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: 25 January 2010

Reviewer: Harold Snieder

Reviewer’s report:

This case-control study in a Tunisian Arab population investigates the influence of three common polymorphisms in the calpain-10 gene on type 2 diabetes. Investigation of common variants on complex diseases in different ethnic populations is of interest. Moreover, although standard, the study is well-conducted and has a decent sample size with 917 cases and 748 controls. I have the following concerns.

1) Abstract: The nomenclature of the 3 SNPs is somewhat strange. What does the UC in UCSNP stand for? I also find the minus sign in front of the SNP number confusing. To me this looks like promoter polymorphisms, which they are not. Furthermore, rs numbers should be mentioned upfront (they only appear in the method section), preferably already in the abstract. Typo: genotyping were done = genotyping was done.

2) Introduction: The available evidence of the involvement of the calpain-10 locus in T2D is patchy with inconsistent results across studies even within Caucasians. Has a meta-analysis been done? Please discuss either here of in the discussion what the evidence from GWA studies tells us about this locus. Typo: was been shown to function = was shown to function; while whereas did not = while some did not.

3) Methods: Were controls matched to cases in terms of geographic area? Please provide distribution (south, central, north) in both groups in Table 1. Please also include information on family history of T2D in Table 1. Was 140/90 used as cut-off for hypertension or 145/90 as stated in Table 1? None of the subjects were taking medication = None of the control subjects were taking medication.

4) Genotyping: please state genotyping success/failure rate and genotyping accuracy rate based on genotyping of duplicates. In general, please provide more detail on measures taken to ensure high quality genotyping results.

5) Statistical analysis: covariates such as age and sex should be included in the multiple regression analyses including those for haplotypes.

6) Results: Per genotype only one overall chi-2 p-value for comparison of genotype distributions should be provided. Providing three separate p-values and ORs for each genotype (Table 2) is incorrect, these are not independent tests. The authors state that SNP19 was associated with body weight. The authors should include BMI in their multiple regression models to investigate whether the
effect on T2D may be explained by the effect on BMI. 
7) It is unclear what the delta coefficient is, it doesn’t seem to be D’or r2? 
8) Discussion: Please carefully check accuracy of citations. It seems at the end of both the 1st and 2nd paragraph the study on Mexican Americans (ref.11) should have been cited? In the 3rd paragraph, OR should be 1.61 instead of 2.17'; Is ref. 20 really on Scandinavians? 

**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’