Reviewer’s report

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

Version: 1 Date: 19 July 2011

Reviewer: Frederic Pene

Reviewer’s report:

The authors assessed the role of TLR2 in splenectomized hosts subjected to a pneumococcal pneumonia. The question is of interest to understand the physiological role of TLR2 in pneumococcal infections. Indeed, though TLR2 is clearly involved in sensing S. pneumoniae, it appears quite dispensable in non-immunocompromised hosts subjected to pneumococcal infections. In this straightforward paper, the authors concluded that TLR2 is also dispensable in the defense of splenectomized animals. Thus, the own role of TLR2 in pneumococcal infections remains questionable. I have several comments:

Major comments

The main goal of the study was to investigate if an intact spleen can compensate for a TLR2 deficiency, or, in other terms, to evaluate the protective role of TLR2 in the setting of splenectomy. The authors used a bacterial load known to be innocuous for non-splenectomized animals, and it appears clearly that this dose is highly lethal for both WT and TLR2 KO splenectomized animals. Although this model clearly shows that splenectomized animals are highly susceptible to pneumococcal pneumonia, it is not appropriate to reveal a higher susceptibility of TLR2-deficient mice. The authors should rather use a non-lethal or sublethal model of pneumococcal pneumonia in TLR2-sufficient mice without spleen, and then check whether TLR2-deficient mice are more susceptible or not to the challenge.

Studies that assessed the role of the spleen in pneumococcal infections were performed using bacteremia models which are not the physiological route of infection in most S. pneumoniae infections. So it is likely that the spleen might rather prevent systemic spread of the disease, and blood bacterial loads should also be displayed as scatterplots.

I would be interested in having the survival curve of WT and TLR2KO mice subjected to serotype 3 S. pneumoniae pneumonia, and of splenectomized TLR2/4 -/- mice subjected to serotype 2 S. pneumoniae pneumonia.

Additional comments

There is a trend towards decreased histological inflammation in TLR2/- mice. This mentioned in the discussion section but not reported in the results section.
Since the number of animals per point is low, the boxplot distribution of variables is not relevant. Data should be displayed as scatterplots.

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

**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