Reviewer's report

Title: In situ pepsinogen I production and stepwise progression from normal mucosa, superficial gastritis, atrophic gastritis to gastric cancer

Version: 1 Date: 7 January 2013

Reviewer: Thomas Wex

Reviewer's report:

The study targets a question that is clinically important, but there are numerous studies published in this field already. The main aim of the study remains somehow unclear. The title refers to the “in situ production” of pepsinogen I in context to the stepwise progression towards gastric cancer (according to the Correa cascade).

There are several issues that need to be addressed by the authors.

Major issues:
- It is well known that pepsinogen I (Pep I) is secreted by corpus mucosa, and that the presence of atrophic gastritis with/without intestinal metaplasia reflects a loss of parietal and chief cells. Naturally, if there are less cells producing PepI, there should be less intensive staining of the mucosa. The authors do not address the question whether the existing chief cells in the corpus mucosa express different amounts of PepI (based on the individual cell type). The current findings of this manuscript do not add significantly new knowledge to this field.
- The definition of an overexpression (IRS >6) is arbitrary and does not reflect the in vivo situation. As mentioned above, the PepI expression level/rate needs to be based on the numbers of PepI-secreting cells.
- What is the purpose of the face-to-face interview mentioned on page 5 in relation to this manuscript?
- Staining of PepI by an antibody provided from someone else needs to be described in more detail and supported by previous publications in which the same antibody was used already.
- How the positive and negative H. pylori status was defined (page 8, based on histology or serology or both?) Based on data from Table 1, H. pylori-positive rates were 41.4% (SG), 50% AG, and 38.7% (GC). This numbers seem very low considering the well-known association of H.pylori infection (here analyzed by IgG levels) with gastric tumorgenesis.
- Primary data of serum-based PepI levels needs to be shown.
- Final conclusion (analysis of in situ PepI expression rate could help …) is not supported by data from this study.

Minor issues:
- Please use xg instead of rpm for centrifugation (page 7)
- Check for typos e.g. -20°C; absent instead of absence (page 5); gastriyis (page 20).
- Stay consistent with SG /GS for the superficial gastritis group (see Table 3, Table 1 and text)

**Level of interest:** An article of limited interest

**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'