Reviewer’s report

Title: TCF7L2 Gene Polymorphisms do not Predict Susceptibility to Diabetes in Tropical Calcific Pancreatitis

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Reviewer: Cedric Le Marechal

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The work presented by Mahurkar et al. is dedicated to look for genetic factors predisposing to diabetes in tropical calcific pancreatitis (TCP) in India which is often the natural evolution of the disease. Because diabetes pathophysiology in TCP is not well known, they hypothesized that SNPs located in the TCF7L2 gene, recently associated with type 2 diabetes may be also associated to FCPD. A previous work confirmed the association of TCF7L2 SNPs and diabetes in indian population (ref 15).

Based on their cohorte (478 patients) that allowed them to identify SPINK1 mutations associated to TCP (ref11), they conducted a case-control study for attempting to find an association of two SNPs in TCF7L2 gene (rs7903146 and rs12255372).

Stratification of the cohorte was done based on ethnicity (table 2a) and clinical diagnostic (FCP vs. FCPD) (table 2b). In order to avoid mistyping, 15% of the genotypes were validated with another set of PCR and sequencing primers. Statistical methods are clearly describied with 80% power to detect OR=1.3 at alpha=0.05.

These points reflects the carefull design of the study which allows to be confident in the result that doesn't show association of TCF7L2 SNPs with TCP nor FCPD in any subgroup (ethnic or clinical) at the allelic and genotypic level.

Minor revision :
In the discussion p.8, the sentence "evidence for association...significance criteria" must be clarified.

Discretionary Revisions :
Previous work of the same team (ref 11) showed a strong association of SPINK1 (p.N34S) with TCP. SPINK1 genotype would have been another criteria for stratification. Did they look at the association between carriers and non carriers of SPINK1 mutations ?

Level of interest: An article of limited interest

Quality of written English: Acceptable
**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