Reviewer’s report

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

Version: 1 Date: 26 August 2010

Reviewer: Janet Powell

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The work presented here is the awaited follow up to earlier publications from this group, focusing on the 9q13 region.

1 It would be very helpful to have a map of the region studied to accompany the manuscript

2 The manuscript is long and probably would become much more readable if the focus was restricted to PEPD rather than PEPD and CD22 as presently. There are several reasons for this including the unconvincing power of any association with CD22 given the amount of multiple testing conducted, unclear mechanistic associations and no evidence of enhanced B-cell expression of this protein in aneurysm tissue (it is well recognised that aneurysm tissue is infiltrated with B cells whereas normal aorta is not).

3 The abstract states that 3 genes were sequenced in 23 individuals. At other points in the results 21 and 25 individuals are mentioned. Were these all AAA cases or were they mixed cases and controls and why the inconsistency in numbers? Again in the abstract, given the multiple testing the nominal associations should be those with a p value much less than 0.05. It is not clear whether the multiple testing was considered in the power calculation or whether, in reality, a much larger cohort of cases and controls is necessary.

4 There is no demographic data for the 7 control aortas used for immunohistochemical studies.

5 I wonder whether the 3 genes selected for sequencing were chosen rationally? After all it is perhaps more important to identify novel pathways associated with AAA than it is to find supporting data for candidate genes. Cost is not always a valid reason to justify the scientific approach. Please can the authors comment.

6 An A to T amino acid change is clearly non-synonomous but can the same be said for an L to F amino acid change? Both L and F have bulky hydrophobic side chains.

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

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the
statistics.

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