Reviewer’s report

Title: Gene-diet interaction effects on BMI levels in the Singapore Chinese population

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Reviewer: Marilyn Cornelis

Reviewer's report:

Chang and colleagues present results for a series of gene-diet interaction tests for BMI in the Singapore Chinese population. The paper is well written, organized and straightforward with regards to results and discussion. As a strong supporter for replication of previous studies I believe that with minor revisions this paper will be a welcome contribution to the field of nutrigenetics.

1. I would suggest the authors refer to the use of two sample populations rather than 6 data sets. The latter suggests independent sampling which is not the case. It is also not clear why (incident) cases and controls were examined separately for SCHS. Wasn't diet and BMI measured prior to event? Please add rational to methods section.

2. The FFQ for SP2 captured diet during the month prior to the interview. What time period did the FFQ for SCHS capture? The SCHS FFQ serving options ranged from never/hardly to 2 or more times/d. What serving options were allowed in the SP2 FFQ?

3. Please provide justification for the choice of 10 dietary factors. Previous high impact papers have reported interactions with sugar sweetened beverages. Might the latter be tested for replication in the current study? This would be an important analysis and aligns with the authors' broader motivation for conducting the study. This would further qualify the authors' conclusions: stated in the abstract and discussion: "In conclusion, similar to studies performed in large-scale European ancestry samples, our data indicates that, in aggregate, most known BMI risk loci do not interact with dietary intake to modify BMI levels in East-Asian subjects."

4. The significance threshold chosen is unclear. The authors state that 89 tests were conducted when in fact at least 78 SNPs x 11 dietary variables= 858 tests were conducted.

5. Discussion page 9 lines 227-233. These are 'results' and should be moved to the results section.

6. Only 9 of the 78 BMI SNPs were 'significantly' associated with BMI in the current study. Were these tests corrected for multiple testing? The supplementary table suggests they were
not and thus even a few the 9 'significant' snp-bmi associations might be chance findings. Regardless, can the authors speculate on the low reproducibility of these SNPs in the current sample? The very weak association between FTO and BMI is especially surprising. Might this have impacted power to detect or replicate gene-diet interactions?

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