Reviewer's report

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

Version: 1 Date: 22 March 2008

Reviewer: Klaus Fellermann

Reviewer's report:

Major compulsory revisions

The submitted manuscript presents serum levels of TIMP1, 2 and 4 in inflammatory bowel disease. Sera from more than 150 patients were investigated. TIMP1 showed a marked increase during inflammation whereas TIMP2 was almost unchanged. Conversely, serum TIMP4 was downregulated during the inflammatory process.

TIMP’s are inhibitors of MMP’s and an imbalance of this system may favor ECM degradation. It is of crucial importance whether this occurs at the tissue or systemic level. What is the meaning of systemic TIMP levels in inflammatory bowel disease at all? Do TIMP’s originate from blood cells or rather reflect a spillover from local inflammation into sera. This is open to question and the report does not provide an answer.

Mucosal TIMP1 has been shown to be correlated with proinflammatory cytokine responses as well as endoscopic grading in inflammatory bowel disease. On the other hand TIMP2 is known to be constitutive and no change has been demonstrated in mucosal biopsies from inflammatory bowel disease compared to controls. In both situations the ratio of TIMP/MMP may be affected in the same manner if the corresponding MMP levels do increase. Thus, serum levels of TIMP with unknown MMP levels are of limited value. I am concerned and critically recommend a consecutive determination of serum MMP’s (e.g. MMP-1, 2 and 9) in the same set of patients. This will help to clarify this issue.

However, the observations of TIMP1 and 2 are in line with previous reports while the findings regarding TIMP4 are novel.

Nevertheless, the paper is well written and concise.

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

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

Quality of written English: Acceptable
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