Author’s response to reviews

Title: A coding polymorphism in Matrix Metalloproteinase 9 reduces risk of scarring sequelae of ocular Chlamydia trachomatis infection

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Author’s response to reviews: see over
Dear Sirs,

Thank you for considering our manuscript MS: 1383133168941857 - A coding polymorphism in Matrix Metalloproteinase 9 reduces risk of scarring sequelae of ocular Chlamydia trachomatis infection- for publication in your Journal.

We are thankful for the valuable comments of the reviewers; our manuscript has been revised accordingly. Please find below our answers (in bold) to each of the reviewers’ comments with a description of the changes made to our paper. Please note that no major compulsory points were raised by the reviewers.

Please don't hesitate to contact us if you have any problems or questions regarding our manuscript.

Yours sincerely,

Dr Angels Natividad-Sancho
Dr Robin Bailey

1-Answers to Professor Peng Tee Khaw comments

- Minor Essential Revisions

The reference abbreviations need to be consistent e.g. reference 15 should be Br J Ophthalmol. Reference 1 also needs checking.
We have checked our reference abbreviations to include only the official journal abbreviations
- Discretionary Revisions

The authors need to mention that MMPs have been shown to be important in ocular fibroblast-mediated collagen contraction (Daniels et al Invest Ophthalmol Vis Sci 2003; 44:1104-1110)(Sheridan et al Am J Pathol 2001; 159: 1555-66) which underlies the dramatic change in tissue leading to lid contraction and scarring of the cornea due to the lashes turning in. This is also important for other fibroblasts and this may be relevant for scarring elsewhere, for example genital infection (Scott KA et al FEBS Lett 1998; 441:137-140) It is also important to mention that inhibiting MMP function may have a dramatic effect on cell mediated collagen contraction in vivo (Scott et al 1998, Daniels et al Invest Ophthalmol Vis Sci 2003) and in vivo in conjunctival scarring (Wong et al Invest Ophthalmol Vis Sci 2003, 2005) which emphasises the potential importance of their finding and also possible treatment avenues.

We agree with the reviewer for a potential role of MMPs in pathological contractile scarring. Two references addressing this point have been included in our paper. Please see discussion section: “Later during the tissue repair phase, excessive MMP activities may contribute to contractile scarring, characteristic of TS and TT, through their role in ocular fibroblast-mediated matrix contraction [15,16]”.

2-Answers to Dr. Ryle Ramsey comments
- Minor Essential Revisions

Under Results, Single marker analysis, 2nd from last line. Table 1 shows results for TT only but not TS? TS also had a significant difference in the frequency of the allele in question did it not (p=0.004 in text)? However, this data is not in Table 1 as indicated in the text describing it.

A table (table 1) showing the genotype results for the TS phenotype has been added in the result section

- Discretionary Revisions

Statistical analysis of allelic differences is somewhat complex and difficult (for me) to follow. There will be others who are interested in this work but who know little of these tests. For convenience, more detail (even brief overview or description) could be helpful to readers for ease-of-reference.

We have included a paragraph in analytical methods describing Conditional Logistic Regression analysis: “Conditional logistic regression is the analysis of choice for dichotomous paired data (in our case paired cases and controls) where the risk estimates associated with specific attributes (e.g genotype) are required to be adjusted for potential confounders”