Reviewer’s report

Title: Genetic variations in APPL2 are associated with obesity in a Chinese population with normal glucose tolerance

Version: 1 Date: 1 December 2011

Reviewer: Zainab Samaan

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Genetic variations in APPL2 are associated with obesity in a Chinese population with normal glucose tolerance

Reviewer’s comments

Title: APPL2 is associated with obesity: a case control study

1. Major Compulsory Revisions

The study design is not a case control study. The title is misleading. This study was based on individuals participating in a diabetes study. APPL2 was tested for an association with adiposity and a single SNP showed a significant association with BMI and WHR.

Abstract

2. Major Compulsory Revisions

“APPL2, an isoform of APPL1 that forms a dimer with APPL1, function as a negative regulator of adiponectin signaling via interaction with adiponectin receptors in muscle cells.”

This paragraph has very close resemblance to Wang et al, J Biol Chem. 2009 November 13; 284(46): 31608–31615.

[APPL2, an isoform of APPL1 that forms a dimer with APPL1, can interacts with both AdipoR1 and AdipoR2 and acts as a negative regulator of adiponectin signaling in muscle cells.]

3. Minor Compulsory Revisions

Please use sex instead of gender throughout the manuscript. Gender is a social construct while sex is a biological construct.

4. Major Compulsory Revisions

BMI and WHR are usually associated and are co linear. Therefore testing for an association with each separately does not add any new information.

Background

5. Minor Compulsory Revisions

Obesity is already an epidemic. Please revise the introductory paragraph.

6. Minor Compulsory Revisions
“are two adaptor proteins, which binds to adiponectin receptors and mediate adiponectin signaling and function [4-6].”

Methods

Participants

7. Major Compulsory Revisions

“according to the criteria set by WHO that classified all individuals into three groups: normal weight (BMI<25 kg/m2), overweight (25 BMI <30 kg/m2) and obese (BMI #30 kg/m2) [10].”

Minor Compulsory Revisions: Please remove additional characters.

8. Major Compulsory Revisions

In addition, the BMI cutoffs provided here are more appropriate to Caucasian populations. Several studies showed different cutoffs for Asian populations. Based on ROC curve, the appropriate BMI cutoff for Chinese adults is 24 and waist circumference of 80 cm (for e.g. see Wildman et al. American Journal of Clinical Nutrition, Vol. 80, No. 5, 1129-1136, November 2004).

9. Major Compulsory Revisions

A description of the study participants should be given in a simple demographic table to include age, sex distribution, BMI and WHR. It is also important to show how many individuals are in each group of BMI cutoffs.

Single nucleotide polymorphism (SNP) selection and genotyping

10. Major Compulsory Revisions

The SNP call rate <95% is low and signify genotyping errors.

Statistical analysis

11. Major Compulsory Revisions

Sample size and power calculations should be provided.

Results

12. Major Compulsory Revisions

Table 1 overweight and obesity category should be revised with more appropriate cutoffs for this population.

13. Major Compulsory Revisions

According to this table there are 552 individuals [based on rs2272495 genotype count] with BMI>25 and 1200 with BMI<25. Total individuals=1752 [96.9% of total sample]. The SNP call rate was stated as 95.3%, were did the additional individuals come from?

14. Similarly other SNPs numbers do not add up. Please explain and account for all individuals.
15. Major Compulsory Revisions
In addition these numbers also show that 31.5% of the study population, described by authors as adults of Hans Chinese ancestry are overweight/obese using an already high cutoff of BMI (25). This rate is much higher than reported statistics on obesity in China. With lack of description of the study sample and unusual rate of obesity, the interpretation of the study results is speculative.

16. The authors should also attempt to replicate these findings in an independent sample.

17. Table 2 is not meaningful as all these measures are co linear and the authors are testing the same association of the SNP with adiposity multiple times to show the same results without correcting for these additional tests.

Discussion

18. The last paragraph is unnecessary. The association with these “quantitative measures of obesity” is the result of co linearity with BMI.

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:

I declare that I have no competing interests