Reviewer’s report

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

Version: 1 Date: 9 May 2007

Reviewer: Robert F Storey

Reviewer’s report:

General
Cavallari et al have genotyped samples from a previous study of subjects who have undergone coronary angiography, assessing the relationship between a P2RY12 SNP that has previously been reported to define H1 and H2 haplotypes in this gene and presence or absence of angiographic evidence of coronary artery disease. They have concluded that the H2 haplotype is associated with an increased risk of coronary artery disease.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
The authors should state whether the determination of p values for interaction, which identified non-smoking H2 carriers as being at higher risk of CAD, incorporated an adjustment for multiple analyses and whether this interaction remained significant after such an adjustment. This is particularly important since the OR for the association between H1/H2 haplotype and CAD is less than the OR which the study was powered to assess for.

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

Discretionary Revisions (which the author can choose to ignore)
The small study by Fontana et al suggesting an associated between P2RY12 genotype and PAD raises an interesting hypothesis but is not conclusive. Some investigators have failed to confirm the findings of Fontana et al that the H1/H2 haplotype influences platelet reactivity (e.g. Hetherington SL et al), which undermines the rationale for this haplotype to influence risk of atherosclerotic disease. In the 14th line of the Discussion, I suggest insert ‘might’ before ‘lead to an increased atherothrombotic risk....’ and refer to data that questions the relevance of the H1/H2 haplotype to provide a balanced discussion.

What next?: Accept after minor essential revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests