Reviewer’s report

Title: Contribution of different pneumococcal virulence factors to experimental meningitis in mice

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Reviewer: Matthijs Brouwer

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The manuscript by Ricci et al presents interesting work on virulence factors of the pneumococcus. They use a murine pneumococcal meningitis model and microglial cell-line experiments to determine capability of TIGR4 strains lacking PspC, PsPA and the entire capsule to cause disease and evade microglial killing. In general the methods are sound and the manuscript is well-written, though a bit lengthy (introduction can be shortened by 30-50%).

Major Compulsory Revisions
1) It is unclear when mice are considered moribund. Was a specific score used to determine when to euthanize the mice? If not was the study performed in a blinded fashion or were the animals randomized to receive specific strains? Knowing which mice was infected with which strain and a subjective definition of moribund may have influenced the results.

2) The novelty of the findings using the rough TIGR4 strain is limited as it has been reported in ref 42 as well.

3) In the discussion the authors should attempt to link their data on experimental meningitis with potential implications for improvement in patient care in a specific way instead of concluding experimental studies are "important to elucidate the pathogenesis". They could for instance discuss the use of the identified virulence factors for vaccination (e.g. see ricci et al, vaccine 2011)

Minor Essential Revisions
1) The number of mice per experimental group should be specified instead of giving the range e.g. 3-14. It is unclear how the group size was determined?

2) The authors describe using PBS controls. However, the results of the negative controls are not mentioned in the results or figures. Were they identical to the FP23 strain infected mice? This should be described.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a
statistician.