Reviewer's report

**Title:** The role of TLR2 in the host response to pneumococcal pneumonia in absence of the spleen

**Version:** 1  **Date:** 6 July 2011

**Reviewer:** Xavier Wittebole

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**GENERAL COMMENT:**

The question addressed in the manuscript is: “Does an intact spleen compensate for TLR2 deficiency during pneumococcal pneumonia?”

To answer this question, the authors report on the effect of TLR2 and, or, TLR4 deficiency in splenectomized mice intranasally infected with 2 different strains of streptococcus pneumoniae.

They demonstrate in splenectomized mice an absence of significant role for TLR2 and TLR4 in host defense against S. pneumoniae. Indeed, mortality, bacterial loads in lung and blood, cytokine lung levels and lung histological alterations, were equivalent in splenectomized wild type animals and in TLR2 KO mice, whatever the dose of pneumococcus used. The double KO (TLR2 and 4) mice display the same kind of result.

Together those results suggest a non-significant role for TLR2 and TLR4 in splenectomized animals infected with S. pneumoniae.

**MAJOR COMMENT:**

1. The hypothesis of work report on an intact spleen (abstract). However, all groups studied in this manuscript report on the effect on TLR2 and TLR4 deficiency in the absence of spleen. This is somewhat contradictory with the hypothesis. To study the hypothesis, 4 groups of animal should be evaluated (spleen+/TLR2 +, spleen+/TLR2 -, spleen -/TLR2 +, spleen -/TLR2 -). Do the authors have those data? Otherwise, they should rephrase their hypothesis.

2. As reported in the manuscript (page 3 line 19 and further) TLR2 does not seem to play a major role in host defence against pneumococcal pneumonia (reference 8,11,12). Therefore, the authors should explain why they thought TLR2 could have any effect on the various outcome studied after pneumococcal pneumonia in the absence of spleen. (an explanation can be found in the latter part of the discussion but this should be described in the introduction, since it is related to the hypothesis).

3. The authors specifically address the problem of TLR2 and TLR4 in this manuscript. We now know that TLR 9 is of particular importance (Albiger B et al. Cell Microbiol.2007 – reference 11) as is MyD88 (Albiger B et al. Cell Microbiol.2005). Why didn’t the author study TLR9KO mice or MyD88 KO mice?
4. Pneumolysin was demonstrated to act through TLR4. Therefore the authors studied the effect of TLR4 in splenectomized animals. However, pneumolysin also acts through the nlrp3 inflammasome, in a TLR4 independent manner (McNeela et al. PLoS Pathog. 2010; Witzenrath M et al. J Immunol. 2011). A comment should be added to the manuscript.

5. The authors conclude their discussion with a suggestion (“TLR2 mediated immune response might be dependent on the spleen as an effective organ:”). As described in comment #1, this could be answered by studying the above-mentioned groups of animals.

**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