Reviewer's report

Title: MMP28 (epilysin) as a novel promoter of invasion and metastasis in gastric cancer

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Reviewer: Barbara Fingleton

Reviewer's report:

The article by Jian et al focuses on the protease MMP28 in gastric cancer. The authors initially looked for genes associated with invasive potential in a gastric cancer cell line, and discovered MMP28 based on a microarray. They subsequently examined expression in a relatively large group of gastric cancer patient samples and were able to show reduced survival correlated with MMP28 expression. Returning to cell lines, they demonstrated that ectopic expression of MMP28 could promote invasive behavior in vitro and more aggressive tumors in vivo, culminating in enhanced metastasis. These data definitely expand the available information regarding MMP28, which is relatively understudied compared to other proteases.

Major Compulsory Revisions

There are three areas that require more information.

(1) The authors need to describe the microarray - for example, was this a targeted array?

(2) The data shown in Fig 3B suggest an increased growth rate for the MMP28-expressing tumors. This is a different phenotype to the enhanced invasive ability that is the focus of the paper. There is no discussion regarding this effect. The authors should at very least discuss this phenotype. Performing some staining for a proliferation marker such as Ki67 within the xenograft tumor specimens could provide confirmation that MMP28 is associated with enhanced growth.

(3) Although enhanced metastasis is described in the text, there is no data to support this suggestion. Authors should include a graph or table indicating number and/or size of metastatic nodules to support their claim.

Minor Essential Revisions

(1) In the Background section 2nd paragraph, line 15, a sentence begins "This type of role for MMP28....". It is unclear what "This" refers to, and the authors should clarify.

(2) Data in Figure 3A and description of matrigel chemoinvasion assay in methods state use of t-test. This is not suitable when greater than 2 groups are being compared, and the authors should use ANOVA with a post-hoc test for analysis.
Minor Issues not for Publication

Fig 1A - axis label on graph has misspelling of 'invasive'

In the methods for semiquantitative RT-PCR, it is stated that expected sizes of PCR products are given but they are missing.

In the methods for matrigel chemoinvasion, need to superscript number for cell count

In Results, 2nd paragraph - delete "a" from first line after title, i.e. "....expression of MMP28 in [a] gastric carcinoma tissue....."

In Results, 2nd paragraph, 5th line after title, change high to higher, i.e. "...also showed highER MMP28 expression..."

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I have received funding for testing of MMP-inhibitory drugs from Dyax Corp. However, these did not target MMP28.

Otherwise, I have no competing interests.