Reviewer's report

Title: The PstI/RsaI and DraI polymorphisms of CYP2E1 and head & neck cancer risk: a meta-analysis based on 21 case-control studies

Version: 1 Date: 2 March 2010

Reviewer: Silvia Rogatto

Reviewer's report:

General

In this manuscript, Tang and collaborators performed a comprehensive meta-analysis in order to investigate the possible association of single nucleotide polymorphisms of CYP2E1 gene and the risk of development of head and neck carcinomas. The highly polymorphic P450 enzyme superfamily is the most important system involved in the biotransformation of many endogenous and exogenous substances. In the last decades, several reports showed evidences of association between gene polymorphism in several genes of this superfamily and cancer susceptibility. CYP2E1 gene is among of the most responsible for the biotransformation of chemicals, especially for the metabolic activation of pro-carcinogens as alcohol. Pathways of carcinogen metabolism are complex, and are mediated by activities of multiple genes, while single genes have a limited impact on cancer risk. Although the focus of this meta-analysis is the two most frequently studied SNPs of the CYP2E1 gene, the data just confirm the association of these polymorphisms in the Asiatic population and do not reveals new relevant data.

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

The authors presented clearly the objectives of the present study and the methods were appropriated and well described. However, several confounders bias were not considered such as sex, age and tumor heterogeneity. In this sense, some points should be considered as:

1. Although apparently the number of literature reports is still so little to reach a
homogeneous group of cancer patient’s, head and neck cancer as a single group may have obscured important biological differences of cancers at different locations (oral cavity, pharynx and larynx).

2, Ethnicity: The meta-analysis failed to confirm any association between the polymorphisms and head and neck cancer among Caucasians. However, the authors should consider that in this group were included three papers from Brazilian population (totalizing 487 cases and 459 controls). Historically, Brazilian population always experienced large degrees of ethnic and racial interbreeding, including Amerindians, Europeans, Africans and Asians. Since Brazilian population is known to be highly miscegenated, the authors could review their data considering the impact of the inclusion of Brazilian data among the Caucasian group.

3, The criteria for study classification in high or low quality is very subjective.

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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)

Although historically single nucleotide polymorphisms were identified by the corresponding restriction enzyme used in the genotyping by PCR-RFLP, the authors should be encouraged to update allele/genotype nomenclature recommended by the Human Cytochrome P450 (CYP) Allele Nomenclature Committee (available at http://www.cypalleles.ki.se/). Also, the SNP identifier of PstI/RsaI polymorphism should be given as described to the DraI polymorphism, a T7632A transversion corresponding to the SNP ID rs 6413432 (see page 4, introduction section, second paragraph, line 11).

Page 2, Abstract, first line: This phrase should be corrected for "CYP2E1 encodes a member of the cytochrome P450 superfamily of enzymes which play.". Besides, the authors should follow the recommendations of Guidelines for Human Gene Nomenclature (http://www.genenames.org). Thus, CYP2E1 should appear in italic.

Pages 2 (abstract) and 3 (introduction): head & neck cancer or head and neck cancer? The tumor type should be described in the same way throughout the text.

Page 3, Introduction section, first paragraph: A bibliographic reference should be included in the end of this paragraph.

Page 3, Introduction section, second paragraph, lines 1-2: "The CYP2E1 gene, located..catalysis of xenobiotic. It specifically activates." should be changed for "The CYP2E1 gene, located.. The protein encoded by this gene activates.".

Page 5, Materials and Methods section, line 2: The acronym HCSCC should be changed to the correct form HNSCC. The same observation is valid to page 6 (line 3) where appears NHSCC.
Page 11, Discussion section, line 2: 

"..and it is therefore probable that the the observed ethnic differences".should be corrected for "..and it is therefore probable that the observed ethnic differences"

Legends of Figures 1, 2 and Begg´s funnel plots should be corrected for head and neck cancer instead lung cancer.

The reference section should be completely reviewed and standardized according the BMC recommendations for authors.

Discretionary Revisions (which the author can choose to ignore)

Table 1, Since RFLP was used by 20 studies and just one was based on real time PCR (RT-PCR). Thus, the column of methods should be deleted.

What next?

Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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

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

Statistical review: Needs statistical evaluation.

Declaration of competing interests:

I declare that I have no competing interests.