Reviewer's report

Title: Effect of freeze-dried Carica papaya leaf juice on inflammatory cytokines production during dengue virus infection in AG129 mice

Version: 0 Date: 19 Sep 2018

Reviewer: Ilango Balakrishnan

Reviewer's report:

Evaluation of this manuscript entitled "Effect of freeze-dried Carica papaya leaf juice on inflammatory cytokines production during dengue virus infection in AG129 mice", address the therapeutic need of the Alternative / Natural medicine for the treatment of dengue viral infection. Few clarifications need to be addressed:

1. Did author used any positive drug control for this study?

2. Did author find any major constituents of the Carica papaya extract which repress the viral infections?

3. In all figures except figure 2, statistically significant (*)*P<0.05 value is missing.

4. Supplementary figure S2 is typo error as figure S1.

5. Does author perform PCR array analysis in duplicate or triplicate for each group?

6. PCR array analysis of 84 genes for both control and FCPLJ treatment groups should be represented in Venn diagram or Volcano plot for both up and down regulated genes. Heat map and graphic bar diagram can be shown up for mRNA expression levels of genes in comparison of both groups.

7. Since the author focused on liver cytokines does any changes seen in the section of liver H&E stains?

8. Since author claimed that FCPLJ treatment significantly down regulated 8 genes: CCL6/MRP-1, CCL8/MCP-2, CCL12/MCP-5, CCL17/TARC, IL1R1, IL1RN/IL1Ra, NAMPT/PBEF1 and PF4/CXCL4. CCL6/MRP-1, CCL12/MCP-5, and IL1R1 after the
viral infections invitro or patients, can author further provide any evidence confirming any of these genes by Immunofluorescence or Immunohistochemistry study?

9. Does the author studied any of liver protein expression of IL6, TNF, IL1, IL8, CCL2 and CCL8?

10. Any changes in macroscopic examinations of PBMC using GFB and Giemsa staining of post infection group and after 7 days of FCPLJ treatment.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable
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