Glutathione S-Transferase P1 (GSTP1) Gene Polymorphism Increases Age-Related Susceptibility of Hepatocellular Carcinoma

This study analyzes the effect of two common SNPs in GSTP1 and GSTA1 Genes with regard to hepatocellular carcinoma (HCC) risk in 102 patients and 386 control subjects.

Although the study has some merit, a deep review is required before the manuscript can be accepted.

Compulsory revisions:

In the first place, it should be stated clearly what this study adds to the present knowledge. Authors mention that only two previous studies addressed this problem, although actually at least another one did it (Pharmacogenomics 2007 8(8), 895-899), but they argue that this study is important because “no study has been investigated the association between these two gene polymorphisms and hepatocellular carcinoma in Taiwanese”. Authors should explain why results obtained in Taiwanese subjects might be different of those obtained in other oriental populations, and specifically whether a different genetic background, diet or environmental factors or other risk factors for HCC are present in Taiwan but not in other regions.

The manuscript is too long and it has too many references. In addition, some sentences and arguments are repeated in the introduction and in the discussion section.

Writing is careless. Some sentences make no sense (for instance in page 5 “Since liver is the major organ of metabolizing endogenous and exogenous toxicant [32, 33].”) and many words are misspelled (for instance in page 5, polymorphisms). Please revise the text carefully and seek the advice of a native English speaker.

Specific comments for compulsory revisions:

Abstract: In the sentence “However, in the younger group, age # 56 years old, the individuals with GG alleles of GSTP1 had 11.68 fold risk (95% CI: 1.4-94.9) of inducing hepatocellular carcinoma …”, the adjusted P value should be included here and in the results section.
If, as expected, the P value is not significant after multiple comparison analysis, the last sentence in the abstract (and throughout the text) should be modified. The conclusion cannot be that “GG alleles of GSTP1 gene polymorphism is considered as a factor…” if the P value is not statistically significant.

Introduction:
The sentence “To our knowledge, only two papers and one papers have been investigated the roles of GSTP1 [34, 35] and GSTA1 [34] gene polymorphisms, respectively, on HCC susceptibility” is wrong. Please include and comment all relevant literature on the topic.
The introduction is too long. It can be reduced to one and a half page without loss of relevant information.

Methods:
The statistical power of the study, calculated on the basis of the number of participants, allele frequencies and an expected OR of at least 2.0 (alpha 0.05) should be included. In the statistical analysis it should be specified how the results were adjusted for multiple comparison testing.

Results:
Authors should explain how the differences in age between patients and controls may bias the findings.

Page 10, Authors should explain how they calculated the adjusted Odds Ratio (AOR).

Discussion:
The sentence “However, GG allele polymorphism of GSTP1 was significantly associated with age-related susceptibility of hepatocellular carcinoma. In the younger group, age # 56 years old, individuals with GG alleles of GSTP1 had 11.68 fold risk (95% CI: 1.4-94.9) of inducing hepatocellular carcinoma” should be modified. The P values and the statistical power for the comparison should be added here or under Results.

Page 17: Conclusion. Unless a statistically significant P value with a statistical power over 80% is obtained for this comparison, the sentence should be reformulated.
The discussion section should be reduced to about one half of its size. Authors should comment their findings, put them into context with other studies and obtain overall conclusions and clinical implications.

Table 1: P values should be included.

Table 2: It would be better to view these findings in a graph, including error bars and P values.

Table 3, 4, 5, and 6. Since no statistically significant associations were observed, these tables should be removed and overall findings briefly commented in the text.
Figure 1: It does not add to the manuscript. It should be removed.

1. Is the question posed by the authors well defined?
   Not quite.

2. Are the methods appropriate and well described?
   Yes

3. Are the data sound?
   Not sure, because statistics requires review.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
   Yes

5. Are the discussion and conclusions well balanced and adequately supported by the data?
   Not sure, because statistics requires review.

6. Are limitations of the work clearly stated?
   No

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
   No

8. Do the title and abstract accurately convey what has been found?
   Not sure, because statistics requires review.

9. Is the writing acceptable?
   No

**Level of interest:** An article of limited interest

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

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

**Declaration of competing interests:**
'I declare that I have no competing interests'