Reviewer’s report

Title: Association of the RYR3 gene polymorphisms with atherosclerosis in elderly Japanese population

Version: 2 Date: 2 September 2013

Reviewer: Makoto Daimon

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General comments:
The authors examined an association between Ryanodine receptor 3 (RYR3) gene polymorphisms and atherosclerosis determined by macroscopic evaluation using 1391 autopsy cases of a general hospital and found significant association between them. This finding seems to be confirmatory of those observed in several previous GWAS studies with Caucasian subjects. However, the authors examined such association in other ethnic population, or Japanese, and also extend the analysis with other SNPs spanning 31.1 kb region including the Tag SNPs originally reported. Therefore, this study seems to an extended study of the previous ones, and, thus, provide interesting information on this field of interest. However, there are several points, which should be considered for making the manuscript appropriate, and, thus, described below.

Specific comments

Major Compulsory revision:
1. the number of subjects the authors claimed was 1391. However, the number of subjects evaluated for atherosclerosis, or common carotid artery regions appeared to be less, or 1374 according to Table 2. Therefore, better correct the number to the one actually used for the analysis.

2. Related above, the call rate of each SNP appeared to be less that that of the Tag SNP, rs 2229116. The least was that of SNP rs 2132207, that is 1352. These differences may reflect to the results for haplotype analysis. So, please, describe not only the frequencies but the number of each major haplotype and also the others combined in Table 1.

3. Also, the atherosclerosis appeared to be evaluated not in all the subjects enrolled. Especially, PAI was evaluated about 10% less subjects that common carotid artery. These facts should be described in “Methods” properly, and, better, also the possible influence in “Discussion” as well.

Minor essential revision

1. In the last paragraph of “Results”, writing of Table 3 should be “Table 4”

2. In Table1, adjust the number of decimal place.

3. In Table 2. What “none” mean. Not significant? Please, describe the number here, even though those were not significant.
Discretionary revisions
1. English be better revised.

**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:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I have no conflict of interest in regard with the manuscript.