Author's response to reviews

Title: Association of an NFKB1 intron SNP (rs4648068) with gastric cancer patients in Chinese Han population

Authors:
renquan lu (lurenquan66@hotmail.com)
Xiang gao (gxcy2001@hotmail.com)
Yin Chen (1251487447@qq.com)
Jian Ni (jiannihome@yahoo.com)
Yongfu Yu (dearfisher@gmail.com)
Sheng Li (lisheng1996@gmail.com)
Lin Guo (jykca@sina.com)

Version: 4 Date: 10 May 2012

Author's response to reviews: see over
Dear Mr. Editor,

Thank you very much for your kind consideration on our manuscript. And we also want to thank Dr. Megan Hitchins for his enlightening instructions on bioinformatics and data analysis. We have added data-mining and other changes according to the suggestions of the reviewer. We sincerely hope to have an opportunity to publish our study in *BMC Gastroenterology*. And, we tried our best to answer the questions asked by reviewer point by point as follows:

Question 1: No attempt was made to elucidate the potential functional role of the intronic SNP eg if it might be located within an enhancer element, despite clear suggestions of how this could be done; evolutionary conservation or association with H3K9me1. Each of these pieces of information are available and readily accessible via the UCSC browsers and ENCODE databases, they just need to be looked up. In this post-GWAS era, where numerous SNP associations with various cancers have now been identified, the interest now lies in their potential functionality. A little bit of data-mining to shed some light on whether this SNP might have a direct functional role, would perk the interest of readers of this paper. It is possible, of course, that no such potential role will come to light as the SNP may simply be in linkage disequilibrium with something that is functional, however, without any attempt at mining the available database, this will not become apparent. The authors state these ideas should be put forward in their next study, but since it only requires some searches of existing freely-accessible databases, I would strongly suggest they undertake a search in the current paper so it is hypothesis-forming for their ongoing studies. *BMC Gastroenterology* has an impact factor of 2.47 and is thus worthy of some insights into findings that otherwise might seem obscure.

Answer: Thank you very much for the previous advice. We have done some research on UCSC and Encode, and we have written a section in the discussion. In this study, we would like to give our thanks to Dr. Megan Hitchins for his enlightening instruction on bioinformatics.

Question 2: The authors provide the SNP locations and hapmap in the Chinese Han population. However, it is not clear where this information has been derived from. This appears to have been downloaded from the web (maybe the HapMap or 1000 genomes project). If this is the case, a proper acknowledgement and annotation of its source needs to be provided in the figure legend. Furthermore, unless this is data they have themselves acquired, it should be presented as a Supplementary figure, otherwise its source could be misleading. Having said that, since this data is available from the general population of Han Chinese, it could serve as a second control-population from which to source genotyping data to compare with their allele frequencies in their gastric cancer population. One of the other reviewer’s comments is that the association found by Lu et al. needs to be confirmed in a second population. I agree with this in principle, although this is beyond the scope of this study and should not be required for publication of the current paper. However, the HapMap project does provide data from a second Control source that is appropriately matched for ethnic origin. If they are to include this data as a figure in the main text (as opposed to a Supplementary Figure), they should use it to show the significance of the association they found between their gastric cancer cohort and in-house Control population also holds true when compared to this second Control population.

Answer: Thank you for your advice. Exactly, our figure was drawn from CHB (Han Chinese in
Beijing, China) by the International HapMap Project (HapMap Data Rel 27 PhaseII+III, Feb09, on NCBI B36 assembly, dbSNP b126), with Haploview 4.2, to investigate the ungenotyped SNPs tagged by these four SNPs. Therefore, we have moved it to the supplement as shown in our manuscript.

Question 3 (Essential corrections): The authors may have misunderstood the previous comment regarding the Adjusted Odds Ratios. This is only applicable on multivariate analysis where multiple factors are taken into account – for instance it might be of interest to them to provide adjusted odds ratios of the SNP when age and gender are taken into account. Certainly in the tables or their legends they need to make clear which tests were performed, eg if the P value they are showing relates to a Chi-square test or multivariate linear regression. They may wish to seek statistical support to ensure their terminology is correct.

Answer: We really appreciated the reviewer for this good advice. We have asked for support from a statistical expert, so we corrected and provided these data using the multivariate logistic regression analysis in our manuscript.

In addition, we also use of the language editing service by Edanz (www.edanzediting.com/bmc1).

Thank you very much.

Best Regards,
Lin Guo