

ANSWERING REVIEWERS



March 20, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: Format for answering reviewers 8893 doc).

Title: Polymorphisms of methylenetetrahydrofolate reductase and susceptibility to oesophageal adenocarcinoma in a Caucasian UK population

Author: R Keld, M Thian, C Hau, J Sajid, N Kumar, Y Ang

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 8893

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

Reviewer number 1:

(1) We have acknowledged the small sample size and the case-control nature of the study and agree this would not allow for a statistical significant conclusions in a gene polymorphism. This study is limited but it is a pilot study. We have included the limitations in the beginning of the discussion and also future studies including prospective setting and much larger sample size to reduce the chance of type 2 statistical error.

(2) The analysis of data was conducted by a professional University statistician and the limitations of small sample size is acknowledged (see answer to (1)). Due to small sample size, the advice of the statistician was that it is better to use normal, low or high values (proportions) rather than real values for folic acid and B12 (as there were a few subjects showing very high levels which will skew the results). The potential interactions of the

four factors (MTHFR, B12, folate and homocysteine) were considered but because of the small sample size the analysis was focus on individual factor.

Reviewer number 2:

- (1) The title is now changed to: Polymorphisms of methylenetetrahydrofolate reductase and susceptibility to oesophageal adenocarcinoma in a Caucasian UK population
- (2) Introduction is now changed to 'Background' in the abstract section and the aim is now stated more clearly.
- (3) The Introduction is now shortened considerably into 4 paragraphs.
- (4) The statement on limitation of the study owing to case-control nature of the study and small sample size and hence possibility of type 2 statistical error is now inserted in the discussion.
- (5) We have suggested direction for future studies in the concluding remarks.
- (6) We have modified the table according to the reviewer's very helpful suggestion. The Table has been updated, the legends are now put in the footnote.

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

Sincerely yours,



Dr Yeng S Ang, MD FRCP FRCPI FEBG

Editorial Board member WJG (UK)

Consultant Gastroenterologist (Salford Royal University Hospital, Manchester, UK)

Honorary Senior Lecturer, University of Manchester (Institute of Inflammation and Repair and Molecular Cancer Group)

Email: yeng.ang@srft.nhs.uk

Tel: 0044-161-2065794