Reviewer’s report

Title: Inhibition of matrix metalloproteinases attenuates brain damage in experimental meningococcal meningitis

Version: 2 Date: 2 November 2014

Reviewer: Christian Ostergaard

Reviewer’s report:

The study by Ricci et al describes the role of matrix metalloproteinases in the pathophysiology of meningococcal meningitis, and demonstrates that pretreatment with the MMP-inhibitor, batimastat improves the outcome of the disease. The study documents that the authors successfully have developed an animal model of meningococcal meningitis using live meningococci, which is an important achievement in future research for more effective treatments of meningococcal meningitis.

Major compulsory revisions.

A limitation of this study is lack of statistical power, which has to be addressed in the discussion. Pretreatment with MMP-inhibitor have likely not only a beneficial effect on cerebral bleeding and BBB-integrity, but also on survival (P-value: 0.064, type II-error?). The Kaplan-Meier survival curves should be added as a figure to demonstrate the clinical course of the disease (+/- BB-94 treatment).

Another limitation that should be addressed in the discussion is, what impact it may have on the other results presented that survival was higher in BB-94 group than in the control group (only 20/21 vs. 13/20 mice, respectively, were included in all analyses). Could it be the most severe cases that were excluded from the analyses?

The correlation analysis in Figure 3 is of little value. The positive correlations between MMP-9 and cerebral haemorrhages/brain albumin are most likely due to the documented differences in these data between the two treatment groups. Data of correlation analysis should be shown for each treatment groups individually.

Minor essential revisions.

Page 5, line 24. Please, describe briefly the content and values of the coma scale to help reading the manuscript.

Page 4, line 17, and page 14, line 11. Please remove “adjunctive”, since BB-94 treatment was not given as adjunctive therapy. It should be stated that future studies should explore, whether anti-MMP treatment would have a beneficial effect on meningococcal meningitis as adjunctive therapy (together with antibiotics).
Minor revision not for publication:

Page 8, line 15. Please clarify, whether the strong correlation was solely for MMP-9 or for other analysis included in the Milliplex assay.

Page 9, line 15. Rho > 0? What about negative correlations?

Page 10. line 7-10. Please remove the less important cytokine data to the end of the result section.

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.