Author's response to reviews

Title: C-reactive protein genetic variant is associated with diabetic retinopathy in Chinese patients with type 2 diabetes

Authors:

Danfeng Peng (pdandanf@sjtu.edu.cn)
Jie Wang (jiediana113@126.com)
Rong Zhang (rongzhang11@hotmail.com)
Shanshan Tang (tss8235078@163.com)
Feng Jiang (jiangfeng1031@hotmail.com)
Miao Chen (chenmiao2011@126.com)
Jing Yan (yanjing@sjtu.edu.cn)
Xue Sun (443782999@qq.com)
Tao Wang (502472450@qq.com)
Shiyun Wang (695107677@qq.com)
Yuqian Bao (byq522@163.com)
Cheng Hu (alfredhc@sjtu.edu.cn)
Weiping Jia (wpjia@sjtu.edu.cn)

Version: 3 Date: 13 February 2015

Author's response to reviews: see over
Dear Editor and reviewers,

Thank you very much for your kind positive comments about our work and for the critical reading and critiques of this manuscript, which we found to be greatly helpful in our revising and improving this manuscript. These critiques are addressed as follows and as highlighted in the revised manuscript.

Thank you again for your efforts.

Sincerely,
Weiping Jia, M.D., Ph.D.
Director, Professor of Medicine
Shanghai Diabetes Institute, Shanghai Key Laboratory of Diabetes Mellitus, Shanghai Clinical Center for Diabetes, Shanghai Jiao Tong University Affiliated Sixth People’s Hospital, Shanghai, China
Editor's Additional Request:

1. Requesting for Copy-Edit
   - We recommend that you ask a native English speaking colleague to help you copyedit the paper. If this is not possible, you may need to use a professional language editing service.
   
   Response: Thank you for your suggestion. We have carefully copyedited the manuscript.

Referee 1
Reviewer: Parimala Narne
Reviewer's report:

The authors need to make these compulsory revisions.

1. The location of the tagging SNPs should be given with reference to CRP ‘gene’.
   
   Response: Thank you for your comment. We have added a column named ‘reference position’ in Table 2 showing the location of SNPs with reference to CRP.

2. With reference to the response to the second comment, the authors mentioned that endothelial dysfunction and atherogenesis play an important role in the pathogenesis of DR. However, no suitable references have been provided.
   
   Response: Thank you for your comments. We have added the reference papers.

3. ‘DR grade was based on the level of the more severe eye’. The sentence is ambiguous and has to be removed. In turn, the list of ocular changes associated with DR and its severity have to be mentioned.
   
   Response: Thank you for your comments. We have modified this part in the revised manuscript. We wrote, ‘A five-stage disease severity classification for DR was applied according to the International Classification of Diabetic Retinopathy [21]: no apparent retinopathy (no abnormalities), mild nonproliferative diabetic retinopathy (NPDR) (microaneurysms only), moderate NPDR (more than just microaneurysms but less than severe NPDR), severe NPDR (more than 20 intraretinal hemorrhages in each of 4 quadrants and/or definite venous beading in 2 quadrants and/or prominent intraretinal microvascular abnormalities in 1 quadrant and no signs of proliferative retinopathy), or proliferative diabetic retinopathy (PDR) (neovascularization and/or vitreous hemorrhage and/or preretinal hemorrhage). DR grade was evaluated for both eyes, and higher grade was recorded for each person’.

4. Details concerning the number of patients in the respective DR categories need to be mentioned in the materials and methods section.
   
   Response: Thank you for your suggestion. We have added the details in the ‘methods’ section. We wrote, ‘Of the 618 patients with DR in this study, there were 395 with mild NPDR, 103
with moderate NPDR, 84 with severe NPDR, and 36 with PDR’.

5. Line 157: ‘Rs’?
Response: We have changed it to ‘rs’.

6. The manuscript needs to be thoroughly checked for scientific notations, syntax and spelling errors.
Response: We have checked the manuscript carefully. Hope it is better now.

7. Table 1: Remove ‘samples’ and place the number of patients enclosed in brackets (as n=593) under the respective categories. Remove ‘subjects with’. The demographic and anthropometric traits should be grouped under ‘Characteristic’.
Response: thank you for your careful comments. We have modified this table according to your suggestions.

Referee 2
Reviewer: Daniel Petrovic
Reviewer's report:
The revised paper “C-reactive protein genetic variant is associated with diabetic retinopathy in Chinese type 2 diabetic patients” is well written research paper. In their study on a large sample of cases and controls they demonstrated that CRP rs2808629 was associated with DR in the Chinese type diabetic patients.
The authors improved the paper as suggested.
Response: Thank you very much for handling this manuscript and helping us improving this study.

Referee 3
Reviewer: Monika Buraczynska
Reviewer's report:
Major Compulsory Revisions :
None.
Minor Essential Revisions :
None.
Discretionary Revisions :
1. In the Methods section : The part concerning the number of patients with DR still needs to be clarified. Since in the study population out of 1,018 patients with T2DM 618 (61 %) had diabetic retinopathy, this number is much higher than the prevalence of DR reported for
Chinese population. The Authors’ explanation suggests that their subjects were not consecutive patients from the Shanghai Diabetes Database, but intentionally selected for affected or not affected with DR (especially that all those without DR had diabetes for over 10 years). This should be clearly stated in the Participants subsection of Methods, to avoid confusion.

Response: Thank you for your kind suggestion. We are sorry we had not stated it clearly in the previous manuscript. We have modified this part in the revised manuscript. We wrote, ‘Of these patients, 618 were diagnosed with DR, 400 were patients without DR, considered as cases and controls for DR, respectively. For controls selection, patients with diabetes for over 10 years were chosen deliberately’.

2. As for the information on macrovascular complications in the study subjects, is it really that hard to obtain these data? Cardiovascular disease is a very common comorbidity in patients with diabetes so this information is certainly included in the Shanghai Diabetes Database.

Response: Thank you for your comment. Information on macrovascular complications was included in the medical records of patients. However, as we have not systemized this part of data, it is not available for further analysis now.

3. The Authors state that they genotyped 438 non-diabetic subjects with rs2808629 and compared the results with three other studies of Asian populations. These information should be mentioned either in the Results or Discussion section.

Response: Thank you for your comment. We have added this point in the ‘results’ section. We wrote, ‘In addition, rs2808629 was genotyped among 438 subjects with normal glucose regulation. The distribution of this SNP was similar to those reported in three other studies of Asian populations in the HapMap database (G allele frequency 0.453 vs 0.419/0.297/0.537), indicating that there was no technical error in this study.’