Reviewer's report

Title: Association of the apolipoprotein A5 gene -1131 T>C polymorphism with fasting blood lipids: a meta-analysis in 37859 subjects

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Reviewer: Nicole Soranzo

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The manuscript describes a literature meta-analysis of APOA5 gene -1131 T>C association with fasting blood lipids (HDL-C, LDL-C, TG, TC) in 38k adult individuals from 37 studies. They show a significant association of this polymorphism with increased TC and TG, and decreased LDL-C.

Not being an expert in literature meta-analysis methods, I am unable to judge fully the appropriateness of methods applied, but from my viewpoint the analyses appear thorough and well-conducted.

I'd like however to enquire about some interesting aspects of the results.

- Association with TG (and partially LDL) is highly heterogeneous, not so with TC. Can the authors speculate on the reasons (biological or otherwise) of this heterogeneity? Could this due to more sensitivity to lab measurement errors for some measurements, unexplained environmental perturbations or other effects? From Table 1, the association with TG shows remarkably similar associations and effect sizes in all groups tested, while TC is clearly more associated in East Asians - so what is heterogeneity reversed in this case? Finally, are there local differences in LD patterns that can explain such heterogeneity?

- What have the more recent waves of GWAS added to knowledge of this locus? particularly, has the exhaustive analysis of the locus through GWAS arrays that are more comprehensively representative of this locus revealed additional variants with less heterogeneity/more significant evidence for association?

- Page 6 last sentence - what is the minimum sample size for the subgroup analyses?

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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