Reviewer's report

**Title:** Genetic variations in the TIRAP gene are associated with increased risk of sepsis-associated acute lung injury

**Version:** 1 **Date:** 9 August 2010

**Reviewer:** Bart Ferwerda

**Reviewer's report:**

Comments:

1- Page 7 describes study enrollment and design. At the end it mentions that the source of infection of patients is known. It would strengthen the article if a brief summary of this information were also included in the article.

2- Page 13: “Previous studies showed ........in Asian populations” mentions the difference between the European and Asian frequencies. Here it is shown that the minor rs595209 A allele has association with sepsis related ALI. In Europe and Africa this allele is the major allele having a frequency of 79.2 and 92.5% (Source: HapMap). Hereby I miss the discussion about the differences in the population frequency of the found SNPs and the consequences for other populations. Are the findings likely to be (Han) Chinese population specific or can the finding have a broader implication?

3- Although the upset of the research is mainly focusing on genetics authors have collected data on source of infection, Acute Physiology and Chronical Health Evaluation II scores and mortality (page 7 and table 1). Despite the presentation of the figures in table 1 it would be interesting to see the differences between those data and the found associated genotypes, which can be used for a better translation to the clinical relevance of the findings. Also strong support for the involvement of the SNPs and haplotypes can be strengthened if the higher mortality within the sepsis related ALI group is due to the TIRAP genetic variation? If possible these analysis should be included and also discussed.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**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'