Author's response to reviews

Title: The hOGG1 Ser326Cys Polymorphism and Prostate Cancer Risk: A Meta-Analysis of 2584 cases and 3234 controls

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Author's response to reviews: see over
Dear Editors

Thank you for your letter and for the reviewers’ comments concerning our manuscript entitled “The hOGG1 Ser326Cys Polymorphism and Prostate Cancer Risk: A Meta-Analysis of 2584 cases and 3234 controls” (ID: 2062343863563559). We are very grateful to the reviewers for their positive and helpful suggestions. We have studied comments carefully and have made correction which we hope meet with approval.

Please find an amended version of the manuscript with changes highlighted in blue and a point-by point response to the reviewers’ comments (below).

Please also see below for a response to the Editor’s comments. We are pleased that the reviewers agree that the manuscript will be a valuable contribution to the literature in this area.

We would like to express our great appreciation to you and reviewers for comments on our paper. Looking forward to hearing from you. We look forward to seeing our manuscript in your journal.

Thank you and best regards.

Yours sincerely,

Yong Xu

Response to Editor’s comments

1) Please adhere to PRISMA.

**We will adhere strictly to PRISMA.**

We would be grateful if you could address the comments in a revised manuscript and provide a cover letter giving a point-by-point response to the concerns.

**A point-by-point response has been provided below.**

Please also highlight (with ‘tracked changes’/coloured/underlines/highlighted text) all changes made when revising the manuscript to make it easier for the Editors to give you a prompt decision on your manuscript.

**The changes have been highlighted in blue.**
Reviewer 1

Reviewer's report
Title: The hOGG1 Ser326Cys Polymorphism and Prostate Cancer Risk: A Meta-Analysis of 2584 cases and 3234 controls
Version: 4 Date: 12 August 2011
Reviewer: Sevtap Savas

Reviewer's report:
Zhang et al. describes a meta-analysis on the OGG1- Ser326Cys polymorphism and its association with susceptibility to prostate cancer. The manuscript is succinct, generally written well, both the title and the abstract convey the work undertaken by the authors and the major findings of the study.

We are pleased that this reviewer feels that the manuscript is succinct, generally written well, both the title and the abstract convey the work undertaken by the authors and the major findings of the study. We are very grateful to the review for her helpful comments regarding the manuscript and we feel that the suggested changes have improved the standard of the paper significantly. Please find below details of how each point has been fully addressed.

1. This reviewer is not very familiar with some of the statistical tests performed in the manuscript. Assuming that not all of the readers would also be familiar with them, the manuscript would benefit from briefly describing some of the tests. For example, why the heterogeneity test was used? What does it mean to have heterogeneity between studies? For example, for the Caucasian populations,“...there was a significant between-study heterogeneity in all the comparisons...”. How does this affect the authors’ analysis and conclusions?

Information regarding those problems above has been added to the manuscript. We agree that this has strengthened the manuscript.

2. 2. Pages 6-7: This section may benefit from a clear indication of populations examined when presenting the statistical results. For example, the first part of the Results, is it for the entire 2584 cases and 3234 controls? Similarly, the second part of the Results where additive, recessive, dominant, and Cys vs Ser comparisons are mentioned, we need to look at the Figures to understand that these results are for the mixed populations; can the population information be added to the text as well? Also, the last paragraph of the results is not clear. For example, the sentence with“ except for the dominant model comparison.......” Please make sure that the readers understand that the authors do not show this data in Figures (for example, add at the end of the sentence (data not shown). In “Cys versus Ser (OR: 0.88........”, please specify that it is the Cys allele versus Ser allele comparisons.

These errors have now been amended.

3. Page 9 and 10: this reviewer would prefer statements such as “statistically significant (or insignificant) increase or decrease in Pca risk”, rather than “trend”, which may confuse some readers.
4. Page 9: How can we explain that significant decrease in Pca risk for mixed populations? Is it because of the large sample size in this group, for example?

**The explanation has now been addressed in the manuscript.**

5. Page 3. Define PCa before using the abbreviation.

**PCa has now been defined before using the abbreviation.**

6. OGG1-Ser326Cys polymorphism is referred as a functional polymorphism in the manuscript; can the authors add information on the functional consequences of this polymorphism?

