**Reviewer’s report**

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

**Version:** 1  **Date:** 20 Jan 2016

**Reviewer:** Marcus Hollenbach

**Reviewer's report:**

Comments to the authors:

The aim of this study by Wang et al was to determine the role of metalloprotease meprin-alpha (MEP1A) as prognostic biomarker, in proliferation and invasion of colorectal cancer (CRC). In this study MEP1A was overexpressed in CRC in mRNA and protein levels and high MEP1A expression was associated with poor survival, tumor size, nodal and AJCC tumor stage. Furthermore MEP1A silencing resulted in reduced cell proliferation and invasiveness. The authors conclude a promising role for MEP1A expression as a prognostic biomarker and therapeutic target in CRC.

This work has several limitations. Before considering this article for publication in "BMC Cancer", important findings should be clarified.

**Major comments**

The quality of written English is insufficient. A complete grammatical and orthographical revision of the manuscript is recommended. In this way some statements and descriptions in material/methods and results section are very difficult to follow when reading the manuscript the first time.

The authors compared mRNA and protein reexpression of MEP1A in 36 CRC patients with paired normal controls. In my understanding this cohort is different from the 88 CRC patients which were analyzed in high and low MEP1A expression group and correlated with clinical scores and...
survival (and this group had no control cohort!). Why did the authors study a second group of CRC patients? Which criteria were used for matching with healthy controls (age and gender?)? For this cohort clinical data (tumor growth, N and M stage and differentiation) are needed since the authors conclude a positive correlation for these parameters in the 88 CRC patients group.

This issue with 2 different cohorts is very confusing and difficult to understand and must be clarified. Maybe it would be helpful to rearrange the material/methods and results section.

Furthermore it would be interesting if it is possible to determine a cutoff for the MEP1A mRNA expression.

As mentioned by the authors, only patients who had undergone tumor resection without chemotherapy or radiotherapy were included in this study. This important point might be a potential selection bias. Further data regarding patients with advanced and palliative disease should be included to correlation and survival analysis. Otherwise this limitation has to be clearly stated in the discussion which completely is lacking limitations of this study.

The laboratory results regarding effect of MEP1A attenuation to proliferation and invasion in vitro and in vivo are promising. To my point of view the results of the authors would be strengthen by another experimental setting regarding MEP1A silencing and overexpression. In this way overexpression of MEP1A should lead to elevated proliferation, invasion and migration compared to control. Alternatively, the authors could compare Caco2 or LoVA cells (high MEP1A expression) with NCM460 cells (low MEP1A expression). These analyses would further support the findings of the authors.

In vitro analyses regarding E-cadherin silencing and overexpression could lead to further insights relating to clinical findings of MEP1A/E-cadherin association.
Minor comments

The abstract section of p2 is not congruent with title page, especially results paragraph is very different and therefore confusing.

The third paragraph of introduction has no relation to the rest of the manuscript and is dispensable to my point of view.

In materials and methods cell culture is described without antibiotics. Were P/S used for cell culturing?

I hope my critics are helpful to enhance the quality of this manuscript

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

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I am able to assess the statistics
Quality of written English
Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

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