Reviewer's report

**Title:** A tagging SNP in INSIG2 is associated with obesity-related phenotypes among Samoans

**Version:** 2  **Date:** 18 August 2009

**Reviewer:** Christian Dina

**Reviewer's report:**

This manuscript is much improved and it is of interest in the context of the evaluation of INSIG2 effect in obesity.

Still, there remain some disappointment as to the "dissection" of the association (provided we consider this p-value of 0.009 is a signal of association).

We observe a decrease of D' between third and fourth (presumed associated) hence, possibly, a recombination. Do we observe this in Europeans (and in Chinese?) HapMap?

A comparative map of the LD and haplotypes between Samoans, CEU and CHN should be provided. This could help understanding where the association could lie.

To sum up, is it plausible, given the LD data available both in databases and in the present study's data that an unobserved causal variant can explain the discrepancy in results?

Let's suppose that the functional SNP is on the 3' side of the recombination - explaining the absence of association with rs7566605... in Asians: then this difference is not due to an excess of LD in Samoans (Asians) but to a decrease, in this case. Maybe this should be discussed when the difference between Samoans and other ethnies is discussed.

It is important to emphasize that the recessive model was really proposed in the initial study as the best describing the association. This should be added to the sentence which gives results of the recessive model. Obviously if the causal SNP is elsewhere, the model at the causal SNP may be different from the one at the "marker" SNP.

Has rs9308762 been typed on any other population?

It would be helpful to have a Table (similar to Table 3) where the effect sizes could be displayed. This can help spotting any possible "heterogeneity" of effects.

**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:

No financial competing interest. Have worked on this topic already but nothing that can cause embarrassment.