Reviewer’s report

Title: Renal Injury is Accelerated by Global Hypoxia-inducible Factor 1 Alpha Deficiency in a Mouse Model of STZ-induced Diabetes

Version: 0 Date: 30 May 2017

Reviewer: Wenzheng Zhang

Reviewer’s report:

This study examine if global deletion of one copy of Hif1α gene affects the development and progression of DN in early stages of diabetes, using streptozotocin-induced diabetic mouse models. The authors compared four groups of mice (non-diabetic and diabetic WT and Hif1α +/- ) and used RT-qPCR, immunofluorescence staining and blood biochemistry to evaluate changes in molecular, histological and biochemical parameters related to kidney injury. The authors claimed that diabetic Hif1α +/- vs. diabetic WT mice had more prominent changes in serum parameters associated with glomerular injury, increased expression of podocyte damage markers, and loss of podocytes, but no significant changes in kidney fibrosis. They concluded that HIF-1 plays a critical role in the early response to prevent diabetes-induced tissue damage and that partial HIF-1 deficiency accelerates progression of DN. The topic is interesting and appropriate to the readers of the journal. The writing is acceptable.

Major concerns:

1. The images in Fig. 2, 4 and 5 are of very poor quality for any assessment. The reviewer is not sure if the poor quality is due to the original files or the reduction of pdf file.

2. Negative control omitting primary antibody of VEGF should be included in Fig. 4.

3. Western blot analyses should be included to verify changes at the protein level. Fig. 6 should be eliminated, unless a time course study is added to establish the causative relationship shown in the diagram.

Minor concerns

1. Fig. 1. Body weight gain after 6 weeks of what?

2. Fig. 1. Parameter should be included in the vertical bars.

3. Fig. 1. For "after 6 hours fasting", at what time point?

4. P8, "the renal medulla was discarded". Why?

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

No

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

No

**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:

Acceptable

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