Reviewer's report

Title: The E670G SNP in the PCSK9 gene is associated with polygenic hypercholesterolemia in men but not in women

Version: 2 Date: 24 May 2006

Reviewer: AJ Marian

Reviewer's report:

General

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

1. Authors should provide a formal power calculation. As any other null study, regarding the lack of an association between the genotypes and plasma LDL-C, the possibility of type II statistical errors need to be excluded (ï¢ error).

2. The potential confounding effects of lipid lowering agents should be analyzed. The number of patients on statins and other lipid lowering agents should be given. Analysis should be repeated in those not on lipid-lowering medications.

3. Please expand table 1 to include additional demographic and clinical characteristics of the study population, including prevalence of other risk factors for atherosclerosis, history of coronary artery disease, medications (particularly statins), ethnic background, etc.

4. Please specify the number in parenthesis in Table 1 mean.

5. Please provide the N for each group in Figure 1.

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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)

6. Sex-dependent association between 50th percentile of LDL and genotypes were noted in secondary data analysis. It does not appear to be based on a priori hypothesis. Authors provide for a plausible biological basis for the observed sex-dependent effect.

1. The baseline plasma LDL-C levels also should be reported and analyzed.

2. Please comment whether and how the genotyping method was validated.

3. First page of the background, line 3rd from the bottom. Please clarify â€œI475VGF SNPâ€

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Discretionary Revisions (which the author can choose to ignore)

1. The study is restricted to analysis of a single SNP, which is not sufficiently comprehensive of the locus information. Authors are encouraged to expand the genotyping to encompass the common haplotypes of the locus.

What next?: Reject because too small an advance to publish

Level of interest: An article of limited interest

Quality of written English: Acceptable
Statistical review: No

Declaration of competing interests:

No conflict of interest.