Author's response to reviews

Title: Influence of IL17A polymorphisms on the aberrant methylation of DAPK and CDH1 in non-cancerous gastric mucosa

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

Thank you for your kind e-mail on April 24, 2012. We have tried to revise our manuscript entitled “Influence of IL17A polymorphisms on the aberrant methylation of DAPK and CDH1 in non-cancerous gastric mucosa” (MS: 5389996076629468). I am sending the revised manuscript. Our responses to reviewers were added in this letter.

I hope that these revisions are satisfactory and that the revised version will be acceptable for publication in BMC Med Genet

Sincerely yours,

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To reviewer 1:

Thank you very much for your important comments and interests in our study. I hope that these revisions are satisfactory. Our responses to your comments as follows:

major

1. How did the authors estimate sample size? To reduce the risk of type I error, it is critical to set the major outcome of this study first. Otherwise, the readers may feel these kinds of significance are due to multiple testing. Furthermore, the reason why they divided the subjects in two groups at 60 years old should be stated.

   In HapMap-JPT, the frequency of IL17A -197 A allele frequency was 45.3%. We assume that a 20% decrease in the prevalence of an allelic frequency would be clinical relevance (non CIHM:40% vs. CIHM:50%). Assuming an alpha value = 0.05 and a power = 0.80, at least 200 non CIHM subjects and 200 CIHM subjects would be sufficient to identify a clinical relevant difference. Accordingly, 400 subjects would be clinical relevance for the study.

   This statement was added in p.7 lines 5-10.

   The data of 1-βpower were added (in p.13 line 10, 18 and p.15 line 7).

   A sentence was added in p.11 lines 1-2 from bottom.

   The mean age of our subjects was approximately 60 years old. So, the subjects were divided in two groups at 60 years old.

   This statement was added in p.14 lines 9-10.

2. Who were the authors of this manuscript? Although three authors were listed in the title page, there were many contributors in the “Authors’ contributions”. Only substantive intellectual contributors to the study can be the authors.

   Sorry for my mistake. Author’s contribution was changed (in p.23 lines 13-14).

minor

Page 7, line 6. How many biopsy specimens did the authors take?

   A word “one or two” and a sentence were added in p.7 line 11 and lines 15-16, respectively.

Page 17, lines 10-14. This part was already stated in the Background section, these sentences are redundant.

   According to suggestion, sentences were deleted.
Page 7, line 11. CIHM should be spelled out the first time the terms appear in the text.

(CpG island high methylation) was inserted in p.7 at bottom line.
Correlation coefficients should be stated for the data of Figures 1 and 2.

$|R|$ values were added in Figure 1 and 2.

Table 2. Unify the font of the letters.
Tables 3 and 4. The row order of “CIHM (…” and “IL17A…” should be changed.
Table 5. IL17A should be italic.

The authors should carefully follow the instructions for authors (ex. Email addresses for all authors should be listed in the title page. All pages should be numbered.)

Thank you very much for your kind indications. All corrections were completed.
To reviewer 2:

Thank you very much for your important comments and interests in our study. I hope that these revisions are satisfactory. Our responses to your comments as follows:

1. The studied population comprised 401 subjects, but only 286 subjects were performed the evaluation on the severity of chronic gastritis according to the updated Sydney system. How to analyze the data and get the results? What’s the relationship among the gastric mucosal inflammation, H. pylori infection and IL17A polymorphisms?

- The histological evaluation in the subjects who consented to only one biopsy was not performed.
  A word “one or two” and a sentence were added in p.7 line 11 and lines 15-16, respectively.
  *H. pylori* infection happens at infant age, and continues all life. The severity of mucosal atrophy progresses with infection period, but the degree of inflammation does not. In general, activity and inflammation scores were decreased in severe atrophy and metaplasia. In our study, there was no significant correlation between age and inflammation score. In addition, there was no significant difference of inflammation score among genotypes. That is, it is difficult to assess the degree of inflammation at one point. Indeed, these findings suggest that *IL17A* polymorphisms may associate with gastric mucosal atrophy by the mechanism other than promoting the inflammation.
  The genotypes of *IL17A* in *H. pylori* negative and positive subjects were 61GG, 83GA and 15AA, and 94GG, 121GA and 26AA (-197G>A), and 130CC, 23CT and 5TT, and 210CC, 19CT and 11TT (*1249C>T), respectively. The influence of *IL17A* polymorphisms on *H. pylori* infection was not seen. Sentences were added in p.19 lines 2-8.

2. Please give more explanation or evidence to discuss the influence of IL17A polymorphisms on the aberrant methylations of DAPK and CDH1 in non-cancerous gastric mucosa.

- According to your suggestion, some sentences were added in “Discussion”.
  However, overestimation for our data was avoided as possible.