Reviewer’s report

Title: MORG1+/- mice are protected from histological renal damage and inflammation in a murine model of endotoxemia

Version: 0 Date: 26 Aug 2017

Reviewer: Mark De Caestecker

Reviewer’s report:

Data showing increased sensitivity of MORG mutant mice to LPS induced renal damage are convincing, as are the data on NF kappa B activation and T cell infiltration. However, I am not convinced by the data shown in Figures 3 and 4 suggesting that MORG mutants have lower levels of PHD3 protein and higher levels of HIF 2 alpha protein after LPS treatment as these are based on "quantitative" analysis of IHC. Two issues here: PHD3 staining is not convincing in Fig 3A, and while HIF2A staining in Fig 4A is nice, quantification of staining intensity in this way is not a valid method to quantify protein expression. You could either: a) quantify positive cell numbers; and/or b) use western blots to quantify protein.

Minor concerns:

Abstract: the statements that "although accumulation of renal HIF-2 was significantly higher in the kidneys of MORG1+/- mice than in wild-type mice, we detected diminished phosphorylation of IB-and IKK ," needs to be better explained

Background: is rather disorganized and difficult to follow and should be rewritten in a more linear fashion. In addition, remove "hypoxic preconditioning" from the last sentence as you are not studying this

Methods: a) state whether analyses were blinded or not; b) state time tissues, blood and urine were analyzed after LPS treatment; and c) IHC quantification, see previous comments

Results: a) including timing of analyses in figure legends for clarity; b) format of Fig 6C is different from all of the others: suggest this is changed

Discussion: an alternative interpretation of the data is that MORG mutant are less sensitive to the effects of LPS because they have lower levels of TLR receptors and/or LPS is metabolized differently. This cannot easily be addressed in vivo but should be discussed

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.

No

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:

Needs some language corrections before being published

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