Reviewer’s report

Title: Analysis of positional candidate genes in the AAA1 susceptibility locus for abdominal aortic aneurysms on chromosome 19

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Reviewer: Per Eriksson

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In the present paper, the authors have conducted a further evaluation of the 19q13 AAA1 locus previously identified by a genome-wide linkage analyses. Nine candidate genes were selected based on their functions and 41 SNPs were genotyped in 394 cases and 419 controls.

Major comment:

The main weakness of this study is the approach of selecting nine candidate genes based on their known function for further SNP analyses in a region containing more than hundred genes. Genes that have been identified by previous genome-wide and unbiased approaches e.g. CDKN2AB/Anril and DAB2IP, would probably not have been chosen in a pre-selection of candidate genes. A dense genotyping over the whole region would significantly increase the interpretation of the study.

Major Compulsory Revisions

Sequencing identified several SNPs in the PEPD and CD22 genes but these were not analyzed in the larger AAA and control cohorts. Were any of these SNPs associated with AAA?

The in silico protein structure prediction and the prediction of miRNA binding sites are premature and do not add to the interpretation of the paper.

Was the analysis of the selected 41 SNPs corrected for multiple testing?

Minor Essential Revisions:

It is unclear how the gene expression profiles were used in the selection process. What criterias were used?

It is difficult to interpret the immunohistochemical staining. The localization of the sections should be defined in the figures. Intima, media, adventitia, intraluminal thrombus etc? How was fibroblast and myofibroblast identified? Staining of the B-cell marker CD22 in AAA tissue has been described previously.

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