Reviewer’s report

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

Version: 0 Date: 30 Aug 2017

Reviewer: Charles Edelstein

Reviewer’s report:

The study concludes that the suppression of MORG1/PHD3 complex has renoprotective and anti-inflammatory effects in a murine endotoxemia model through modulation of HIF-2α stabilization and/or simultaneous inhibition of the NF-κB signaling. There is a lot of data in the paper. In general, experiments seem well performed and data is well presented. Conclusions in the most part, except for PHD3, are well supported. Major criticism is that data on PHD3 is weak and this needs to be discussed and conclusions about PHD3 toned down

Abstract:

Too long

Introduction:

Also too long. Typo "gramm" negative

Methods:

Were +/+ controls age, sex and weight matched? Were they littermate or purchased controls?

Does the dose of LPS cause hypotension in the mice?

Results:

Fig 1 Tubular injury is less in+/− mice. There should be arrows in the pictures demonstrating the different features of tubular injury

Fig 2: Plasma NGAL is not really a marker of KIDNEY injury but rather a systemic response. Comment on this

Was BUN, serum creatinine or inulin GFR measured. Inulin GFR, but not BUN, SCr, has been found to be decreased with LPS (Knotek at el. Kidney Int 59, 2243, 2001)

Fig 3:
The decrease in PHD3 protein expression in +/- is very small (does not seem to merit P<0.05) and there is no decrease in mRNA. Major conclusions are drawn about PHD3 in Abstract and Discussion based on this weak data. Conclusions about PHD3 should be toned down, limitations of data discussed OR more experiments performed to look at PHD3.

Fig 4

HIF 2 alpha protein expression is increased in +/-.

Fig 5

IL-6 and INF (/typo for IFN) data is not new.

Fig 6

TNF protein not increased in +/-.

Fig 7

NF-KB not increased in +/-.

Fig 8

CD4 T cells and Caspase-3 not increased in +/-.

Should say "Caspase-3" and not extrapolate to apoptosis without showing changes in apoptosis on histology (Fig 1).

Fig 9

Is there a way of determining whether the data is statistically significant?

Discussion

Too long.

A lot of previous studies and background data is discussed rather than commenting on each of the multiple findings.

**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

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