Author's response to reviews

Title: The CD14 functional gene polymorphism -260 C>T is not involved in either the susceptibility to Chlamydia trachomatis infection or the development of tubal pathology

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Author's response to reviews: see over
Dear Editor,

Herewith we resubmit our manuscript entitled: "The CD14 functional gene polymorphism –260 C>T is not involved in either the susceptibility to Chlamydia trachomatis infection or the development of tubal pathology", by S. Ouburg for publication in BMC Infectious Diseases.

We have changed the manuscript as suggested by the reviewers. In general, we have reduced the length of the manuscript by reducing the introduction and discussion as suggested. This textual reduction has resulted in a reduction in references and we have omitted more as suggested by the reviewers. We have deleted one of the figures, which was redundant according to the reviewers. However, we feel that figure 1 does have an additional value for the manuscript since many researchers in the Chlamydia field will not be that familiar with these immunogenetic approaches and we would like to maintain this figure in the manuscript. One of the reviewers commented on the poor quality of the figures, which is most likely a editorial conversion issue since the originals are in powerpoint and of high quality. If needed we could provide the powerpoint files

Below our responses to the reviewers. We hope the introduced changed will make our manuscript suitable for publication in BMC Infectious Diseases.

Kindest regards,

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Responses to reviewer #1: Heljä-Marja Surcel

General
This manuscript describes analysis of CD14 functional gene polymorphism in the susceptibility to C. trachomatis infection or the development of tubal pathology. The subjects is an important step in the field of Chlamydia research where host immunogenetic factors are studied in purpose to know the possible risk factors that could explain the enhanced susceptibility of certain individuals for development of Chlamydia associated destructive disease sequelae. The manuscript is well written, methods and results are clearly presented. Some discretionary revisions can be considered for the discussion which is long and hypothetical compared to the presented data. Moreover, the number of references seems overwhelming.

Answer: We thank the reviewer for her kind words. As suggested we have shortened the discussion and introduction. The textual reduction has resulted in a reduced number of references. Furthermore, we have critically reviewed our reference list and removed references where possible and appropriate.

Although antibody analysis plays a role of minor importance in this study, using two different methods for antibody analysis is disturbing and requires explanation. Are the two methods comparable? A type of method obtained from Medac should be added in the text.

Answer: Indeed the reviewer is right that two different kinds of assays are used. We have commented on this topic in the Material and Method section and included the fact that we have made a comparison between the tests previously (Morré et al. J.Clin.Microbiol. 2002)

Figures: The figures, that are not referred in the text, are purposeless. Especially Figure 1 goes beyond the subject.

Answer: We regret to have forgotten to properly refer to the figures in the text and have corrected this.

Responses to reviewer #2: Brunhilde Blomeke

Reviewer's report:
The paper of Ouburg and colleagues focuses on the impact of susceptibility factors such as CD14 -260 C>T on Chlamydia trachomatis infection or the development of tubal pathology. The authors did not find an association with this polymorphism. Overall, the study is sound, well-written and adds on the ongoing discussions about the impact of SNPs in CD14 and TLR receptors for infections or corresponding disease severity. The quality of the manuscript is good, and I recommend publication without any revisions.

Answer: we thank the reviewer for these kind words regarding the quality of our manuscript
Responses to reviewer #3: Mihai G Netea

General
The current manuscript by Ouburg and colleagues investigates the impact of the CD14 –260C>T polymorphism, on the susceptibility to genital Chlamydia trachomatis infection, as well as to long-term complications of genital infections such as tubal infertility. The study is well-designed and present solid data which strongly suggests that this particular polymorphism is unlikely to play a major role in genital C. trachomatis infection. The manuscript is clearly written.

Answer: We thank the reviewer for his positive review of our manuscript

1. Figures 1 and 2 depict well-known aspects of TLR4 and CD14 biology, and are unlikely to enhance the value of the manuscript.

Answer: We thank the reviewer for his critical appraisal of the figures. We have removed figure 2. However, we feel that figure 1 has value for this manuscript since this model is relatively unknown to many Chlamydia researchers since these immunogenetic approaches in the Chlamydial field are still quite new.

2. There are no mentions of the figures in the text of the manuscript: should be added.

Answer: The reviewer is right, we apologize for the missing links to the figures and have added these where appropriate.

3. The quality of the figures in my version was rather poor.

Answer: The quality of the figures was most likely poor due to converting issues. The originals were made in powerpoint. The automated conversion to the PDF file resized and stretched the figures, resulting in a rather poor representation of the figures. We will address this issue with the editor, and submit new figures in different formats if required.

Discretionary Revisions (which the author can choose to ignore)

1. Introduction is rather long and it could be shortened.

Answer: We have shortened the introduction

2. One aspect which could be touched in the Discussion is fibrosis, and the role played by TGFbeta in this process. TGFbeta is an anti-inflammatory cytokine with an important role in fibrosis (and thus very likely in post-infection tubal pathology), which is mainly synthesized through TLR2-dependent pathways. TLR2 is important for recognition of Chlamydia, and its involvement in Chlamydia-induced TGFbeta, through CD14-independent pathways, may explain why CD14 polymorphisms may not impact tubal pathology.

Answer: This is an excellent point made by the reviewer and we have gladly included this relevant point to our discussion.