Reviewer’s report

Title: Association between Tumor necrosis factor alpha-238G/A polymorphism and tuberculosis susceptibility: a meta-analysis study

Version: 3 Date: 27 August 2012

Reviewer: Sergey Nejentsev

Reviewer’s report:

The authors report meta-analysis of 9 studies that investigated association between TNF -238 G/A variant and TB. They found no evidence of association.

*Major Compulsory Revisions*

1. In Introduction the authors cited two papers (refs 14 and 15) as examples of studies that reported positive association between TNF -238 and TB. Why these studies were not included in meta-analysis? If they did not satisfy any of the selection criteria, the authors have to discuss it.

2. In Discussion: “However, on account of the limitation of the current studies and the important role of TNF-# to controlling TB, future large sample studies using standardized unbiased genotyping methods, homogeneous TB patients and well matched controls are still required, especially among no-Asian population.”

Why further studies of this particular variant in the TNF gene are needed, if the authors’ meta-analysis shows no association? Was there any real evidence of association in the first place? Fig 2 and Fig 3 suggest that none of the nine original studies found association with TB.

*Minor issues not for publication*

No need to repeat in the text results that are shown in Table 3

Several statements have to be rephrased, as it is not clear what the authors want to say:

“A few studies have investigated significant association between the TNF-238G/A polymorphism and susceptibility to TB.14, 15”

“(3) it provided enough (basically genotypic) data to calculate odds ratios”.

“Sensitivity analysis was also performed by sequence excluding individual study.”

“The failure of the present meta-analysis (including the majority of individual association studies to date) proves an association between the TNF 238 G/A polymorphism and TB susceptibility was attributed to several factors.”

“Otherwise, three studies specifically addressed targeting PTB patients were involved into the pooled analysis on different TB types, despite other TB types
did not include enough information, and the result was not significant,”

“A few of studies have already verified the association between HLA and THF, and the important role of the balance between TNF-# and IL-10 for control or dissemination of MTB was also demonstrated”. Two parts of this sentence do not make sense together.

**Level of interest:** An article of limited interest

**Quality of written English:** Not suitable for publication unless extensively edited

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