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: 17 August 2007

Reviewer: Krzysztof (Chris) Szyfter

Reviewer's report:

General
I accept your finding but some points require your explanation/revision

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

1. The term "gastric cancer" is in use, although there different meanings. What was your point: oesophagus to anus?, stomach to intestine? There is a partial answer in "study population" section; 57.8% were located in intestine, other? I am raising this point to refer to the first sentence in INTRODUCTION. Gastric cancer is the second most common? To my knowledge there is a sequence: lung, breast, gastric (in males: lung, breast)...

2. Study groups.
- an attempt used to have as clean as possible selection of Italian population regarded Caucasian (appearance?) and Italian birthplace as criteria. This is a way used by many researchers; sometimes national names are also included. However, still European nations were formed in wars, slavery, peaceful migration etc. and we cannot avoid heterogeneity. Anyway, you have to decide if you are going to generalize your results on Italian population (as it sounds in the final section, p.15) or is restricted to the study group only (p.3, "this population").
- control group is usually recruited from healthy individuals; non-cancer (but not healthy!) subjects served as controls. Were they at least non-gastric patients?
- study group is rather small; you have verified your results by statistical calculations but doubts remain open.

3. The ethical approval and patient information were observed.

4. Alcohol intake. I guess that alcohol consumption in Italy means wine drinking. Did you take into account a beneficial effect of moderate consumption of red wine?

5. Gene variants distribution, gene-gene interaction, impact of tobacco smoking and alcohol consumption are shown in Tables 1-3. Familial cancer is given only as the information and was not confronted with gene polymorphism. It means you
did not confirm an association of gastric cancer risk with familial clustering (p.12).

6. Perhaps my knowledge of statistics is not sufficient to understand Table 4. A heading says age and gender were confronted with, gene distribution. I can't see it.

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

---- p.3....polymorphisms (plural) appears (singular),
- p.4. (A major part of) carcinogenic substances require metabolic activation,
- p.14. 1-hydroxyacetyl not...acetyl

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Discretionary Revisions (which the author can choose to ignore)

I suggest to continue your studies including more subjects (multicenter study?)

What next?: Accept after discretionary 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.