Reviewer’s report

Title: Genetic risk factors for intestinal metaplasia in a high risk Singapore-Chinese population: a cohort study

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Reviewer: charles S rabkin

Reviewer’s report:

This manuscript examines the relationship between certain polymorphisms in candidate genes and intestinal metaplasia in a Singapore-Chinese population. Significant associations are detected between intestinal metaplasia and the three polymorphisms examined. The manuscript is well written and commendably concise. The findings are of interest, but any conclusions should be tempered by the small sample size.

Major Compulsory Revisions
None.

Discretionary Revisions

1. It is laudable that the authors did a systematic literature review to select the studied SNPs. Readers would benefit from detailed information provided in a summary table (maybe as a supplemental material). The additional table would list the 18 candidate genes/SNPs found to be significantly associated with the risk of gastric cancer, and the following: study design, sample size, ethnicity of participants, and risk estimates of the studies should be included, if available.

2. Description of genotyping methods should include quality control procedures (i.e. genotyping success rate, reproducibility).

3. If data are available, authors should discuss their allele frequencies against other published data involving Singapore-Chinese populations.

Minor Essential Revisions

1. Given the study design (cross-sectional), the word “risk” should be avoided and the title of the manuscript modified. Furthermore, information on the study design of the cohort study from which these subjects were selected should be provided. Criteria of inclusion, and recruitment time period should be clearly stated.

2. Additional information on Helicoblot assay must be provided. It is not clear how the test was interpreted, and what determines a positive status. The lack of this information prevents this reviewer of fully evaluating the analytic approach of the study.

3. Results of multivariate analysis (Table 4) suggested that H. pylori status is an effect modifier of the association between the presence of IM and PTPN11
(GA/AA vs. GG). Please provide evidence of the statistical significance of this interaction.

4. Authors should mention the guidelines used to classify the gastric lesions. Please specify if the following classifications were used.


5. The IM negative group should be fully described in terms of gastric pathology (i.e. number of subjects with atrophic and non-atrophic gastritis). Were there any subjects with gastric dysplasia? If so, please indicate how those were handled in the analysis.

6. Authors should mention genetic models (i.e. dominant, recessive or codominant) used to guide data analyses.

7. How were “drinker” and “smoker” defined?

8. It is apparent from Table 3 that there were fewer than 374 subjects successfully genotyped for all the SNPs. Please explain reasons for incomplete genotyping data.

9. Absolute numbers rather than frequencies are presented in Table 3. Please alter the title to reflect the results more accurately. Given the uncertainty of the genetic models, it will be useful to present the three genotypes of each locus. In addition, rs numbers should be included.

10. Given the large number of SNPs examined, a p-value of <0.05 may be inappropriate. Authors should discuss the problem of using multiple comparisons.

11. Reference #3 is incomplete.

**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:**

Reviewed with Dr. M. Constanza Camargo.

We declare that we have no competing interests.