July 10, 2013

Dear Editor,

We thank the editors and reviewers of the *World Journal of Gastroenterology* for taking their time to review our article. We have made some corrections and clarifications in the manuscript after going over the reviewers' comments. The changes are summarized below:

Please find enclosed the edited manuscript in Word format (file name: 3049-review.doc).

Title: *ITGA1* polymorphisms and haplotypes are associated with gastric cancer risk in a Korean population

Author: Dong–Hyuk Yim, Yanwei Zhang, Sang-Yong Eom, Sun In Moon, Hyo-Yung Yun, Young-Jin Song, Sei-Jin Youn, Taisun Hyun, Joo-Seung Park, Byung Sik Kim, Jong-Young Lee, Yong-Dae Kim, Heon Kim

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 3049

The manuscript has been improved according to the suggestions of reviewers:
1. The format for the figures has been updated
2. Revision has been made according to the suggestions of reviewers

Reviewer A

(1) It would be great if the author could provide the reason of choosing codominant and recessive genetic model.

- We would like to choose one most appropriate genetic model which could explain the association between polymorphic distributions of *ITGA1* SNPs and gastric cancer. But, we could not choose any one model from them, because we could not find any information about genetic models for the SNPs, and their statistical significances were not much different between the models. Therefore, we presented all the results for codominant, dominant and recessive genetic models.

(2) In the method section, it would be better to address the potential function of selected SNPs if possible.

- We have made a correction as follows.

"We applied public databases of SNPs related with gastric cancer and assessed the potential functions of selected SNPs through SNP function prediction software. Among those 15 SNPs, only two were located in the exons, and one of them was non-synonymous. The potential function was not predicted for all the SNPs except rs*2447867* which was predicted as an exonic splicing enhancer (ESE)."

Reviewer B

(1) There are 15 SNPs of *ITGA1*, whether the gene-based association is effective?

- We have tried a gene-based association test for the 15 SNPs. We used web-based VEGAS (versatile gene-based association study) approach (http://gump.qimr.edu.au/VEGAS/). When the p-values for the minor alleles of codominant, dominant or recessive models were applied, no significant gene-based association was found. However, if the lower p-value among those for dominant and recessive models was input for every SNP, the test statistics was 29.622, which was statistically significant (p-value = 0.037). We have added following sentences in Materials and Methods, Results and Discussion.

"Gene-based association tests were performed were applied with the VEGAS (versatile gene-based association study) method (http://gump.qimr.edu.au/VEGAS/)."

"When the p-values for the minor alleles of codominant, dominant or recessive models were applied to VEGAS test, no significant gene-based association was found. However, if the lower p-value among those for dominant and recessive models was input for every SNP, the test statistics was 29.622, and statistically significant (P = 0.037)."

"*ITGA1* gene was found to be significantly associated with gastric cancer in the VEGAS test."

(2) For a mediate sample size 477 pairs and 15 SNPs, please calculate the study power and FDR (false discovery rate) for their findings.

- We have added following phrases.

"Study power was calculated with 'case - control for discrete traits' mode of Genetic Power Calculator (http://pngu.mgh.harvard.edu/~purcell/gpc/cc2.html). Following parameters were applied; risk allele frequency - 0.4, alpha error - 0.01, and disease prevalence - 0.1%. The power for a codominant model was 0.7768, when the heterozygous odds ratio was set as 1.5. For dominant model, if the odds ratio for genotype with one or 2 risk allele(s) was considered as 2, the power was 0.8821. When the 2 was input for the odds ratio for genotype with 2 risk allele(s), then the power for recessive model was 0.8182."

"Multiple testing corrections were carried out by Benjaminin and Hochberg's methods for strong control of the false discovery rate (FDR). A two-sided adjusted P value < 0.05 was considered as statistically significant. FDR Q values were calculated separately for the SNPs and haplotypes based on those numbers."

"After controlling FDR, only the SNP *rs2432143* significant in the codominant was statistically model."

3 References and typesetting were corrected

- Additions have been made as the reviewer's recommendation

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Thank you again for reviewing our manuscript.

Sincerely yours,

Heon Kim, M.D., Ph.D.
Professor
Department of Preventive Medicine, College of Medicine,
Chungbuk National University.
410 Sungbong-ro, Hungdok-gu, Cheongju,
Chungbuk, 361-763, Republic of Korea
TEL: +82-43-261-2864, FAX: +82-43-274-2965,
E-mail: kimheon@cbu.ac.kr