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: 4 Date: 22 March 2010

Reviewer: Simin Liu

Reviewer's report:

The authors addressed some of the issues raised by the reviewers, but the manuscript still needs major revision to clarify several important aspects regarding study population, SNPs selection, statistical methods, and the interpretations of findings.

Major Compulsory Revisions

1. The authors only selected three SNPs based on previous reports; and as such, limitations of such a narrow focus should be discussed in the discussion section. Specifically, the authors restricted their study population to only Tunisians of Arab descent, the authors should address whether three SNPs are sufficient to capture the genetic variability in the population of Arab descent.

2. More details on matching method would be helpful. Was it an individual matching or a frequency matching? If individual matching, how close a set of controls with respect to matching factors was chosen for each case?

3. Need to provide more detail regarding statistical analyses:
   (i) The authors stated that they used two-way ANOVA in table 2 to compare genotype distributions between groups. Two-way (or two-factor) ANOVA (analysis-of-variance) is generally used to compare a continuous variable by two factors.
   (ii) It is recommended that, in matched case-control studies, we should control for matching factors regardless of “statistical significance” for the difference between cases and controls to reduce bias introduced by matching (Rothman KJ, Greenland S, Lash TL, Modern Epidemiology, 3rd. ed). Thus, the authors' response, “We did not include them (i.e. age and gender) in the model, since they were not significantly different……” , is not justified.
   (iii) The authors should consider clearly stating the reference groups they used to calculate odds ratios (Table 5 and 6). For example, you may write as “odds ratios were calculated for carriers versus all non-carriers”. In this case, all non-carriers would be a reference group.

4. Authors wrote that homozygosity for the UCSNP-19 was associated with increased body weight among patients. Does this suggest that CAPN10 plays an important role in determining adiposity? Is there any previous reports regarding the relation between CAPN10 and measures of adiposity such as BMI or
waist-hip-ratio? How does this relate to the risk of diabetes? Authors might well consider describing the findings in detail and discussing about this issue in discussion section.

Minor Essential Revisions
1. Please provide the results of the Hardy-Weinberg Equilibrium test.
2. Please provide the number of patients and controls for each cell in Table 5.

Discretionary Revisions
1. Typographical error in Introduction section:
   (i) “and as at-risk diplotypes….. were reported for many populations” was written twice in the same sentence.

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.