Reviewer's report

Title: WWOX gene is associated with HDL cholesterol and triglyceride levels

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Reviewer: Gang Shi

Reviewer's report:

The authors investigated the associations between SNPs in WWOX region with HDL cholesterol and triglyceride phenotypes. The association was previously reported by Lee et al., and this study tried to replicate it with independent data. The results presented in the paper are novel and interesting, the paper was well written. There are still some issues need to be addressed or discussed:

1. The results presented in this paper need to be discussed under the context of current GWAS findings. For example, adjacent region on chromosome 16q22 has been reported to be associated with HDL by multiple GWAS (Aulchenko et al., 2008; Kathiresan et al., 2008; Sabatti et al., 2008; Willer et al., 2008), which is about 10 Mbp away from the WWOX gene. It is of interest to discuss if the association between HDL and WWOX is due to long-range linkage disequilibrium or they represent two independent signals.

2. WWOX was found to be associated with left ventricle wall thickness phenotype (Vasan et al., 2009), which is cardiac structure and function trait. This biological relevance needs to be introduced in the background section.

3. Since 1,045 SNPs were tested for association in this study, multiple testing issue needs to be dissussed or addressed.

4. The authors mentioned their experiment on genotype imputation using genotyped SNPs from 250k NspI chip and CEU HapMap samples. It is not clear how the 96.7% concordance rate was derived, e.g., if they were based on the SNPs that were both genotyped and imputed, which are expected to have high concordance rate.

5. Note that the sample size in this study is smaller than the discovery sample of SNP rs2548861, it would be interesting to discuss the power of replication with the sample used in this study.

6. Many imputed SNPs were used in this study, and most significant results were from imputed SNPs, it would be useful to include some information about the imputation quality in Supplementary Table 1-3.

7. Page 3, line 5: “heriTable” should be “heritable”.

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.