Reviewer's report

Title: Matrix metalloproteinase-10 promotes tumor progression through regulation of angiogenic and apoptotic pathways

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Reviewer: Jiunn-Liang Ko

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This is a well constructed manuscript on the relationship between MMP-10 and tumor progression. Collectively, this is a well paper with clearly presented results that may have considerable clinical impact. The authors demonstrate a correlation between MMP-10 expression and invasive cervical and bladder cancers, supporting a role for MMP-10 in human tumor progression. In their series of in vitro and in vivo experiments, MMP-10 activity was shown to be pivotal in the tumor growth in a mouse model of cancer, and the expression of this MMP is associated with the upregulation of key molecules related to angiogenesis, metastasis, and apoptosis, being very important in the clinical application. The in vitro and in vivo analyses are well designed and straightforward, and the results are clearly presented. The analysis of MMP-10 and tumor is compelling and clinically important. I suggest the article is acceptable with discretionary revisions. However, I still have some questions that should be address.

1. The spelling MMP-10 and MMP 10 should be in unanimity throughout the article.

2. Is a total MMP-10 staining score, which range from 0 to 6, obtained from proportion and intensity scores by addition or multiplication? This should be clearly stated in supplemental material.

3. In METHODS section, Cells and reagents part, Hela cell line is adenocarcinoma, is there any squamous cancer cell line such as SiHa or Ca Ski cancer cell lines tested? Additionally, is there any control cervical cell line such as immortalized keratinocyte Ect/E6E7 cells from American Type Tissue Culture Collection (ATCC; Rockville, MD, USA) tested? Why bladder cancer cell line was not tested?

4. In METHODS section, Gene transfection for stable cell lines part, it is better to show the MMP-10 cDNA cloned sequence even in the supplementary materials. The MMP-10 content of HeLa cells is low. So, only MMP-10 cDNA transfection but not MMP-10 knockdown was performed in the current study. It is better to describe this in manuscript.

5. In METHODS section, Transfection of small interfering RNA (siRNA) part, The MMP-10 content of UROtsa cells is high. Only MMP-10 knockdown but not MMP-10 cDNA transfection was performed in the current study. It is better to describe in text.
6. In RESULTS section, MMP-10 expression is upregulated in cancer tissues part, does histopathology type affect MMP-10 expression? Because HeLa cells are adenocarcinoma, what about squamous cell carcinoma? The results of adenocarcinoma can be applied to squamous cell carcinoma? Are there any correlation between MMP-10 expression and other clinicopathologic characteristics, such as tumor diameter, depth of stromal invasion or lymph node metastasis?

7. In RESULTS section, MMP-10 expression is upregulated in cancer tissues part, how did the authors define the invasive or non-invasive cervical tumor? On what classification was the invasion based on?

8. In RESULTS section, MMP-10 influences endothelial cell behavior part, in the current study, benign bladder cell line UROtsa is selected. Is there any difference found if bladder cancer cell line is selected, while exposing to conditioned media.

9. In Discussion section, 1st paragraph, how do the authors explain that MMP-10 positive staining localized to the nucleus in begin tissues, low-grade, NMIBC, while the MMP-10 staining seems to be predominantly cytoplasmic staining in high-grade and MIBC? are there any studies or references supporting this? They should be cited.

**Level of interest:** An article of outstanding merit and interest 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.