Reviewer’s report

Title: Metalloproteases meprin-α (MEP1A) is a prognostic biomarker and promotes proliferation and invasion of colorectal cancer

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Reviewer: Margaret Jane Currie

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Metalloproteases meprin-α (MEP1A) is a prognostic biomarker and promotes proliferation and invasion of colorectal cancer.

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General Comments

In this manuscript the authors investigated the role of the metalloprotease MEP1A in colorectal cancer. Using patient CRC samples, they demonstrated that MEP1A was more highly expressed in tumor versus normal mucosa samples. Moreover, high levels of MEP1A were associated with worse overall survival. The authors knocked down MEP1A expression using shRNA and showed loss of CRC cell proliferation and invasion in vitro, and decreased xenograft tumor growth rates in vivo.

In general, the manuscript is well written with good English, sufficient background information, well-described methods, clear ethical statements, and nicely presented and discussed results. I have listed a few minor corrections for consideration below.

Minor Corrections

Abstract

Page 2 Line 9: The first sentence in the methods section is clumsy and could do with rewriting.
P2 L15: It would be good to state the method of 'dampening'. For example, 'shRNA was used to knockdown MEP1A expression…'

P2 L27: Suggest change to 'Several parameters were associated with enhanced MEP1A expression including…'

P2 L40: Suggest change to 'and as a therapeutic target…'

Introduction

P3 L11: Suggest change to 'in CRC development and progression…'

P3 L52-54: Provide reference(s) and correct 'Additionally, human prostate cancer cell models also express MEP1A, where it promotes cellular replication and invasiveness (delete 'in these cells').'

Methods

P4 L19: Please clarify the number of CRC patients. N=36 here. Then n=40 on P5 L37.

P4 L29-32: Suggest change to 'Two pathologists confirmed the diagnoses and performed tumor staging according to the guidelines of the…'

P6 L1: Suggest change to 'protocol used the following conditions:…'

P7 L42: Correct 'describede'.

Results

P10 L1-2: Rewrite 'The mean MEP1A mRNA expression found in tumor tissue specimens and in paired adjacent normal mucosal specimens was significant'. State how it was significantly different.

P10 L13: Correct 'suggests'.

P10 L29: Provide p values for PCNA and Ki-67 mRNA expression differences.
P10 L46: Clarify that migration and invasion assays were only performed in LoVo cells. Either change the subtitle to 'Decreased LoVo cell migration...' or change the first sentence to '..., scratch and migration invasion assays were performed using LoVo cells (Figure 4A and B).'

P11 L27-39: Move Table 1 and 2 under the subheading 'Correlation between MEP1A overexpression and clinicopathological factors in CRC'.

P12 L15: Delete 'Table 3 (in page 21)'.

P12 L35: Which factors were taken into account by the multivariate analysis?

Discussion

P12 L52: Delete the first 'both' in 'both expression of both MEP1a..' 

Figures and Legends

Expand Table 1 Legend to state that these are the n=88 patient samples on the Tissue Microarray.

Figure 1. Correct 'Graycale' on Y axes.

Figure 5B. Use 'Cumulative Survival' on Y axis.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes
Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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