Author's response to reviews

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

Authors:

Yun Cao (yunsirisums@163.com)
Xiao-Ping Miao (Miaoxp@sina.com)
Ma-Yan Huang (hmy220@sina.com)
Ling Deng (dengling81@yahoo.com.cn)
Li-Fu Hu (Lifu.Hu@mtc.ki.se)
Ingemar Ernberg (Ingemar.Ernberg@mtc.ki.se)
Yi-Xin Zeng (yxzeng@gzsums.edu.cn)
Dong-Xin Lin (dlin@public.bta.net.cn)
Jian-Yong Shao (shjiany@mail.sysu.edu.cn)

Version: 4 Date: 17 April 2006

Author's response to reviews: see over
Dear Editor:

Here we send you the revised manuscript MS 6734268418496577, which entitled “Polymorphisms of XRCC1 genes and risk of nasopharyngeal carcinoma in the Cantonese population”. This manuscript is not under consideration by another journal and has not been previously published.

Firstly, we appreciate you for your kindly help for managing this manuscript. We also would like to appreciate the reviewers for their help in improving the quality of this manuscript, their good comments as well as their questions to this manuscript. The answers to the reviewers questions is attached to the next page of this letter. Text of this manuscript has been copyedited for improving the quality of written English again by a professional scientist from USA.

Again, we would appreciate your consideration of this manuscript for publication as an research article in *BMC Cancer*.

Best regards

Sincerely yours

Jian-Yong Shao, M.D., Ph.D., Professor
Dept. of Pathology
Sun Yat-Sen University Cancer Center
651 Dong Feng Road East
Guangzhou 510060
P.R. China
Tel/Fax: 86-20-87343391
Email: shajiany@mail.sysu.edu.cn

*Answers to the questions and comments of reviewers of this revision*

Reply to Reviewer Allan Hildesheim (Version 3, 27 March 2006)
1. The evidence for correlation between polymorphisms in codons 194 and 280 of XRCC1 is not tested in this study. Though Cheo EY et al had reported the correlation between NPC and polymorphism in codon 280 and 399 of XRCC1, it will be better to further test the correlation between polymorphism in condon 194 and 280 of XRCC1. We will do this further study in our future research project.

2. According to your suggestion, Table 3 along with the sections in Abstract, Results and Discussion are removed from the latest revision.

3. There were 44 (44/123, 36%) women smoked in cases and 5 (5/259, 2%) women smoked in controls. To answer this question, we visited epidemiologist in the School of Public Health of Sun Yat-Sen University. We believe that the results was credible for the analysis of polymorphism in codon 194 in male population; and for the femal population, the results was not confident for few smoked women.

4. The quality control results has been added in page 6, in the last paragraph of Genotyping section.

5. The sentence of “Because of the use of frequency matching” in Statistical Analysis section was deleted.

6. Errors of the number of allele frequency was corrected in the text in this revision.

Reply to Reviewer Jae Yong Park (Version 3, 11 March 2006):

Figure 1 and Figure 2 were deleted in this revision.
Answers to Reviewer JaeYong Park:

**Comments 1.** The selected criteria for cases were histologically confirmed, untreated cases, and Cantonese, the selected criteria for controls included cancer-free individuals and Cantonese. For each eligible case subject, we tried to match one control subject by age (±5 years) and ethnicity (Cantonese). Overall, 520 eligible cases and 520 eligible controls agreed to a detailed risk factor interview administered by a trained nurse-interviewer. During interview, among the 520 eligible NPC cases, thirty-three cases were ever accepted radiation treatment, and 15 cases couldn’t collect detailed smoking information, 10 cases refused to blood sample collection, so these 58 cases were wiped off. Among the 520 eligible controls, nine controls were wiped off due to deficient smoking information. Finally, 462 cases (88.8% of eligible) and 511 controls (98.3% of eligible) were included finally.

We notice that the controls were not matched to cases on gender ratio (339:123 in the cases and 252:292 in the controls) and smoking status (298 in the cases and 158 in the controls). We tried to match the cases and controls on bases of gender and smoking status, but if gender or smoking status factors were matched to cases, the controls need more individuals to recruit, it is difficult for us, so we remain the controls to conduct the study. Since the gender frequency and smoking status are not matched between cases and controls in this study, we further analyzed the association of XRCC1 Arg194Trp and Arg399Gln polymorphism and risk of NPC separately by stratification by gender and smoking status in the revision of this study.

**Comments 2.** The author’s original idea was to observe the joint effect of two XRCC1 polymorphisms and the risk of NPC, but the term was misused as ‘interaction’. Combination analysis indicate that individuals with the Trp194Trp and Arg399Arg or the Arg194Trp and Arg399Gln genotypes present, respectively, a 0.44-fold (OR = 0.44, 95% CI, 0.23-0.83) and 0.58-fold (OR = 0.58, 95% CI, 0.36-0.93) decreased risk of NPC development compared to individuals with the Arg194Arg and Arg399Arg genotypes. The P value (0.01) for Trp194Trp and Arg399Arg genotypes is statistically significant after Bonferroni’s correction. We can not exclude the joint effect of Trp194Trp and Arg399Arg genotypes in risk of NPC. Since the OR value does not reduce significantly, it is considered that the joint protective effects is mainly contributed by the polymorphism of XRCC1 Trp194Trp genotype.
Answer to Minor Essential Revisions:

**Comment 1.** Description of the previous studies results is rewritten in a clear way.

**Comment 2.** Figure 1 and figure 2 are cut back in the revision. In addition, to verify the results, 15% of the random sample were repeated for genotyping, it included 63 cases and 74 controls in condon 194 polymorphism, and 64 cases and 75 controls in condon 399 polymorphism. This was added in the section of methods.

**Comment 3.** All the data were recalculated and Bonferroni’s correction of $P$-value was evaluated when multiple comparison used.

**Comment 4.** For genotyping, 417 cases and 495 controls were able to perform analysis of XRCC1 condon 194; 425 cases and 501 controls were able to perform condon 399 polymorphism analysis. The problems for this difference may due to DNA quality or other technique problems.

**Comment 5.** The unadjusted OR has been added to the Table 2 and Table 3.

**Comment 6.** The data of stratification analysis according to age, gender and smoking status was performed in this revision. The results of this analysis are described in sections of results and are presented in Table 4, Table 5 and Table 6.

**Comment 7.** The data of this study has been compared to the data of previous study regarding the role of these polymorphisms on the risk of NPC conducted by Choe EY et al. in section of discussion. Both studies reported a similar result, the XRCC1 399 genotypes was not associated with risk of NPC.