Reviewer's report

Title: Host cytokine responses distinguish invasive and airway isolates of the Streptococcus Milleri/Anginosis Group

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Reviewer: John McCormick

Reviewer's report:

This paper uses a set of clinical isolates from the Streptococcus Milleri/Anginosus group (SMG) to test the hypothesis that the host immune response may contribute to the overall pathogenesis of individual strains. Although the SMG includes 3 species, the authors make the argument that SMG bacteria show very heterogeneous phenotypes making species/strain/phenotype correlations with particular diseases impractical. The key data set in the paper shown in Figures 2 and 3 where increased cytokine responses occur with strains isolated from invasive infections, compared with respiratory isolates, but this does not correlate with species, phenotypes (e.g. production of hyluronidase, chondroitin sulfatase, hemolytic activity or protease production), genotype, or what the authors refer to as biotypes, and that this also does not correlate with TLR2-dependent activation. The overall findings are quite interesting. Below are some specific comments that may improve the manuscript.

- Major Compulsory Revisions

I do not have any compulsory revisions.

- Minor Essential Revisions

L50: the wording is unclear and may be interpreted as female respiratory tracts are colonized.

L116: Please check the wording of this sentence.

L240: Please expand on what is meant by phenotypically "active" and "non-active". This was not clear.

L250: The title to this results section should be reworded to reflect the findings.

The data presented in Figure 1 is shown on a logarithmic scale – I believe this was done to include all the data on the same graph. It may be better to present each cytokine on an individual graph and this may show the IL-17 differences better. Alternatively, the graph needs to be enlarged. Table I appears to repeat the data shown in Figure 1.

The resolution of Figure 2 needs to be increased.

The supplementary figures should have figure legends.
- Discretionary Revisions
I do not have any discretionary revisions.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests