Reviewer's report

**Title:** Common genetic variants and type 2 diabetes in urban Ghana: a hospital-based case-control study

**Version:** 1  **Date:** 10 June 2013

**Reviewer:** Per Medbøe Thorsby

**Reviewer's report:**

The study present markers in four genes which confer genetic risk for type 2 diabetes in 675 self-reported diabetes, compared to 377 healthy, younger and more educated control individuals with FBG < 7 mmol/l and no hypertension from Ghana. The main finding is that the T allele of TCF7L2 rs 7903146 confer risk of type 2 diabetes and that one haplotype of CALP10 confer mild protection. The risk of the TCF7L2 rs 7903146 risk allele is comparable to that found in other studies and populations.

**Mayor concerns**

To use unmatched controls may influence on the genetic risk observed. Since these controls were younger and may also differ from the cases in ethnicity and SES background that may influence heavily on diabetes prevalence. Also to use only 50% of controls compared to cases may give rise to selection bias.

Diagnosis of diabetes were mostly self-reported (97%) or on the basis of medication, but medication used is not stated in the paper. Since only one FBG sample were used to exclude diabetes in the controls, undiscovered diabetes among controls and some non-diabetics among cases may further contribute to selection bias between the groups. FBG < 5 mmol/l rather than < 7 mmol/l should be used to exclude diabetes, but preferably HbA1c <6,5% or OGTT.

Did the control individuals all have BP below 120/80?

About the power calculation, does it indicate that there should be 525 in each group? Then the study is underpowered.

One should always address the question about multiple testing in such studies, when the P values are only mildly significant.

**Minor concerns**

The description of possible additive effects of the risk allele of TCF7L2 is not clear.

I think nearly 60 risk genotypes of type 2 diabetes is found so far (Page 3, 15 ref to 40 genotypes)

Was C-peptide or anti-GAD measured to exclude other forms of diabetes?

How was glucose measured? In plasma?

CV for the laboratory measurements should be mentioned.
Genotypes KCNJ11 and PPARG should be presented in the paper
Tab 3 and 4 is unnecessary
The discussion is much too long

**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:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests