Reviewer's report

Title: Overexpression of activated protein C hampers bacterial dissemination during pneumococcal pneumonia

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Reviewer: Clifford S. Deutschman

Reviewer's report:

This nicely performed study is interesting from several viewpoints. The most remarkable is the stark contrast between the effects of pneumococcal pneumonia and a previous study by the same group examining gram-negative pneumonia. The authors (and, indeed, this reviewer) seem to be at a loss to explain the difference. That said, there are several issues that might be addressed to improve the manuscript. Addressing them would significantly enhance enthusiasm for the manuscript.

1. The APC-high animals are generated to have an inborn error in their coagulation system. Are there other phenotypic differences between these and WT mice?

2. The difference in neutrophil recruitment seems counter-intuitive. One would suspect that fewer neutrophils would promote infection, yet the opposite appears to be the case. How might this be explained? And why would a deficit of an important component be associated with improved outcome? Is there some effect on neutrophil function, as opposed to accumulation?

3. The authors suggest that the difference in neutrophil accumulation might reflect decrease chemotaxis. In this regard, it would be important to measure levels of chemoattractant cytokines such as gro.

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

Quality of written English: Acceptable

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

Declaration of competing interests:

I declare that I have no competing interests