Author's response to reviews

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

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Author's response to reviews: see over
Dear Mr. Danolf de Jesus,

Thank you for your email correspondence dated 7 Sept 2012, in which you encouraged us to revise our manuscript entitled “Functional promoter -31G/C variant of Survivin gene predict prostate cancer susceptibility among Chinese: a case control study”.

Below please find our point-by-point responses to the reviewers’ comments. We have also attached the revised manuscript, which contains changes to the document based on the comments and suggestions of the reviewers (highlighted in red). We would like to thank the editor and the reviewers for their valuable comments and recommendations that have greatly improved the quality of this paper. We hope our responses are satisfactory.

We confirm that our manuscript has not been, or will not be submitted elsewhere for published, and all authors have read and approved the manuscript. If accepted, the article shall not be published elsewhere in the same form, in either the same or another language, without the consent of the Editors and Publisher of Biomed Central.

All authors agree with the content and the submission of this manuscript. All authors do not have any conflicts of interest.
Sincerely,

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Reviewers’ comments

Reviewer #1 (Comments to the Author):

Introduction, 1st paragraph, last sentence: “Furthermore, these conclusions were advocated by some animal studies …”

Response: Thanks a lot for the comments. We have revised this sentence as your suggestion.

Paragraph 3 of Introduction, lines 3, 4, 6: there are what appears to be PubMed Id numbers included after the references that should be removed (20166933, 2196211, and so forth).

Response: Thank you for the valuable advice. We have deleted the Pubmed Id numbers.
Materials and Methods, DNA extraction and polymorphism genotyping section: the symbols for degrees (°) are showing up as box-formatting or font issues?

**Response:** Thank you for your suggestion. The symbols for degrees were performed with Chinese format, we have revised them.

Results, Characteristics and clinical features of study population subsection, line 8:

“Among these patients, 40.9%...” – how this is worded it sounds like the authors are referring to a subset of the cases (the nonsmokers from the previous sentence); however, I believe they mean to refer to all of the prostate cancer cases.

**Response:** Thank you for the valuable advice. We have revised the sentence to indicate that the 40.9% patients represented the individuals in our study.

Discussion, first paragraph, 4th line: the gene name (survivin) has an extra ‘g’ at the end (surviving) which will not be found by spell check.

**Response:** Thank you for your comment. We have deleted the extra ‘g’.

Discussion, second paragraph, 5th line: “Growing evidence is accumulated that...” should be modified to either “Growing evidence is accumulating that...” or “Growing evidence has accumulated that...”.

**Response:** Thank you for your suggestion. We have revised the sentence to “Growing evidence has accumulated that...”
Results, Characteristics & clinical features of study population subsection: The text states that 330 of 665 men were defined as localized stage, while Table 1 states it is 390.

Response: Thanks a lot for the valuable suggestion. It was our mistake and the number should be 390. We have revised it in the line 9 of Characteristics & clinical features of study population subsection.

Results, Stratification analyses subsection: In the second sentence, they state that individuals with “GG/GC genotypes had a significantly increased risk of PCa than those with CC genotype”. However, according to the rest of the manuscript, the alternate allele is C, and it should be that those with CC/GC genotype have a higher risk than GG (this would match the data in Table 3).

Response: Thanks a lot for the comment. We are so sorry that we did not correct the mistake before submission. We have revised this sentence to “We found that individuals with CC/GC genotypes had a significantly increased risk of PCa than those with GG genotype…”

Discussion, third paragraph: Authors mention a second SNP, rs8073069 that is in LD with the SNP under study. They state that it may be the causal loci influencing prostate cancer prognosis, not the SNP they studied. The authors should comment on why they think this second SNP (rs8073069) may be the causal SNP and if there is any evidence that would support it being a functional SNP.
Response: Thanks a lot for the valuable advice. The SNP rs8073069 is in LD with rs9904341, so we only analyzed rs9904341. We didn’t express clearly, so we revised the sentence to “we only selected rs9904341 for genotyping and analyzing”.

Reference #49 does not appear to be correct.

Response: Thanks a lot for the valuable suggestion. We have searched www.ncbi.nlm.nih.gov/pubmed/ and revised the reference #49.

Reviewer #2 (Comments to the Author):

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.

**Response:** Thanks a lot for the valuable suggestion. The standard of smokers in our paper was based on the median of the number of smoking package among the smokers in the control group. We have used this standard in several published papers.

Reference:


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.

**Response:** Thank you for your advice. We found that the variant allele C of rs9904341 was associated with a higher risk of PCa. So we focused on the differences between the wild type G and variant type C and analyzed the diversity of the three genotypes, CC/GC vs. GG, and G allele vs. C allele to discuss the influence of gene mutation for PCa. All the results were showed in table 2.

**Response:** Thank you for your comment. We referred the association between the

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

**Response:** Thank you for your comment. We referred the association between the
polymorphism of survivin and other malignancies to indicate that rs9904341 would effect the risk of PCa. We have revised the discussion section in page 11.

*English drafting should be extensively polished to make this paper more readable.*

Many typos throughout the manuscript should be corrected. Abbreviations should be specified (GWAS, HWE for example). Gene symbol should be italicized as well as mRNA and cDNA, whereas the corresponding protein should be written in regular format.

**Response:** Thank you for your valuable advice. We have specified the abbreviations and revised the fonts of gene symbols and proteins.

*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.*

**Response:** Thank you. The data of incidence and mortality of PCa was collected in 2010 in the U.S. We have indicated this in page 4.

*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.*

**Response:** Thank you for the valuable advice. We have correct this mistake in page 9.
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.

Response: Thank you for your suggestion. We have deleted the row “0” in table 3