Reviewer's report

Title: Gene sequence variations of the platelet P2Y12 receptor are associated with coronary artery disease.

Version: 1 Date: 9 July 2007

Reviewer: Dirk Sibbing

Reviewer's report:

General

Genetic polymorphisms in platelet receptor genes may in part explain part of the individual risk for atherosclerotic disease. The H2 haplotype of the P2Y12 receptor has been shown to be associated with peripheral arterial disease and an increased ADP-induced platelet aggregation ex vivo in healthy volunteers.

Cavallari and co-workers sought to assess in a large population of 1378 unrelated patients the impact of the H1/H2 haplotype on coronary artery disease (CAD). The study population comprised 991 patients with angiographically determined CAD and 387 patients without CAD. The major results of the study were that (a) H2 haplotype carriers were more frequent in the CAD group and that (b) this association was strongest in the non smoking population. Based on their results the authors conclude that gene sequence variations of the P2Y12 receptor are associated with the presence of CAD.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

None

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. The authors state that consecutive patients were included into the study. However, gender distribution and the different mean age of both patient groups (CAD and CAD-free) might be the result of inhomogeneity between the two groups. The authors should comment on this and should furthermore add a flow chart to the Methods section of their manuscript describing the generation of their study population.

2. Gender distribution differed significantly in both groups (79.8% vs. 65%; P<0.001) and gender specific differences for associations of genotypes with a clinical phenotype have been observed in other studies (e.g. McDermott et al. Circulation. 2005;112:1113-1120; Wu et al. Ann Hum Genet. 2007 Jul;71:519-25.). The authors should comment on this and should add a separate
gender specific calculation (male and female) for haplotype distribution and CAD association.

3. In addition to genotype distribution allele frequencies should be presented in the Results section.

4. The heterozygous genotype (T/C) of the minor allele C was found more often in CAD group, whereas the homozygous genotype (C/C) of the minor allele was found more often in the CAD-free group. The authors should comment on this (lack of gene dose effect etc.).

5. Background section (line 1): “atherosclerotic” should read “atherosclerotic”

6. Background section (line 5): the words “high risk” can be deleted.

7. Discussion section (line 15): the sentence “…and smokers exhibit higher platelet P2Y12” should read “… and smokers exhibit higher P2Y12 expression”.

8. Table 1: “Oligonucleotyde” should read “Oligonucleotide”

Discretionary Revisions (which the author can choose to ignore)

None

What next?: Accept after minor essential revisions

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.