Reviewer’s report

Title: Functional promoter -31G/C variant of Survivin gene predict prostate cancer susceptibility among Chinese: a case control study

Version: 3 Date: 20 August 2012

Reviewer: Xiaoyi Huang

Reviewer’s report:

Polymorphism rs9904341-31G/C is an important SNP located in the promoter region of the survivin gene which has been implicated during cancer development by its aberrant expression. Many studies have been carried out using cancer cell lines, as well as in cancer patients, to clarify how this SNP impact on the expression level of survivin, though the correlation remains controversial so far. This study recruited 665 prostate cancer patients and 710 healthy controls to genotype the rs9904341 polymorphism with purpose of unraveling the association of this SNP with development of prostate cancer in Chinese population. By means of several statistical analyses, the author found a significantly increased frequency of CG/CC genotype among the patients, which might contribute to susceptibility of prostate cancer. Further analysis stratified with smoking condition, drinking status and family history revealed an increased frequency of GC/CC alleles in prostate cancer patients with high level of PSA. This study is novel because it is the first one implemented in Chinese population with intent to address the possible relationship between rs9904341 polymorphism and prostate cancer.

Major Compulsory Revisions:

1. The standard for smokers in this paper is different from widely accepted standard which is classified by WHO (World Health Organization. Guidelines for the Conduct of Tobacco Smoking Surveys for the General Population. Geneva, Switzerland: World Health Organization; 1983. Document WHO/SMO/83.4.). According to their guidelines, Smoking status was defined as follows: general or ever-smokers included persons who had ever smoked for at least 6 months; current smokers were smoking at the time of the survey while former smokers were not; regular or daily smokers were persons smoking at least 1 cigarette daily; and heavy smokers smoked at least 20 cigarettes daily. Quantity of tobacco consumption can be otherwise calculated by virtue of smoking index (SI), which is represented by daily consumption of cigarettes times years smoked. SI#200 is considered as mild smoking, SI=200~400 is thought as moderate smoking#while SI#400 means heavy smoking. To define the extent of smoking, either way of the above, but not subjective threshold, is acceptable when stratification analysis was performed.

2. It is acknowledged that single model will generate biases during the process of statistical analyzing on the raw data. In order to make the readout more convincing, researchers usually use multiple genetic models within groups to
access the significances of genetic variations. Based on this, the author of this study should have also included several other genetic models to strengthen the conclusions substantially.

3. In the discussion section, it is not appropriate to draw a conclusion regarding to prostate cancer based on the evidences from other diseases.

Minor Essential Revisions:
1. English drafting should be extensively polished to make this paper more readable.
2. Many typos throughout the manuscript should be corrected.
3. Abbreviations should be specified (GWAS, HWE for example).
4. Gene symbol should be italicized as well as mRNA and cDNA, whereas the corresponding protein should be written in regular format.
5. In page 4, the place where the incidence and mortality of prostate cancer occurred should be indicated and the corresponding reference should be added. Also in the same page, please specify the meaning of the figures.
6. In page 9, the section of Stratification analyses, line 8, genotypes were mixed up. The genotype should be GC/CC in the first part of the sentence and GG in the followed part.

Discretionary Revisions:
1. In table 3, the data in row “0” is duplicated to the data in row “Never”. Since they are integrated in a same table, data in row “0” is unnecessary.

**Level of interest:** An article whose findings are important to those with closely related research interests

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

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests