Reviewer's report

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

Version: 2 Date: 4 October 2008

Reviewer: Charles Foster

Overview: This study tests the hypothesis that a polymorphism in the gene selenoprotein S, enhances the pro-inflammatory cytokine response and modulates the risk for progressing from H. pylori induced gastritis to gastric cancer. The G-105A polymorphism was typed in 268 men with gastric cancer and 306 controls. The major finding was that in patients with Lauren's Intestinal type cancer GG homozygotes were over represented (OR 1.99, p = 0.047). The authors conclude that these data support the hypothesis that selenoprotein S polymorphisms may modify the risk of Intestinal type gastric cancer.

Major Compulsory Revisions:
1) The statistical analysis should include a discussion of whether the data is in Hardy-Weinberg Equilibrium.
2) The discussion should comment on whether selenium status is known to influence susceptibility to H. pylori, gastritis, or gastric cancer. Is it known whether selenium deficiency is common in your population?
3) Cigarette smoke exposure is known to modify the risk of colon and prostate cancer in selenium deficient patients. Were patients asked about smoking status? Does smoking modify the strength of the association?
4) In rats selenium deficiency induces eosinophilic enteritis (Hong CB. Exp Mol Pathol. 1988 Apr;48(2):182-92.); does the polymorphism correlate with the degree of eosinophilia on gastric biopsies?

Minor Essential Revisions:
1) There are quite a few awkward phrases throughtout the manuscript. A native English speaking scientific editor should be consulted to assist with revisions. For example: "Selenoprotein S is the molecule related with the control of inflammatory response in Endoplasmic reticulum." This might be re-written as "Selenoprotein S is an Endoplasmic reticulum localized protein that may control inflammatory response." AND "It is suggested this SEPS1 polymorphism possibly associated with the process of chronic gastric inflammation to carcinogenesis." This could be re-written as "Since polymorphisms in SEPS1 influence inflammatory cytokine response, it is possible that the G-105A polymorphism influences progression from chronic gastric inflammation to gastric cancer."

2) In the discussion, the authors say that the results of previous association
studies exploring the role of the G-105A polymorphism in chronic inflammatory disease are controversial. Without further elaboration, it is not clear to the reader why these results are controversial.

Discretionary Revisions:
1) If tissue is available, it would be most interesting to directly determine whether the polymorphism correlates with tissue mRNA or protein levels of pro-inflammatory cytokines such as IL-1β.

**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:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.