Reviewer's report

Title: Common Polymorphisms of Calpain-10 and the Risk of Type 2 Diabetes in a Tunisian Arab Population: a case-control study

Version: 2 Date: 4 January 2010

Reviewer: Simin Liu

Reviewer's report:

This case-control study investigated the association of the 3 SNPs (UCSNP-43, -19 and -63) in the CAPN10 gene with T2D risk among Tunisian patients and controls. Below are some comments and suggestions that would hopefully help improve the paper.

Major Compulsory Revisions

1. How can the authors justify the sufficiency of the three SNPs to capture the genetic variability of CAPN10 in Tunisian population?

2. The author may consider providing more details about subjects selection.
   (i) How were the cases and controls enrolled? Were they recruited by mailed questionnaires?
   (ii) What were the exclusion and inclusion criteria?
   (iii) What were the participation rates for cases and controls?
   (iv) Because the mean duration of T2D was 12.6 years (table1), it appears that most cases are prevalent cases. Would there be any problems of using prevalent cases?

3. What were the matching criteria and the number of controls per case used?

4. More details should be provided in the statistical analysis section. For example:
   (i) What specific genetic models did the authors use to estimate the odds ratios in table 2, 3, and 5?
   (ii) What variables were included in the multivariate regression analysis apart from the genotype or haplotype? In particular, the authors matched on age and gender, thus the authors should state whether they have adjusted for these matching factors.
   (iii) The authors should consider including odds ratios in Table 6. In general, odds ratios should be presented together with the p-values (instead of just the p-values) to provide more information. Also, the author may consider including confidence intervals, which are more informative than the p-values and the point estimates. What methods did they use to compute p-values and odds ratios? What are their interpretations of the odds ratios?
Minor Essential Revisions

1. The authors should consider including the followings in their manuscript:
   (i) was genotyping done blind to case-control status in this study? Please discuss in the SNP genotyping section.
   (ii) discuss more about the biology of CAPN10 affecting what specific cellular compartments for T2D.
   (ii) possibility of population stratification
   (iii) issues identified in the previously reported meta-analysis (Song et al AJHG 2004)
   (iv) limitations of their work
   (v) sample size in Table 3 and 5

2. Briefly explain what kind of expectation maximization algorithm was used to determine the haplotype and diplotype frequencies.

3. The definition of hypertension described in table 2 is not consistent with the one in the method section.

Discretionary Revisions

1. The authors described that the findings in this paper were in agreement with those reported for the Scandinavians, Koreans, and Mexicans. More importantly, however, Song et al. have also shown, both in a meta-analysis (Song et al AJHG 2004) and a prospective cohort of multi-ethnic Americans, essentially the same null findings (Song et al, HMG, 16:23, 2007). The authors should also consider citing this article to further support their findings.

2. Typographical errors in Introduction section:
   (i) dipoltypes and dipoltypes -> diplotype
   (ii) (diplotype]->(diplotype)

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

Quality of written English: Needs some language corrections before being published

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.