Author’s response to reviews

Title: Association study of two inflammation related polymorphisms with susceptibility to hepatocellular carcinoma: a meta-analysis

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Author’s response to reviews: see over
Dear Editor,

We would like to submit the enclosed manuscript entitled "Association study of two inflammation related polymorphisms with susceptibility to hepatocellular carcinoma: a meta-analysis ", which we wish to be considered for publication in BMC Medical Genetics.

Recent study indicates inflammation and abnormal immune may promotes malignant progression in the development of cancers. Our study was performed to evaluate the two inflammation related polymorphisms, miR-146a rs2910164 C>G and miR-499 rs3746444 T>C, and the susceptibility of hepatocellular carcinoma. Its’ mechanism in regulating human bioprocess has been a hot topic since the discovery of miRNA. Existing evidence still remain controversial and inconclusive. Our meta-analysis of all eligible studies, provide more credible evidence by systematically summarizing existed data and detected the statistical significant association between miR-146a rs2910164 and the susceptibility to HCC for the first time.

We are informed that previous meta-analyses have already reviewed the potential association of the miR-146a rs2910164 polymorphism with susceptibility to HCC, but our study improves upon them in the following aspects:

(1) Most of these analysis were performed to detect cancer risk despite the difference of tissue origin. This may damage the reliability of the result due to the heterogeneity brought by various type of cancer that was unable to remove.

(2) The only study (hongxia Wang et al. in PLoS One) specified in hepatocellular carcinoma failed to detected the association between the SNP and HCC risk.(i) That may at least partly due to the fact that this meta-analysis has not been able to identify all eligible studies related to the analysis (Wang et al. in 2010). (ii) Also, after the publication of this study, two important well-designed studies (Li et al. 560 patients and 560 controls in Chinese, Kim et al. 159 patients and 201 controls in Korean) with large sample size of more ethnic groups has performed to further clarify the association.

(3) Our meta-analysis specified in HCC and by far contains the largest numbers of studies and observed objects. Thus the result successfully detected the significant association between rs2010164 and HCC.

Regard to miR-499 rs3746444, 3 meta-analysis was performed to detect this SNP polymorphism and cancer risk and the result was limited by the heterogeneity introduced by tissue orinigin. We focused on HCC in order to avoid inherent difference between cancers from distinct tissue origins, which may limit the reliability of the conclusions of the previous meta-analyses of miR-499 and cancer risk. However, none meta-analysis concerning the relationship of this SNP and specified in HCC has found.

The mechanism passways those inflammation related SNPs regulate in HCC also plays an important role in immune disease such as SLE. Our study of those two inflammatory cytokines stimulation miRNAs can also enlighten further study in other autoimmune diseases for scholars in this field.

We would like to express our thanks to Editor Aldrin for his constructive advises concerning our manuscript. We read through the paper he provided line by line and carefully fill and add the MOOSE check list to our manuscript. We also add the “Comparisons with other Meta-analysis” section to demonstrate our study has improved upon previous meta-analysis. We learn much from this process.

Each author of this manuscript has reviewed the final version of the manuscript and
approved it for publication. To the best of our knowledge and belief, this manuscript has
not been published in whole or in part nor is it being considered for publication elsewhere.
Your favorable consideration would be greatly appreciated.

Sincerely yours,

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