Reviewer’s report

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

Version: 3 Date: 31 March 2012

Reviewer: Megan Hitchins

Reviewer’s report:

In their revised version, the authors have addressed/corrected some of the minor comments/errors raised by the three reviewers. For example, they have now included a table describing cohort characteristics, and made some additional changes in the Discussion. While these changes are commendable, they still have not addressed some of the other queries, which may not be considered by the Editors as essential, but would nevertheless improve the overall quality of the paper.

For example:

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.

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.

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.

Final comment re Reviewer 3 and power calculations:

Reviewer 3 has stated that the numbers are too small and thus the study underpowered to reach an adequate conclusion. I do not agree with this opinion. Power and numbers of cases are inter-related. The stronger the association, the fewer the numbers of cases that are needed to identify an association. The larger the cohort, the greater the power to detect associations that may be weaker. The fact that this group has found an association in their cohort atests to its strength. However, a power calculation based on their numbers available in each cohort and a P value of 0.05 would be helpful to include in their Statistical Methods section (see Reviewer 2 comment 1 – projected power calculations were requested but have still not been provided). If a power calculation were also to be provided for the 30 cases and controls, then this would provide justification for proceeding only with the one SNP in the rest of the populatin. I agree that this interesting finding needs to be replicated in an additional cohort, but do not agree with Reviewer 3 that this needs to be performed before acceptance of the current study. The current study reports the initial finding of a SNP association with gastric cancer, which is worthy of publication with existing numbers, and other groups may wish to follow this up in due course in their own populations.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interests.