Reviewer’s report

Title: Large effects on body mass index and insulin resistance of fat mass and obesity associated gene (FTO) variants in patients with polycystic ovary syndrome (PCOS)

Version: 2 Date: 14 October 2009

Reviewer: Margrit Urbanek

Reviewer’s report:

Tan et al have significantly improved the manuscript. Two issues remain to be addressed/clarified.

1) In table 3 are the p-values the nominal P-values or the corrected p-values?

2) Some aspects of the power analysis needs to be clarified.
   a. What is meant by standardized additive genetic risk. Does it refer to genotype relative risk or % of relative risk explained by locus?
   b. The authors should be more specific with regards to phenotype when stating that markers for FTO or TCF7L2 have a standardized effect size of 0.1. Is it with obesity, type 2 diabetes or a quantitative trait?
   c. If the standardized effect sizes that have been observed for FTO or TCF7L2 are 0.1 and even under the most informative conditions of MAF of 46.2% there is only sufficient power to detect and effect of 0.2, then the study is not “well-powered.” The authors need to indicate that. This is especially an issue for the variants where they did not detect an effect since these loci are even more underpowered.

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.