Reviewer's report

Title: Genetic polymorphisms at SIRT1 and FOXO1 are associated with carotid atherosclerosis in the SAPHIR cohort

Version: 1 Date: 15 July 2014

Reviewer: Sébastien Robiou du Pont

Reviewer's report:

In this manuscript, Kedenko et al. assessed the predisposition of 5 SNPs in FOXO1 and 6 SNPs in SIRT1 individually and their respective haplotypes with different traits related to atherosclerosis risk in the SAPHIR population. The authors identified that a subset of the SNPs was associated with common carotid intima-media thickness and with a higher effect size for the women.

Major Compulsory Revisions:

1- The main problem in this publication is the SNP selection. Indeed, the authors selected their SNPs using ‘SNP tagger’ but they found SNPs in high linkage disequilibrium in both genes leading to redundant results. Could you please present results only for the most associated SNP and not for all the SNPs?

2- In the ‘Statistical analysis’ section, the authors explained that the beta estimates were reported in the original scale whereas the regressions were log transformed. Could you please provide more explanation about how the back transformation of the betas had been performed?

3- In the ‘Introduction’ and ‘Discussion’ sections, please use the international nomenclature in an appropriate manner to differentiate gene and protein.

4- The authors mentioned that SITR1 and FOXO1 genes interacted with each other, if an interaction between the genes are already known why they did not try to perform SNP x SNP interaction analysis.

Minor Compulsory Revisions:

1- In the ‘Statistical analysis’ section, could you please give in this section the Bonferroni threshold used.

2- In the ‘Results’ section, could you please explained which threshold you used to estimate the number of loci for each gene especially for the FOXO1 gene.

3- In the ‘Results’ section, could you please check the sentence, ‘(3 for the SNPs at the FOXO1 … at the SIRT1 gene locus)’, you probably inverted the gene names.

4- In the ‘Haplotype analysis’ section, could you please present the haplotype results in a table.

5- In the second part of the ‘Haplotype analysis’ section, could you please precise the IMT (common carotid IMT).
Level of interest: An article of importance in its field

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