Author's response to reviews

Title: Methionine synthase A2756G polymorphism may predict ulcerative colitis and methylenetetrahydrofolate reductase C677T pancolitis, in Central China

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Author's response to reviews:

Point-by-point Response to the reviewers' and Editor's comments

Response to Editor’s comments
Q: Peer review of your manuscript (above) is now complete, and we are delighted, in principle, to accept the manuscript for publication in BMC Medical Genetics. The reviews are accessible in PDF format via the web links provided below. Do let us know if you have any problems opening the files. However, before acceptance, we would urge you to further improve the manuscript in response to the comments made by the reviewers.
A: We thank you for your decision regarding our manuscript. We took into account all your comments as well as reviewer 3’s comments (please see below) in the revised version of our manuscript.

Q: We would also request that you go through the manuscript formatting checklist one more time and ensure that your revised manuscript conforms to all of the points. The link to the formatting checklist is provided at (http://www.biomedcentral.com/info/ifora/medicine_journals ). It is important that your files are correctly formatted.
A: As requested, the revised manuscript has been formatted according to the author guidelines.

Response to reviewers’ comments

REVIEWER 3:

Q: In Table 2, indicate which OR is for dominant and recessive models of the allele

at risk.
A: It is now stated in the legend of Table 2 “Comparison with dominant genotype” and which are the “dominant genotypes”. We confirm here that ORs were calculated correctly.

Q: Tables 2 and 3 should be merged. Omit the 95% CI for the frequencies in Table 3.
A: As suggested by reviewer 3, tables 2 and 3 have been merged, and 95% CI for the frequencies have been deleted in Table 2 of the revised manuscript. Accordingly, the title of the new table has been modified as following: “Genotype frequencies and minor allele frequencies of genetic polymorphisms in UC patients and controls”.

Q: Clarify where and how Bonferroni’s correction was used.
A: Bonferroni’s correction was used when several dependent or independent statistical tests were performed simultaneously. We have added this information in the paragraph of statistics. As the reviewer probably knows, the Bonferroni correction is a multiple-comparison correction: while a given alpha value alpha may be appropriate for each individual comparison, it is not for the set of all comparisons. In order to avoid a lot of spurious positives, the alpha value needs to be lowered to account for the number of comparisons (n) being performed, with the correction alpha/n.

Q: Test for LD in your study population.
A: There was no linkage desequilibrium among different genotypes. This is now mentioned in the revised manuscript.

Q: Provide data on combined genotypes.
A: Our study was underpowered to perform such analysis.

Q: In Introduction, specify the position of the SNPs.
A: We indicate in Introduction of the revised manuscript the position of the SNPs.

Q: Test for HWE using an exact test according to Weir (see Book by Bruce Weir).
A: To test for HWE, we used the chi-square two tailed calculation of Knud Christensen, population genetics, www.kursus.kvl.dk.

Q: Calculate sample size and power taking into consideration the frequency of the minor allele in the study population and the prevalence of the disease.
A: This is already mentioned in the current version of the manuscript (Page 6, 1st paragraph: Statistical analysis section) as following: “The minimal size of our sample was estimated at 150 patients, with a study power 1- # = 0.8 and # = 0.05, assuming a 1.5-fold difference in the less frequent alleles between controls and patients.”

Q: Why gender should influence HWE?
A: We have no explanation for this. However, we believe that this result does not modify the main results and the take-home message from our study.

Q: What type of matching was done and how? There are 168 cases and 219 controls!
A: The controls were extracted from a larger cohort and were matched for age and sex with UC patients. This is now mentioned in the Methods section (1st paragraph) of the revised manuscript.

Q: In addition to unadjusted ORs in the merged Table (see above), also provide adjusted ORs for all relevant clinical variables (and for age and sex (if there is no sufficient explanation for the matching)), altogether at the same model.
For extensive UC provide unadjusted and adjusted ORs for clinical variables and for age and sex (a hypothetical matching was performed only for UC).
A: The adjusted ORs are given in the result section, last paragraph.

Q: In Results, delete the section that presents percentages, and show the unadjusted and adjusted ORs.
A: We respectfully disagree. Indeed, we think that comparing numbers of cases and providing percentages is more informative for the reader.

Q: Delete Table 4 and their respective results.
A: Table 4 and their respective results have been deleted in the revised manuscript.