Reviewer's report

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

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Reviewer: Keitaro Matsuo

Reviewer's report:

Li et al. conducted a cross-sectional evaluation of in situ PGI expression according to various levels of gastric mucosa. They found significant difference in PGI expression across normal, superficial gastritis, atrophic gastritis, and gastric cancer. PGI expression reduces as its progress of malignant transformation. Although the question authors challenged is interesting, there remains several points to be considered.

Major points:
1. Background characteristics of subjects examined should be presented because it may influence comparability of each group such as age and sex distribution, helicobacter infection status, serum PG I/II and smoking status. The result presented in table 2 is not good enough to convince people in this point. For comparison across groups, considering these different characteristics in the analysis such as multinominal logistic regression as necessarily is of interest to see robustness of their finding.

2. For table 2, they concluded no difference across based on p-values less than 0.05. However, taken small number of subjects in mind, it is difficult to conclude. More conservative interpretation is recommended.

3. It is of interest to see PG II expression in these subjects. As noted by the authors, PGI levels coupled with PGI/II is commonly used indicator for gastric mucosa atrophy. Therefore, it is very questionable why authors did not see it within the study.

4. In the figures, authors described different expression of PGI across site of mucosa in the stomach. It is very questionable which sites to be evaluated in each individual. If mucosa in each site from all the subjects were evaluated comprehensively, result should be presented as it was. If site of mucosa differ across subjects, it should be presented in the baseline characteristics. Without clarification of this, it is difficult to conclude as authors did. For gastric cancer patients, mucosa of actual cancer site was examined or mucosa around the cancer was examined?

5. It is of interest that authors found lack of correlation between serum PGI levels and PGI expression. It is of interest to have a box and whisker plot for that showing serum PGI levels according to histological PGI levels or a scatter plot.
showing correlation between IRS scores and PGI levels to have overview about correlation.

6. In discussion, authors noted discrepancy in grading/recognition of atrophic gastritis between those from endoscopy and from microscopy. In this study, it is rather unclear how authors categorized subjects into four groups.

Minor points:
1. Expression and production should be distinguished. They evaluated expression rather than production. Title should be changed.

2. The statistical testing they applied was chi-squared test. Taken small subjects in the analysis especially in the subgroup analysis, Fisher's exact test seems more appropriate.

**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:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.