Reviewer's report

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

Version: 1 Date: 16 February 2014

Reviewer: Mathurose Ponglikitmongkol

Reviewer's report:

1. Is the question posed by the authors well defined?

Zhang Ge et al. have tried to correlate the mechanistic roles of matrix metalloproteinase 10 (MMP-10) to cancer progression and have used both in vitro and in vivo experiments to demonstrate the correlation between MMP-10 and the invasiveness and resistance to apoptosis in cervical and bladder cancers. The authors have shown the effects of MMP-10 over-expression and of MMP-10 ablation by siRNA on cell invasion/ migration in cervical cancer cell lines, HeLa and benign bladder cell lines, UROtsa, respectively. Further effects of MMP-10 on metastasis using in vitro PCR Arrays and also on angiogenesis and apoptosis using both in vitro and in vivo xenograft models were demonstrated only with HeLa cell lines. They concluded that the increase in MMP-10 expression is associated with up-regulation of key molecules involving in cell invasion, migration, angiogenesis and apoptosis and suggest that MMP-10 may be a novel biomarker or provide a molecular target for therapeutic intervention.

Although these findings provide useful information for cervical cancer research, I have a number of points that should be addressed before the manuscript is accepted (Please also see below). My comment is therefore “minor essential revisions”.

1. As the background on MMP-10 study in cervical cancer is missing (Please see no.7), the question is not so clear why they are interested in looking at MMP-10 in cervical cancers.

2. To show the effect of MMP-10 on apoptosis, the data in the absence of the apoptosis inducing agent, staurosporine, is missing (already mentioned in the first paragraph of results under the heading of “MMP-10 influences apoptosis”). The x bar in Figure 5 indicated the effects of staurosporine at 0 hr not in the absence of it.

2. Are the methods appropriate and well described?

Mostly yes. The reference for endothelial cell tube formation assay should be added.

3. Are the data sound?
Yes.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
   Yes.

5. Are the discussion and conclusions well balanced and adequately supported by the data?
   We see the correlation between MMP-10 and the mechanistic changes in angiogenesis and apoptosis pathways leading to tumor progression from your results but we do not see much from your discussion. Please elaborate more on possible mechanisms that MMP-10 regulates angiogenesis and apoptosis. This should support the meaning of the title.
   The authors might also speculate why invasion results was not clearly observed in bladder cells.

6. Are limitations of the work clearly stated?
   Yes. The author stated that the subcutaneous xenograft model that they used did not readily become invasive or metastasize, therefore the factors related to MMP-10 in this model could not be assessed.

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
   The authors should mention about previous studies on MMP-10 in cervical cancers for examples, A.D. Santin et al Virology 331 (2005) 269-291 and G. Vazquez-Ortiz et al Archives of Medical Research 36 (2005) 448-458. Vazquez-Ortiz et al reported that overexpression of MMP-10 was observed only in HPV positive cervical tissues.

8. Do the title and abstract accurately convey what has been found?
   The title might be too general. Most of the experiments (both in vitro + in vivo) were performed in HeLa cervical cell lines. No data of MMP-10 expression on apoptosis profile or on xenograft was shown in bladder cell line. It is therefore recommended that the title specify the effect of MMP-10 on cervical cancer cells.

9. Is the writing acceptable?
   Yes, however, to prevent confusion and to make it easier to follow the minor changes should be made as follow:
   1. The word “normal” cervical tissue in Figure 1 (also in results) should be changed to benign cervical tissue. Types of tissues shown in the text and in the figure should be written in consistency.
   2. The heading “Membrane Potential Analysis” in “Methods” should be changed to “Mitochondrial Membrane Potential Analysis”.
   3. Where is caspase 9 in Figure 5? Please make sure that the results under the
heading of “MMP-10 influences apoptosis” correspond well with the figure and the Legend and please correct if this is due to the typo-errors.

4. There is a typo-error in the address of author #4.