Author’s response to reviews

Title: Selenoprotein S (SEPS1) gene -105G>A promoter polymorphism influences the susceptibility to gastric cancer in the Japanese population

Authors:

Tomoyuki Shibata (shibat03@fujita-hu.ac.jp)
Tomiyasu Arisawa (tarisawa@fujita-hu.ac.jp)
Tomomitsu Tahara (ttahara@fujita-hu.ac.jp)
Masaaki Ohkubo (mohkubo@fujita-hu.ac.jp)
Daisuke Yoshioka (dyoshioka@fujita-hu.ac.jp)
Naoko Maruyama (nmoruyama@fujita-hu.ac.jp)
Hiroshi Fujita (hfujita@fujita-hu.ac.jp)
Yoshio Kamiya (ykamiya@fujita-hu.ac.jp)
Masakatsu Nakamura (mnakamura@fujita-hu.ac.jp)
Mitsuo Nagasaka (mnagasaka@fujita-hu.ac.jp)
Masami Iwata (miwata@fujita-hu.ac.jp)
Kazuya Takahama (ktakahama@fujita-hu.ac.jp)
Makoto Watanabe (mwatanabe@fujita-hu.ac.jp)
Ichiro Hirata (ihirata@fujita-hu.ac.jp)

Version: 3 Date: 15 November 2008

Author’s response to reviews:

BMC-series journals Assistant Editor

Dear Dr Dunckley,

Thank you very much for reviewing our manuscript entitled “Selenoprotein S (SEPS1) gene -105G>A promoter polymorphism influences the susceptibility of Japanese to gastric cancer” (MS: 1983473344218508). We are grad to obtain many good suggestions to our paper. We attempted to revise our paper according to reviewers comment as thoroughly as possible. And we asked a professional editing service, American Journal Experts, for copyediting of our manuscript. By professional copyediting, the title has been changed to “Selenoprotein S (SEPS1) gene -105G>A promoter polymorphism influences the susceptibility to gastric cancer in the Japanese population”. Please reconsider of its suitability for publication in BMC gastroenterology.

Sincerely yours,

Tomoyuki Shibata, M.D., Ph.D.

-------------------------------------------------------------------------------------------------

Answer to Reviewers
Referee 1

Thank you for your very important comments and suggestions. We corrected and added these points as below.

About major compulsory revisions

1. We only have 74 healthy volunteer DNA (all are H. pylori negative). We examined these DNA about SEPS1 polymorphism -105G>A. As a result, the numbers of GG were 70, the numbers of GA were 4 and none of them was AA. From these results, we thought our comparison between gastric cancer patients and non gastric cancer patients was proper comparison for analyzing the association risk of gastric cancer and SEPS1 polymorphism other than the association of H. pylori.

2. As suggested, we described the details of the study populations and exclusion criteria in Methods section. These patients were consecutive, therefore the averaged age of two groups were different.

3. As suggested, in subgroup analysis, the results were preliminary in these analyzed numbers. We added the comment about the limitations of these numbers in the Results section.

About minor essential revisions,

1. We copyedited our original manuscript by professional copyediting service as described above.

Referee 2

Thank you for your many important suggestions and comments about our manuscript. We carefully read these comments and answered.

About the comments,

1. As suggested, the significant differences between gastric cancer group and non-gastric cancer group was borderline significance. We think the most influenced factor for gastric cancer development is H. pylori. We analyzed these data with adjustment of H. pylori, age and sex (we described in Methods section). And we added the comment about these adjustment in Discussion section just after the sentence “……, we found significant associations between carrying the A allele and the odds of specific types of gastric cancer”.

2. We performed histological evaluation (immunohistochemistry with anti-H. pylori Ab) in almost all patients. In impossible cases for taking biopsy sample or histology negative patients, we considered the results of other evaluation methods (serum anti-H. pylori antibody or urea breath test). Because the specificity and sensitivity are both very well in immunohistochemical examination (Sao Paulo Med J 2001 Mar;119(2):67-71).

3. As suggested, we described the details of control patients and exclusion
Referee 3

Thank you for your very important comments and suggestions. We corrected and added these points as below.

About major compulsory revisions,

1. As suggested, we calculated and added the data of Hardy-Weinberg Equilibrium analysis in Methods and Results section.

2. As suggested, we commented about the relation of selenium and H. pylori, gastritis and gastric cancer in Discussion section. It is not common of Selenium deficiency in Japanese population from previous reports.

3. We are sorry that we did not ask about the smoking status. For future cohort study, we would like to ask about the smoking status, because the smoking status is important for some cancer risk. Since we did not the smoking status, we did not have the answer about the association of smoking and selenium. In previous cohort study about gastric cancer risk and selenium concentration, it was not obvious that the smoking modified the selenium concentration (Am J Clin Nutr. 2004 Jan;79(1):80-5).

4. In these polymorphism patients, no severe eosinophil infiltrations were found.

About minor essential revisions,

1. As suggested, we copyedited our original manuscript by professional copyediting service as described above.

2. As suggested, we added further description about this controversial result about the association of SEPS1 polymorphism and inflammatory desises.

About the discretionary revisions,

1. We agree with your suggestion. But currently, we don’t have good tissue to analyze the cytokines or mRNA.