Author's response to reviews

Title: Influence of HRH2 promoter polymorphism on aberrant DNA methylation of DAPK and CDH1 in the gastric epithelium

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Author's response to reviews: see over
Dear Sir,

Thank you for your kind e-mail on Oct. 17, 2012. We have tried to re-revise our manuscript entitled “Influence of HRH2 promoter polymorphism on aberrant DNA methylation of DAPK and CDH1 in the gastric epithelium“(MS: 1843810096747648). I am sending the re-revised manuscript. Our responses to reviewer 2 were added in this letter.

I hope that these revisions are satisfactory and that the re-revised version will be acceptable for publication in BMC Gastroenterol.

Sincerely yours,

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To reviewer 2:
Thank you very much for your important comments and interests in our study. The aim of this study is to investigate an association between HRH2 genetic polymorphism and gene methylation by a genetic statistical method. We do not have a lot of data. Our responses to your comments as follows:

Major Compulsory Revisions

As pointed out in my previous report the authors found that the GG homozygote displayed no significant risk for DAPK methylation in subjects with GC (Table 4). The same was also true for CDH1 (Table 5). Nevertheless, this is not mentioned in the abstract or in the conclusion.

- Sentences were added in abstract p.3 lines 14-16 and in conclusions p.20 lines 11-12.

No data was provided to support a functional role of the methylation of the genes, which were detected using a non-quantitative method. In addition, no data was provided to show a functional role of the SNP.

- The aim of this study is to investigate an association between HRH2 genetic polymorphism and gene methylation by a genetic statistical method. Our study cannot reveal a functional role of both methylated gene and SNP. To clarify these points, another study will be necessary using another method and technique. We have no more data. For us to be able to do now is only to speculate them using previous data reported in the other studies.

- A sentence was added in p.16 lines 9-11 and ref.27-30.

Finally, only non-neoplastic tissue was included in the study, and the authors did not investigate whether the methylation in these tissues reflect the methylation in neoplastic cells from the same patients.

- We believe that accumulation of gene methylation shows an increased risk of carcinogenesis as many studies have indicated. However, we do not know whether the methylation of specific genes promote the development of carcinogenesis or not.
From our present study, the mechanism of carcinogenesis via gene methylation cannot be fully discussed.

- Data of gene methylation in cancer lesion in all 115 subjects with GC were added in Table 4 and 5.

- A sentence was added in p.8 lines 8-9 “Materials and Methods”.

- Sentences were added and changed in p.13 line16-p.14 first line and in p.14 line6-10 “Results”.

- A paragraph was added in p.16 “Discussion”.

Minor Essential revisions

There are still some sentences and typos which need to be corrected. For instance, page 10, line 4 ("bislufite-modification" should be "bisulfite-modification"), page 10 line 6 ("1 minutes" should be "1 minute"), and page 18, line 17 ("almost GC patients" should be "almost all GC patients").

- According to your instructions, these words were corrected.