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: Peter Kovacs

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Salopuro et al.

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

The authors analysed association of 9 genetic variants covering the UCP2-UCP3 locus with obesity and diabetes related traits in 507 subjects with IGT from the Finnish Diabetes Prevention study. Several polymorphisms and derived haplotypes were associated with measures of obesity and/or lipid phenotypes. The study appears to be relevant as 5 previously unexplored variants were included in the analyses, thus extending our current knowledge on genetic aspects of UCP2 and UCP3. The paper is clearly written, the design and statistics are sound and appropriate.

Discretionary Revisions:

1) Since the study subjects were overweight and obese, obesity may have masked the effects (particularly the protective ones) of genetic variants in UCP2 and UCP3. This might, among other factors already discussed by the authors, explain the lack of association with obesity (e.g. for rs1800849). I believe it is important to emphasize the “obese” character of the study cohort, particularly when considering controversial genetic findings on UCP2 and UCP3 reported by others.

2) Do the Authors have information on ranking of their most promising UCP2 and UCP3 SNPs in previously reported genome-wide association studies for obesity or type 2 diabetes?

3) Haplotype analyses resulted in association of several haplotypes with lipid phenotypes or measures of obesity. I believe that the Discussion might profit from more clear interpretation of the haplotype data. Do the Authors assume that the associated haplotypes harbour an unidentified obesity risk variant or are these findings just supportive of those observed for individual SNPs?

4) Several studies with Pima Indians are being cited in the Manuscript, which seems to be appropriate considering high mean BMI of study subjects from DPS (BMI>31 kg/m2). While associations of UCP3 variants with energy expenditure (EE) in Pima Indians are mentioned in the Introduction (page 6), association of UCP2 variants with EE (Kovacs et al. Diabetologia 48, 2292-2295, 2005) was left...
out. Any specific reason?

5) Page 13, Haplotype analysis: “In order to confirm the associations with serum lipids and WHR, haplotype analysis was performed for blocks 2 and 3”. What about block 1? Block 1 is included in Table 4 but not mentioned in the text.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.