Reviewer’s report

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

Version: 1  Date: 24 April 2008

Reviewer: Hongbing B Shen

Reviewer’s report:

General comments:
The manuscript of Zhang et al described the H-RAS T81C genotypes and their associations with gastrointestinal cancers in a Chinese population. The authors showed that C allele was significantly increased the risk of gastric cancer when compared with wild type homozygote, but the effect was not observed in colorectal cancer. Though the results in gastric cancer was interesting, the small sample size and some drawbacks in the study design (e.g. absence of Helicobacter pylori infection information, no considerations for other SNPs in linkage with T81C and effects from confounding factors because of unmatched age or gender) may reduce the credibility of the results, which need to be in caution when the authors conclude their findings.

Specific comments:
1. Page 3, line 2, the authors described that the CC genotype was with more risk, which was not appropriate, because the adjusted ORs were 3.67 and 3.29 for TC and CC genotype, respectively.
2. In this study, the cases and controls were not matched by age and gender and they were significantly different between gastric cancer cases and healthy controls. The gastric cancer cases were older and more men than their controls. Therefore, the authors need to describe more details of their study design and exclude the confounding effects of age and gender on the association between genotypes and gastric cancer risk. It was better to perform stratified analysis according to variables shown in Table 1 (age, gender, smoking, drinking and family history ) though the sample size was small. In addition, the interaction effect was not directly estimated from stratified analysis (see Page 9, paragraph 2.).
3. The authors needed to present the definitions of smoking, drinking and family history.
4. Please add the note for adjusting factors in Table 2. In addition, family history should be included.
5. In the meta analysis, another 254 controls from hospital in Johne's study were cancer-free and needed to be included in the meta analysis. Furthermore, the authors should not divide their study into two comparisons because those two case groups shared one control group.
6. The risk effect of variant allele found in gastric cancer was not detected in colorectal cancer, so the eligible explanation was needed in the discussion.

7. Add the rs no. of T81S in the article.

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

**Quality of written English:** Acceptable

**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.