**Information on the functional consequences of this polymorphism and 4 references have now been added.**


7. Page 4. The first sentence of Methods; “.....cancer” or in Medline……”. Is the“or” extra here or is there a word after which was omitted in the text?

**The“or” has now been removed.**

8. Page 6: Can the heading “Meta-analyses Databases” be changed for something more reflective of the contents of this section?

**The heading “Meta-analyses Databases” has been changed for “Meta-analyses and Evaluation of Heterogeneity and Publication bias”**
9. Page 6: “The Cys/Cys genotype carriers did have an increased prostate cancer risk...”. The p-value is not significant at 0.05 level, thus the above statement may confuse some readers. The authors may rather state that there was no statistically significant difference in Pca risk between the patients with these two genotypes.

The sentence has been amended as suggested.


The sentence has now been revised.

11. Page 5: “Then the relationship between allele and susceptibility to Pca was examined”. In this sentence, the authors would like to specify it is the comparison of Cys allele with Ser allele. This will help understanding the results on Page 7.

“Then the relationship between allele and susceptibility to Pca was examined” has now been specified.

12. Page 5: Data extraction section: please add the statistical data to the extracted data.

The statistical data have now been added to the extracted data.

We have addressed all the comments above and are very grateful to you for the helpful suggestions. We appreciate for your warm work earnestly, and hope that the correction will meet with approval.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests:
I declare that I have no competing interests.

Reviewer 2

Reviewer's report
Title: The hOGG1 Ser326Cys Polymorphism and Prostate Cancer Risk: A Meta-Analysis of 2584 cases and 3234 controls
Version: 4 Date: 21 August 2011
Reviewer: Helene Choquet

Reviewer's report:
In this report, H. Zhang and colleagues assessed the association between the Ser326Cys (rs1052133) polymorphism of human 8-oxoguanine DNA glycosylase (hOGG1) gene and the risk of prostate cancer by combining 8
independent studies in a meta-analysis including 2584 cases and 3234 controls. This current study do not include new data, however this meta-analysis is relevant. The paper is globally clear but the discussion subsection might be improved.

We are pleased that this reviewer feels that our article was important in its field. The authors are grateful to the reviewer for the helpful comments that we feel have improved the quality of the manuscript. Please find below details of how all comments have been fully addressed.

The authors may consider to address the following concerns.

Minor points:
1. The Authors should specify at least one time the official rs number corresponding to the Ser326Cys Polymorphism (= rs1052133).

We have now specified the official rs number corresponding to the Ser326Cys Polymorphism (= rs1052133).

2. The Authors should detail the abbreviation “PCa” at the beginning of the Background section and then replace “Prostate cancer” by “PCa” in the rest of the text. This abbreviation should be also added in the List of abbreviations.

PCa has now been defined before using the abbreviation and added in the List of abbreviations.

3. In the Background subsection, following the sentence “In the past years, the hOGG1 Ser326Cys polymorphism has attracted widespread attention”, the authors should specify that this polymorphism is functional.

We have now specified that the hOGG1 Ser326Cys polymorphism is functional.

4. In the Results subsection, the sentence “In the stratified analysis by ethnicity, no significant heterogeneity was detected we detected in all the comparisons in mixed population” is not clear. This sentence should be reformulated.

The sentence has now been reformulated.

5. In the Results subsection, the Authors should specify that results in the sentence “There was significant association ... except for the dominant model comparison” correspond to the Mixed population.

This has now been amended.

6. The “Begg’s funnel plot and Egger’s test” should be added in Statistical Analysis, methods subsection
The “Begg’s funnel plot and Egger’s test” has now been added in Statistical Analysis, methods subsection

7. The authors might specify the name of the model “Cys vs Ser”. Allelic model?

“Cys vs Ser” has now been specified.

8. In my view, the two first paragraphs of the Discussion subsection (from “Several DNA repair pathways ...” to “… to explore a robust estimate of the effect of this polymorphism on prostate risk”) are most background (and not discussion). The authors should simplify and reformulate the beginning of the discussion part.

The two first paragraphs of the Discussion subsection has been amended as suggested.

Special thanks to you for your good comments. We appreciate for your warm work earnestly, and hope that the correction will meet with approval.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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.