Reviewer's report

Title: Genetic Network Identifies Novel Pathways Contributing to Atherosclerosis Susceptibility in the Innominate Artery

Version: 2  Date: 5 May 2014

Reviewer: Ping Zhang

Reviewer's report:

In the manuscript, Albright et al. expands knowledge of the complex process of atherosclerosis by applying a system-based approach. The aim of the work is interesting. They identified 1 module of co-expressed genes that are related to atherosclerosis, which contains a well-studied putative candidate gene Cd44 and a number of previously uncharacterized genes in a complex transcriptional network. The findings of the work may be useful (e.g., potential novel targets). Also the work demonstrates the utility of a network approach to prioritize genetic candidates and to identify potential mechanisms for candidate genes identified in QTL studies. The methods could be used in other problems.

However, some Minor Essential Revisions should be addressed by the authors:

1. Methods and Results parts of the manuscript are not well-organized and not easy to understand. You should provide a flow chart (or a bullet paragraph) to overview the series of bioinformatics approaches you conducted (with their inputs/outputs) before the detailed description.

2. Please provide more detailed information on how you conducted analytics. Otherwise, the readers (especially those who are not familiar with the tools you used) are hard to replicate the experiments.
   e.g., 1> how you used WGCNA to divide 4485 genes into “10-co-expression modules”? Why you set # of clusters as 10? Are there any other parameters for WGCNA software?
   2> how you used SEM to “confirm that Cd44 is the most likely candidate gene”? For instance, what was the model? What were the chi-square statistics and other model fit statistics? What were the estimates of model parameters? What is the difference between NEO score (page 14 line 2) and LEO score when you used NEO software?

3. Please double check your manuscript and make sure the data is correct and consistent.
   e.g., in page 12 line 10, you mentioned “top 10 most connected genes in this module”. However, in the following context and in Table 2, you only listed 9 genes.

4. The manuscript contains some minor typos or grammatical errors, please double check.
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