Reviewer’s report

Title: Variation in the UCP2 and UCP3 genes associates with abdominal obesity and serum lipids: The Finnish Diabetes Prevention Study

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Reviewer: Wolfgang Patsch

Reviewer’s report:

The study addresses possible influences of the UCP2/UCP3 locus with obesity indices and metabolic traits reflecting glucose and lipid metabolism in 507 participants of the Finnish Diabetes Prevention Study (DPS). Eight sequence variations (seven SNPs and one insertion/deletion polymorphism) were typed. The results show moderate associations of SNPs located in haplotype block 2 with obesity indices such as waist circumference and waist to hip ratio, while SNPs located in haplotype block 3 were associated with cholesterol, LDL-cholesterol and the ratio of total to HDL cholesterol.

Overall, these are carefully conducted studies. The number of subjects studied is relatively small for quantifying moderate effects. This point of criticism is mitigated by the fact that the study population is very well characterized and monitored.

Major Compulsory Revisions:

1. Obviously, several subjects were on lipid-lowering medication. The type of drug as well as the number of subjects using such medication in the intensified diet group and the control group should be given. It is stated in the method section that lipid measurements were adjusted for the use of cholesterol lowering medication. Footnotes in Table 3 only mention adjustment for age, sex and BMI. Furthermore, depending on dose and drug used, effects of lipid-lowering drugs may differ. It would therefore be important to analyze the lipid data of study participants not taking any lipid lowering medication and include or describe the results of these analyses in the manuscript.

2. In the longitudinal data analyses, effects of interventions as well as interactions of interventions and genotypes should be considered. The c2 test as used for converters to T2DM in Table 3 does not take into account possible effects of the interventions.

Discretionary Revisions

The rather comprehensive review of the literature on UCP2/UCP3 effects may include a paper showing associations of UCP2 with preclinical atherosclerosis in women (ATVB 2005; 25:604-610) as this paper is consistent with the metabolic
traits investigated.

**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.