Reviewer’s report

Title: Association between H-RAS T81C genetic polymorphism and gastrointestinal cancer risk: a population based case-control study in China

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Reviewer: Jae Yong Park

Reviewer’s report:

General Comments: The authors investigated the potential association of the SNP T81C of HRAS gene with risk of gastrointestinal cancer. This study is basically sound, but is not well designed study. Several major concerns need to be addressed.

Specific comments:

1. A major concern is the selection of cases and controls. 1) In the selection of cases: this study included patients who had survived up to May 2005. Therefore, there is a possibility that only the patients with good prognosis or early stage of cancer may be selected (selection bias). That is, the case population is not truly representative of whole gastrointestinal cancer in the population studied. The HRAS SNP may have an influence on disease progression and/or prognosis, thus the genotype distributions between cancer patients with early stage of disease and those with late stage disease, as well as patients with good prognosis and those with poor prognosis. 2) In selection of controls: Author should explain eligible criteria for the selection of controls. It should be answered to the following concerns: how to match the controls to the cases; and is the prevalence of smoker among the controls (40.0%) comparable to that of authors’ country. - I am impressed with low prevalence of smoking particularly in the control after consideration of the low prevalence of smoking in Chinese women). Would you present the prevalence of smoking (or the trends in smoking habit) in China? 3) It is uncertain why the demographics of stomach cancer cases are statistically different from other cancers and controls (age and smoking rates) – Are these true in the authors’ population. In order to understand these points, the authors would provide the epidemiologic characteristics of gastrointestinal cancers in authors’ population.

2. The authors should be described the potential mechanism(s) for the tumor origin-specific association (The HRAS SNP was associated with gastric cancer; however, it was not significantly associated with colorectal cancer) in the Discussion section.

3. It would be explained why the colon cancer was divided into colon and rectum cancers. Are there differences in the etiology and pathogenesis between colon and rectum cancers?

4. P-values should be provided in Tables.

5. The rs number and reference sequence of the polymorphism should be
6. The results would be shortened.

**Level of interest**: An article of importance in its field

**Quality of written English**: Needs some language corrections before being published

**Statistical review**: Yes, but I do not feel adequately qualified to assess the statistics.