Author's response to reviews

Title: Associations of Complement Factor B and Complement component 2 Genotypes with Subtypes of Polypoidal Choroidal Vasculopathy

Authors:

Koji Tanaka (tanaka.koji@nihon-u.ac.jp)
Tomohiro Nakayama (nakayama.tomohiro@nihon-u.ac.jp)
Ryusaburou Mori (ryu-m@sa2.so-net.ne.jp)
Naoyuki Sato (n-satou@hsri-ei.co.jp)
Akiyuki Kawamura (kw-eye-c@xb3.so-net.ne.jp)
Mitsuko Yuzawa (yuzawa.mitsuko@nihon-u.ac.jp)

Version: 4 Date: 17 May 2014

Author's response to reviews: see over
May 17, 2014

Editor-in-Chief
BMC Ophthalmology

Dear Editor,

Enclosed is the revised version of our manuscript entitled “Associations of Complement Factor B and Complement component 2 Genotypes with Subtypes of Polypoidal Choroidal Vasculopathy” (reference ID number 6905275981236409R3), which we are submitting for possible publication in BMC Ophthalmology.

We appreciate the review of our previous submission of this manuscript and the helpful comments sent on May 10, 2014. We have revised the manuscript based on the reviewers’ comments and have enclosed a list of responses and the changes made. My coauthors and I believe that our revisions adequately address all of the concerns raised by the reviewers, and hope that the revised manuscript is now suitable for publication in BMC Ophthalmology.

Sincerely yours,

Tomohiro Nakayama, M.D.
Division of Laboratory Medicine, Department of Pathology and Microbiology
Nihon University School of Medicine
30-1 Ooyaguchi-kamimachi, Itabashi-ku, Tokyo 173-8610, Japan
Tel.: +81-3-3972-8111 (Ext. 8205); Fax: +81-3-5375-8076
E-mail: nakayama.tomohiro@nihon-u.ac.jp

To the Editor:

Thank you very much for your helpful comments. We have revised our manuscript accordingly. Revisions are underlined in the text.
1) What is the inclusion criteria of tAMD, PCV, RAP and control?
   →We noted the inclusion criteria for the tAMD, PCV, RAP and control cases on Page 4, lines 11-15.

2) There were 376 PCV cases in the first part, but only 282 PCV cases were classified into subtypes in the second part. Whether the 282 PCV cases came from the 376 PCV cases? Why the author did not include all 376 PCV cases in the second part?
   →Why we did not include all 376 PCV cases is explained on Page 4, lines 17-20.

3) There is huge difference of rs2072633 in PCV in Table 2 and Table 5. The frequency of GG, GA and AA genotype is 36.4%, 47.3% and 16.2% in Table 2, 17.7%, 46.5% and 35.8% in Table 5. Did the author revert the alleles?
   →Reviewing the data revealed the AA and GG genotypes of Table 2 to be reversed. We have corrected accordingly, including the statistics. We thank the reviewer for noticing this error.

4) Comparing Table 2 and Table 5, the SNPs in tAMD is similar to Typical PCV, but different from polypoidal PCV. For example, the GG, TG and TT frequency is 88.4%, 11.2% and 0.4% in tAMD, 88%, 11% and 1% in Typical PCV, 95%, 5% and 0% in Polypoidal PCV. Therefore, it is typical PCV but not polypoidal CNV that is closer to tAMD.
   →As you pointed, we could not state with certainty that tAMD was similar to polypoidal CNV in this study. However, when we consider the reason for typical PCV having no associations with the SNPs, our hypothesis is that polypoidal CNV and tAMD are similar. This stems from the results of our prior study and the histopathological characteristics of PCV.
   We added these comments to P8, lines 14-23.

5) The frequencies in Table 5 and Table 8 should keep one decimal number.
   →We have complied with this suggestion.

6) I think that correction for multiple comparison is still required in logistic regression. I would like to suggest the authors to expand their sample size which may result in smaller p value.
   →We also added the results of Bonferroni correction to Table 3 and Table 6. We added the comment that the statistical results did not reach significance after Bonferroni
correction. We hope to add more subjects in a future study and thereby improve the statistical significance of our results.