Reviewer’s report

Title: Selenoprotein S (SEPS1) gene -105G>A promoter polymorphism influences the susceptibility of Japanese to gastric cancer

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Reviewer: caspar grond-ginsbach

Reviewer’s report:

This manuscript presents the findings of a genetic association study with case/control design. A known promoter polymorphism (rs28665122) of candidate gene SEPS1 was genotyped in 268 Japanese patients with gastric cancer (GC) and in 306 Japanese control patients from the same center. The A-allele of the promoter polymorphism was found more frequently in GC patients than in control subjects, but the difference was not significant. However, in some subgroups of patients (patients with intestinal type of GC, patients with tumors located in the middle third) the A-allele of rs28665122 was significantly more frequently than in the control series. This observation suggests, as the authors express in the title of their study, that the SEPS1 promoter polymorphism influences the susceptibility of Japanese to gastric cancer.

This is an interesting study of a gene, that was only recently described as pro-inflammatory, and that is an interesting candidate for the study of inflammation and cancer development in relation with Helicobacter pylori.

Major compulsory revisions

1. The authors did not compare a study group of GC patients with a study group of healthy normal subjects, but analyzed two different patient groups: patients with GC and patients without GC, but with other disease of the digestive system that are also associated with Helicobacter pylori infections (gastric ulcer, duodenal ulcer or gastritis). The conclusion of the study therefore must be that the SEPS1 promoter variant is associated with some differences between GC and gastritis or other infectious diseases of the stomach. The suggestion of the authors that the genetic variant of SEPS1 is related to the risk for GC in the Japanese population requires the analysis of a control group from the healthy population. The authors must either recruit a third study group of healthy control subjects or they must change the interpretation of the results of their study and consider the role of SEPS1 in two study groups, both Helicobacter pylori positive, with different diseases of the stomach.

2. The recruitment of the study populations must be described in more detail. Was the series of patients consecutive? Which were exclusion criteria?

3. The test results in Table 4 reach for some of the different subgroups of patients nominal p-values <0.05. However, the authors did not use any correction for multiple testing. The data are interesting and promising, but their preliminary
nature should be underlined.

Minor Essential Revisions
1. The language needs editing.

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

**Quality of written English:** Not suitable for publication unless extensively edited

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

**Declaration of competing interests:**

I declare that I have no competing interests.

Caspar Grond-Ginsbach