

Responses to reviewers' comments



April 14, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 9927-Research report.doc).

Title: A case-control study of diabetes-related genetic variants and pancreatic cancer risk in Japan

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Name of Journal: *World Journal of Gastroenterology*

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The manuscript has been improved according to the suggestions of reviewers. All the changes have been highlighted in red font.

1 Format has been updated.

2 Revision has been made according to the suggestions of the reviewers.

Very few molecular epidemiologic studies have addressed the issue about the common genetic background which predisposes individuals to developing both diabetes and pancreatic cancer. This a good case-control study, try to examine whether diabetes-related genetic variants are associated with pancreatic cancer risk in Japan. 7 diabetes-related genetic variants were therefore genotyped and it was found that rs1501299 in the ADIPOQ gene may be associated with pancreatic cancer risk, although the role of adiponectin variants has not been clarified yet. Although this is a retrospective study, the result may be helpful for clinical practice. so this manuscript is recommended for publication after Minor reversion.

1) The method of Genotyping assays should be briefly described

We appreciate the reviewer's comment. We have added the following sentences in the Methods.

Page 8 Line 7-13

Genotyping was performed using Fluidigm 192.24 Dynamic Array with BioMark HD Systems and EP1 (Fluidigm Corp., CA). We applied SNPtype assay (Fluidigm Corp., CA) which employs allele-specifically designed fluorescences (FAM or VIC) primers and a common reverse primer. We analyzed the data by the BioMark SNP Genotyping Analysis software to obtain genotype calls. The software defined genotype of each sample based on the relative intensities of fluorescences. All the assay were conducted at the Aichi Cancer Center Research Institute, Nagoya, Japan. The laboratory staff members were blinded to case or control status. Four quality control samples were included in each assay array, and the concordance rate was 100%.

2) A definitive diagnosis newly diagnosed with pancreatic ductal adenocarcinoma was made according to imaging modalities and pathologic reports (if available), and patients without pathologic confirm

should be excluded.

The reviewer is correct. We tried to obtain pathology reports from all cases. As a result, pathology reports were available for approximately 90% of cases. In the analysis restricting to those pathologically confirmed cases, as suggested by the reviewer, we found that the association between rs1501299 in the ADIPOQ gene and pancreatic cancer remained unchanged. So we did not exclude those cases without pathology reports. However, the inclusion of those cases was considered a limitation. We have added the following sentences in the revised paper.

Method Page 7 Line 8-11

A diagnosis was made according to imaging modalities and further confirmed by pathology reports. Pathologically confirmed cases represented approximately 90% of all cases in this study.

Discussion Page 15 Line 8-12

Second, one concern is that pathology reports were not available for all cases. However, we performed an analysis excluding those cases without pathology reports, and found that the positive association between rs1501299 in the ADIPOQ gene and pancreatic cancer remained unchanged.

3 References and typesetting were corrected.

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

Sincerely yours,

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