Author's response to reviews

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

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Author's response to reviews: see over
Dear Dr. Marshall,

Please find below our response to your email dated March 10, 2012, in which you invited us to carry out the changes requested by one of the reviewers (Dr. Frederic Pene).

Our manuscript originally was reviewed by two referees. One reviewer has one remaining suggestion after our resubmission, i.e. to perform an additional survival experiment in splenectomized wild-type and TLR2 deficient mice after a sublethal dose of *S. pneumoniae*. We explained in our first rebuttal that we specifically chose an infectious dose that results in a survival of approximately 50% at 48 hours. Indeed, since overwhelming pneumococcal infection after splenectomy in humans causes irreversible infection leading to mortality within the first 48 hours, we chose to study the role of TLR2 within this relevant period using bacterial loads to cause severe disease without killing the mice before predefined time-points of euthanasia. Considering that in our current model, all mice survived the first 24 hours after inoculation, we think that our data provide information that is relevant for the clinical syndrome of severe pneumococcal infection after splenectomy. We also explained in our first rebuttal that the institutional Animal Care and Welfare Committee does not allow large scale survival studies, especially in experiments wherein bacterial loads do not differ between groups. We specifically asked for approval for the survival study shown in figure 1a. This was “special” since the Animal Care and Welfare Committee generally does not grant approval for survival studies in case other parameters (bacterial loads and inflammation) were found to be similar between groups. Therefore, we are not able to conduct additional survival studies. Nonetheless, we feel that our manuscript contains
valuable data and that the comment raised by this reviewer has been adequately addressed in the Discussion: herein we now state that “We used an infectious dose that caused lethality in virtually all mice beyond the 48 hour time point. We specifically chose this dose considering that overwhelming pneumococcal infection after splenectomy in humans causes irreversible infection leading to mortality within the first 48 hours (references 17,18,37). As a consequence, our data do not exclude a protective role for TLR2 in asplenic animals after infection with a low nonlethal dose of S. pneumoniae” (page 15).

We have corrected the statistical paragraph as suggested by the reviewer (please see high-lighted section).

We kindly ask you to make an editorial decision about the fact that we cannot fully fulfill the last request of one of the reviewers. We sincerely hope our manuscript will be considered suitable for publication in BMC Infectious Diseases.

Sincerely,
Jolanda Lammers & Tom van der Poll