Reviewer’s report

Title: Role of emmprin in endometrial cancer

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Reviewer: Katsutoshi Oda

Reviewer’s report:

In this paper, the authors report that expression of emmprin/CD147, extracellular matrix metalloproteinase inducer, was significantly higher in endometrial cancer specimens, and that knocking down emmprin in endometrial cancer cell lines was associated with cell proliferation, migration and invasion. Although the originality of the manuscript might be limited, their data are sound and well analyzed.

There are several concerns with the paper that should be addressed.

1. It is still uncertain whether high emmprin expression might be clinically useful to predict poor prognostic patients with endometrial cancer. First, they did not perform multivariate analysis. Second, they showed that high emmprin expression is associated with almost all the aggressive clinicopathologic factors, including advanced stage, high grade, lymph node metastasis and deep myometrial invasion. According to these findings, high emmprin expression might not be an independent poor prognostic factor, but might rather mirror the aggressiveness which can be easily diagnosed by pathologic findings. Third, the prognosis of high emmprin expression is still favorable. Although it correlates with various types of aggressive morphological findings, the 5 yr-overall survival rate is over 70%. It might be more precise to describe that “LOW emmprin expression might be a predictor of FAVORABLE prognosis”.

2. Although the authors described that emmprin expression is associated with EMT, they did not include any carcinosarcoma cases in this study. It should be important to see whether emmprin expression is increased in carcinosarcoma cases (and possibly non-endomtrioid adenocarcinomas as type II).

3. All their data are based on experiments with siRNA for emmprin. It would be more confirmative if exogenous emmprin expression was shown to induce phenotypes involved in migration, invasion and EMT. At least, they should refer other papers and discuss the phenotypes by the introduction of emmprin in cancers.

4. Although the expression of emmprin might be low in normal tissues, the low levels of expression might be still important in various organs. It should be addressed whether knock-out mouse of emmprin has been already analyzed.

5. They did not describe treatment protocols of the clinical samples. It should be also important whether the emmprin expression might be associated with
chemosensitivity (or radiosensitivity if provided).

6. They analyzed emmprin expression in five endometrial cell lines. However, the criteria of high emmprin expression in cell lines are not clear. How can they say that emmprin expression levels are high in HEC-50B and KLE cells without controls? It would be good to include appropriate controls for comparison, if possible.

7. This manuscript contains mainly in vitro studies, NOT in vivo studies. The description of the last paragraph in discussion (page 19, line 4) is not appropriate.

**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' below.