Reviewer's report

Title: Polymorphisms of XRCC1 genes and risk of nasopharyngeal carcinoma in the Cantonese population

Version: 3 Date: 27 March 2006

Reviewer: Allan Hildesheim

Reviewer's report:

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

General

The authors have attempted to address many of the issues brought up in the previous review. The following residual issues remain:

1. It is still unclear why the only polymorphism in XRCC1 (codon 280 polymorphism) that has previously been found to be associated with NPC has not been tested for in this study. Is there any evidence for correlation/linkage between polymorphisms in codons 194 and 280 of XRCC1? If so, the finding from the present study (for codon 194) and that from the previous XRCC1/NPC report (for codon 280) might reflect the same phenomenon.

2. Table 3 is not informative. Perhaps it could be removed, along with the sections in the Abstract, Results and Discussion related to that table. If the authors feel strongly about retaining Table 3, it would be important to formally test whether the OR estimate observed for Arg/Trp(codon 194)-Arg/Arg(codon399) [OR = 0.86] is statistically significantly different from that observed for Arg/Trp(codon 194)-Arg/Gln(codon399) [OR = 0.58]. If not significantly different from each other, statements currently in the text that suggest any joint effect of XRCC1-194 and XRCC1-399 polymorphisms are not accurate.

3. Are the observed differences by gender due to gender differences in smoking? How many women in the study smoked? If few, the authors may not have the ability to adjust for smoking in the gender models presented in Table 4 and the gender effect seen might simply reflect differences between genders in their smoking behavior.

4. The authors allude to quality control data in the next-to-last paragraph of the Materials and Methods section. However, those results are not presented. Could those QC results be presented in the text?

5. The matching criteria used to select controls are still unclear. The authors mention in the Study Subject section that controls were individually matched to cases on age (+/- 5 years) and ethnicity. However, in the Statistical Analysis section the authors mention frequency matching on age, gender, and smoking. Please clarify.

6. Some of the numbers still do not match. For example, in Table 2, the allele frequency reported for 399Gln is 0.25 for cases and 0.26 for controls. In the text, the reported frequency is 0.279. The
genotype frequencies also do not match (7.5% and 6.0% in the table and 8.9% in text). The numbers reported in the tables and text should be double checked.

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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)

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Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

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

Statistical review: Yes