

February 28, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 7815-edited.doc).

Title: APE1 polymorphisms are associated with colorectal cancer susceptibility in Chinese Hans

Authors: Shiheng Zhang, Linang Wang, Zheng Li, Yu Peng, Yanping Cun, Nan Dai, Yi Cheng, He Xiao, Yanli Xiong, Dong Wang

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The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

Reviewer 1: The authors analyzed an important aspect of risk factor for CRC. The number of cohort study is adequate and it is very interesting because it has been conducted in Asiatic population that has different genetic characteristics with respect a Western population. Considering the nature of the study (case control) probably a match 1 to 2 instead that 1 to 1 is more adequate.

Answer: We greatly appreciate the suggestion of reviewer, the main reason we did not use a 1 to 2 match in this study was that the behavioral information for control subjects was difficult to collect, as most individuals that took the health examination did not provide many details. However, further studies will attempt to overcome this obstacle and hopefully build a more adequate database.

Reviewer 2: MAJOR POINTS This article is dealing with an interesting, even promising issue, namely the identification of an inexpensive, reproducible agent that could be used as a reliable screening test for colorectal cancer. BER gene polymorphism in cancer and in specifically in colorectal cancer has been extensively studied. Consequently, the novelty of this manuscript is limited to the extent of a study pertaining a geographically specific and homogeneous population. However, the findings are still of value. The manuscript is well-structured and presented. It is readable and comprehensible, but a minor english editing is probably needed SPECIFIC COMMENTS Materials and methods: The only drawback is that of the method itself as a case-control study. According to bibliography, the possible impact of gene polymorphism in colorectal cancer is so far, inconsistent, confounding and multifactorial. Having this in

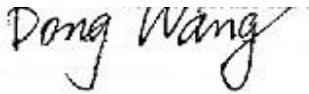
view, the results of a case-control study for this issue could be questioned. Nevertheless, authors acknowledge this parameter.

Answer: We greatly appreciate the comments of this reviewer. As mentioned, these polymorphisms have been studied in various Western populations and regions. However, to our knowledge, research data linking these gene polymorphisms and behavioral factors for CRC are still lacking, especially within the Chinese Han population. The retrospective case-control study may not be adequate for our topic, but as a background study, we consider it sufficient to reveal our hypothesis. We have plans for a case-control study with a prospective cohort to confirm the associations identified by the present study. Furthermore future planned experiments will investigate the exact mechanisms for our findings.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

A handwritten signature in black ink that reads "Dong Wang". The signature is written in a cursive, flowing style.

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