrial tumor cells.

Furthermore, it was reported that SHARP1 regulates the expression of proteins involved in EMT transition, such as E-cadherin, N-cadherin and Vimentin, through interference of NOTCH1 signaling. These results designate SHARP1 as a potential therapeutic target in the treatment of human endometrial cancer.

However endometrial cancer, an estrogen-responsive tumor, in several patients, is resistant to current drug therapies (for example tamoxifen), indicating an involvement of estrogen independent cellular components.

For this reason, it must be demonstrated if the mechanism through which the overexpression of SHARP1 suppresses the NOTCH1 signaling in EC cells, is independent from the estrogen receptor alpha expression, by using, for example, an estrogen receptor negative cell line.

In addition, the authors should evaluate in their in vitro experimental models, the expression of mRNA and protein levels of ERalpha and if its expression changes in the EMT transition.

In vivo histological studies reveal that, the overexpression of SHARP1 is able to reverse the lung metastases: but, did the authors observe metastases in other organs?

The authors show, by microscopic analysis, that the overexpression of SHARP1 is able to reverse in EC cells the EMT phenotype, through a change in cell morphology. It must be demonstrate that the morphological change is related to a new rearrangement of the cellular architecture. For this reason it is possible evaluate the cytoskeleton rearrangement by F-actin filaments expression study.

Finally, the authors should demonstrate in vivo model (xenograft) the ability of SHARP1 to interfere with the NOTCH1/EMT signaling. Therefore they should evaluate the expression of E-cadherin, N-cadherin, Vimentin and NOTCH1 signaling (Jagged1, HES1) by Western Blotting and RT-PCR analysis.

Level of interest: An article of importance in its field
Quality of written English: Acceptable

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'