Reviewer’s report

Title: MicroRNA Expression Signature in Human Abdominal Aortic Aneurysms

Version: 1 Date: 18 April 2012

Reviewer: Jan Lindeman

Reviewer’s report:

Thank you for giving me the opportunity to review this well-written and timely paper. The authors rightly point out that the mechanisms of AAA formation; progression and rupture are unknown as such a study as this is relevant. Yet, an inherent and unavoidable limitation of this study is the fact that all AAA samples were from patients with advanced disease. As such data from the study can not be extrapolated to understanding of processes underlying AAA formation. A second, and again unavoidable limitation of the study is that the findings can not differentiate between cause and consequence. I.e. do the findings from the study reflect involvement and activation of for example apoptotic pathways or do they merely reflect a clear differences in cellular content (i.e. increased cytotoxic T-cells and NK cell content in AAA). These issues should be brought up in the discussion.

Another point is whether correction for multiple testing is indicated, I am surprised by the extremely low number of differentially expressed miRNAs in the AAA and control samples. Although the authors already performed the mildest correction for multiple testing it presumably introduces a major type I statistical error. Given the fact that the authors performed independent validation of their results a much more liberal correction appears to be more appropriate (although I realize that this would not allow for a detailed bio-informatics approach as performed in the paper). Do the differentially expressed (before correction) fit in distinct pathways??

Minor points:
- I am surprised by the fact that PCR failed to confirm the results for the up regulated miRNAs, may this relate to a problem with the use of U6 for normalization
- in the discussion the authors point to an apparent paradox between positive regulation of apoptosis and SMC proliferation. Isn’t this a logical consequence which indicates accelerated SMC turn-over
- many theoretical pathways have been labeled on basis of the context of their initial clustering. Could the authors relate response to organic stimulus etc. to mechanistic pathways involved in AAA?

Level of interest: An article of outstanding merit and interest in its field
Quality of written English: Acceptable

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