

Professor Ze-Mao Gong
Science Editor,
Editorial Office,
World Journal of Gastroenterology
November 6, 2015
Re: ESPS manuscript NO: 21218

Title: Association between polymorphisms of *APE1* and *OGG1* and risk of colorectal cancer in Taiwan

Dear Professor Gong:

Thank you for your inspiring and helpful comments and suggestions for the above referred manuscript. We have carefully revised the manuscript as suggested, and have attached our point-by-point responses to the reviewers' comments. Thanks for your consideration of this article for publication in *World Journal of Gastroenterology*.

Sincerely,

Chih-Ching Yeh, PhD
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Responses to Reviewer 1 (reviewer's code: 02494908)

1. The manuscript is very well written and the methodology well performed. I have no further comments to this.

Reply: Thank you for your comment.

Responses to Reviewer 2 (reviewer's code: 02495844)

This manuscript is well established to investigate the association between BER gene polymorphisms and CRC susceptibility. However, there are still two confusions that needed to be answered.

1. The first one is about the haplotype analysis. As we know, the haplotype was based on the genetic linkage of gene sites located in the same chromosome. So we are curious that whether the two SNP sites of OGG1 or APE1 had a linkage inheritance? Please provide the results of linkage disequilibrium analysis.

Reply: Thank you for your comment. We had conducted linkage disequilibrium analysis for OGG1 Ser326 and 111657A/G as well as for APE1 Asp148Glu and T-656G. The results of the linkage inheritance estimates are described in the latest paragraph of the *Results* section. (Please see the latest paragraph on page 13).

2. The second one is about the SNP site. Since we found several other articles focused on the same rs1760944 SNP were named APE1 -141T/G, which is different with yours as APE1 T-656G, so please confirm the exact name of this SNP site.

Reply: Thank you for your comment. According to the NCBI website [1], we can found that the APE1 rs1760944 is located in the promoter region of the gene. This SNP is named as APE1 -141T/G when calculated from the 5' UTR and is also named as APE1 T-656G when calculated from the start codon. This SNP being indicated as APE1 T-656G was also presented in several journal articles [2-5]. Since we had shown the APE1 T-656G SNP with its identical rs number in the manuscript, the readers will not be confused.

[1]

http://www.ncbi.nlm.nih.gov/projects/SNP/snp_ref.cgi?showRare=on&chooseRs=all&locusId=328&mrna=NM_001641.3&ctg=NT_026437.13&prot=NP_00163

[2.2&orien=forward&refresh=refresh.](#)

- [2] Lo YL, Jou YS, Hsiao CF, Chang GC, Tsai YH, Su WC, Chen KY, Chen YM, Huang MS, Hu CY, Chen CJ, Hsiung CA. A polymorphism in the APE1 gene promoter is associated with lung cancer risk. *Cancer Epidemiol Biomarkers Prev.* 2009 Jan;18(1):223-9.
- [3] Cao Q, Qin C, Meng X, Ju X, Ding Q, Wang M, Zhu J, Wang W, Li P, Chen J, Zhang Z, Yin C. Genetic polymorphisms in APE1 are associated with renal cell carcinoma risk in a Chinese population. *Mol Carcinog.* 2011 Nov;50(11):863-70.
- [4] Zhou B, Shan H, Su Y, Xia K, Shao X, Mao W, Shao Q. The association of APE1 -656T > G and 1349 T > G polymorphisms and cancer risk: a meta-analysis based on 37 case-control studies. *BMC Cancer.* 2011 Dec 18;11:521.
- [5] Dai ZJ, Wang XJ, Kang AJ, Ma XB, Min WL, Lin S, Zhao Y, Yang PT, Wang M, Kang HF. Association between APE1 Single Nucleotide Polymorphism (rs1760944) and Cancer Risk: a Meta-Analysis Based on 6,419 Cancer Cases and 6,781 Case-free Controls. *J Cancer.* 2014 Mar 13;5(3):253-9.