Author's response to reviews

Title: Chandipura virus infection in mice: the role of toll like receptor 4 in pathogenesis

Authors:

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Author's response to reviews: see over
To

The Editor in chief,

Journal Editorial office

BioMed Central

Dear editor,

MS: 1870516978688620

Research article

BMC infectious disease (Section: Viral Disease)

Sub: resubmission of manuscript “Chandipura Virus infection in mice: role of toll like receptor 4 in Pathogenesis”, with changes in text

I had submitted the above said manuscript (MS: 1036439165748662) to BMC infectious disease journal but it got rejected with due comments. The editorial office asked me to revise the manuscript taking into account of reviewer comments and resubmit it. I have addressed the main concerns of reviewer and revised the manuscript accordingly. The changes have been made in the manuscript is described below and the changes also highlighted in text.

I submitted the manuscript today but the changes highlighted are not visible in pdf file generated by BioMed central. So I am resubmitting the manuscript with some format changes.

Major reviewer comments

Comment 1: Quantify the cytokines level and virus titer in both wild type and TLR4 mutant mice

Reply: proinflammatory cytokines (TNF-α, IL-12, IL-6, IL-10, MCP-1 and IFN-γ) were quantified in sera from wild type and TLR4 mutant mice. The virus titer in blood and brain was also titrated. In addition, to eliminate the possibility of antibodies in protection, virus specific IgM level was also quantified in these mice.

Comment 2: cytokine level in NO inhibitor treated animals

Reply: As per my knowledge, it is not necessary to quantify cytokine level in NO inhibitor treated mice because our objective is to test role of NO in pathogenesis.
Comment 3: Excess production of proinflammatory cytokines in a TLR4 dependent manner is the cause of mortality-conclusion

Reply: The conclusion was changed according to the results

Minor comments

Comment 1: Description of the experiments and M&M is not clear

Reply: M&M section was revised and rewritten in elaborate

Comment 2: Virus replication in RAW cells should be measured at later time points

Reply: The virus titer was measured up to 24 h PI, and the titer was similar after 8 h PI even up to 24 h PI so it was not shown in the graph

Comment 3: Legend of figure 2 not clear

Reply: The description of legend has been changed

Comment 4: Fig.3 is not appropriate

Reply: Fig.3 has been changed from tri-dimensional graph to half-offset histogram

Comment 5: Testing of LPS in samples

Reply: The appropriate negative control was used in all the experiments which could negate LPS contamination in the samples.

Modifications in the text

1. Abstract

   Result: modified and included the cytokine quantification in C3H/HeJ mice

   Conclusion: modified and the modification highlighted in the text

2. Introduction

   There is no major correction in this section

3. Materials and Methods

   Cells and virus: no major changes

   Virus infection: revised completely

   Microarray analysis: no major changes

   TLR expression: no major changes

   Quantification of mouse inflammatory cytokines: no major changes

   Mice experiments: the text was revised and included the reviewer comments

   IgM kinetics: new text

   Quatantification of nitric oxide: no major changes

   NO inhibitor treatment: changes highlighted
4. Results: New text

Earlier manuscript the result and discussion was combined but in new manuscript the result was separated from discussion and rewritten completely including all reviewer’s comments.

5. Discussion: New text

The whole discussion was rewritten including all new experiments and data.

6. Conclusion: Modified and highlighted in text

7. References: More references are included

8. Figure Legend:

   Fig.1: completely modified
   Fig.2: completely modified
   Fig.3: Slight modifications were made in the text and highlighted
   Fig.4: modified and highlighted in the text
   Fig.5: no modification
   Fig.6: new legend
   Fig.7: new legend
   Fig.8: new legend
   Fig.9: no changes
   Fig.10: no changes

9. Table: Formatted

I expect that the reply may satisfy the Editorial office, if any further clarification please contacts me.

Thank you

Yours sincerely,

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