Reviewer's report

Title: Polymorphisms in metabolic genes, their combination and interaction with tobacco smoke and alcohol consumption and risk of gastric cancer: a case-control study in an Italian population

Version: 1 Date: 22 August 2007

Reviewer: Mark J Roth

Reviewer's report:

General

The authors describe the distribution and the potential gene-gene and gene-environment interactions for a set of Phase I and II xenobiotic enzymes in relation to gastric cancer risk in an Italian population. They find an increased risk to be associated with having a GSTT1 null genotype or SULT1A1 His/His genotype. In a stratified gene-environment analysis of ever-smokers versus non-smokers, they find a significant association among those who smoke for the SULT1A1 variant genotype and gastric cancer risk. In a gene-gene interaction analysis, an additional increased gastric cancer risk was identified among those individuals with a GSTT1 null and NAT2 slow acetylator phenotype.

The manuscript is, in general, well written and the authors acknowledge in the discussion their most significant limitation, i.e., sample size, especially with regard to the gene-environment and gene-gene analyses.

The authors should clarify how the current group of study participants relates to those previously reported in the authors' Cancer Letters 2005 and Biomarkers (In Press) articles. Do they overlap? If so, its not entirely clear why the results of these efforts were reported separately.

---

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. Page 2, Abstract, Results: the SULT1A1 His/His genotype OR presented in the abstract is different than what is presented in Table 2.

2. Page 2, Abstract, Results: typo involving number of significant figures for the combined GSTT1 null and NAT2 slow acetylators CI.

3. Page 4, Introduction: the last sentence of the 1st paragraph, ‘…, among them those of genes coding for…..’ should be grammatically revised.
4. Page 4, Introduction: similar to above, the last sentence of the second paragraph, ‘…..while conflicting results regarding the etiological relevance in gastric carcinogenesis of several SNPs in metabolic genes results from the literature’ should also be grammatically revised.

5. Page 6, Materials and Methods, 1st paragraph: It is unclear to this reviewer the anatomic significance for the term ‘stumps’ in the setting of curative gastrectomies. Please clarify.

6. Page 7, Data Collection and Table I: Does family history of cancer include non-melanoma skin cancers? Please also revise “Familiarity for,” consider ‘Family history of’

7. Page 10, Results: It is unclear why the authors chose to discuss/highlight the non-significant NAT2 slow acetylator results in the text, when other similar non-significant results are identified. This comment also relates to the inclusion of the NAT2 results in the 1st paragraph of the Discussion (page 12). Please justify.

8. Page 10, Results, 2nd paragraph: grammatical revision suggested, ‘GSTT1 null individuals resulted significant regardless of the smoking status’

9. Page 11, Results: the cell size for the stratified gene-gene analysis is of particular concern.

10. Page 13, Discussion, 1st paragraph: The authors’ comment regarding confirmation of the increased risk of gastric cancer for SULT1A1 homozygotes seems to be a bit of an overstatement, especially given it is explicitly mentioned in the previous paragraph that the study was not sufficiently powered for this homozygous variant. Table 2 lists only 11 cases (10.3 %) versus 13 controls (5.1%) with this genotype.

11. Page 14, Discussion, 1st paragraph: grammar, suggest revision, ‘…the stratified analysis did not allow to see it.’

12. Page 23, Table I: Please clarify in the Material and Methods, Data Collection, and in the Table legend what is meant by “Meals salt addition.”

Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable
**Statistical review**: Yes, but I do not feel adequately qualified to assess the statistics.

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