Reviewer's report

Title: Imbalance of tissue inhibitors of metalloproteinases (TIMP) - 1 and - 4 serum levels, in patients with inflammatory bowel disease

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Reviewer: andrew S Day

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The manuscript by Kapsoritakis and co-authors reports on the patterns of three tissue inhibitors of metalloproteinases (TIMPs) in patients with IBD.

General Comment:
Understanding the complex interactions involved in the pathogenesis of IBD is important in working towards improved managements and ultimately a cure for this chronic condition. The proteins of focus in this manuscript may contribute to complications of gut inflammation (such as tissue remodelling/fibrosis) and also potentially to aspects of the pathogenesis of the gut inflammation itself. This study provides some further insight into the patterns of these proteins, and hints at the potential relevance of them.

Specific Comments:

1. The manuscripts mainly reports the details of TIMP-1 and TIMP-4 levels in these patients with CD and UC. TIMP-2 levels are mentioned in the Methods and Results, but not mentioned at all in the abstract.

2. The Results of TIMP-1 and -4 measurements suggest an imbalance between these proteins: would the expression as a ratio of these two proteins be more helpful to represent this better?

3. The authors show the correlations between the two TIMP proteins and disease activity and standard inflammatory markers. It is intriguing that although TIMP-1 increases with greater disease activity, TIMP-4 does not bear any relationship to disease activity.

4. Furthermore, despite the above relationships, both proteins correlate positively with the two chosen standard markers of inflammation. This seems incongruous, as TIMP-4 levels are less in IBD than in healthy controls.

5. The Background section has large amounts of data and information with no reference to the published literature. This should be amended and appropriate references added.

6. The last sentence of the Introduction suggests that this report will highlight the key mechanisms of these proteins in IBD, but no mechanistic data is presented.

7. The data is reported as mean ± SEM: why is this chosen rather than SD?

8. Further, after advising that all data will be presented in this manner (Statistical
analysis, Page 7), this is repeated many times in the results (e.g. page 9). This is not necessary.

9. In the Discussion (page 10), it is stated that TIMP-1 has a role in the recruitment of inflammatory cells (implying that it leads to recruitment). However, the opposite is subsequently stated. This should be clarified or rewritten to ensure that there is no confusion.

10. The Discussion (page 11) discusses the potential imbalance between MMP and TIMP proteins: suggestions are made here that are not supported by the data presented in this report.

11. The first sentence on page 12 needs to be revised. Similarly, the first sentence of paragraph 2 on this page also needs correction.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

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 declare that I have no competing interests'