Author's response to reviews

Title: Modulation of hepatic PPAR expression during Ft LVS LPS-induced protection from Francisella tularensis LVS infection

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Reviewer 2: The revised manuscript has addressed most of the comments, however, now when the content of figure 5 has been explained, it is difficult to understand why the 24h time point post infection and 48 h post-LPS treatment have been included in the figure. In all other figures, results comparing the effects of infection vs infection with LPS pre-treatment have been included. Since the aim of the paper is stated to be to understand the LPS-induced blunting of the proinflammatory response, then it would be appropriate to include data on the effects of LPS-pretreatment on the gene expression in infected mice. Moreover, it would be logical to include data on both the 24 and 48 time points.

After discovering that LPS causes consistent up-regulation of PPAR### (Figure 4), we explored the changes in expression of these genes (and associated genes of fatty acid metabolism) after challenging the mice with whole bacterium (which also contains LPS on its surface). Figure 5 thus juxtaposes two different effects on host gene transcription (due to LPS and due to whole bacterium) and interestingly reveals opposite trends (up-regulation of most genes by LPS and down-regulation of most genes by whole bacterium).

Moreover, it would be logical to include data on both the 24 and 48 time points.

We thank the reviewer for this suggestion. Accordingly we have added the second time point (48 h post-infection) as another column in the heat map in Figure 5. As shown, both 24 h and 48 h post-infection cause down-regulation
(while LPS causes up-regulation) of most genes associated with fatty acid metabolism.