Reviewer’s report

Title: HIF-1α contributes to Ang II-induced inflammatory cytokine production in podocytes

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Reviewer: Hirofumi Hitomi

Reviewer's report:

General comments

In this study, the authors investigated the roles of HIF-1α in renal cell injury induced by Ang II both in rats and podocytes. The results showed that high HIF-1α expression was observed in Ang II-infused rats. In addition, Ang II increased expressions of HIF-1α, MCP-1 and TNF-α in podocytes. These findings will be potentially interesting; however, the results seem to be preliminary and lack novelty. Moreover, this paper suffers from following critiques and insufficient to support authors' discussion.

1. Similar in vivo results have been already reported by several groups. The detail mechanism of Ang II-induced glomerular injury via HIF-1α was clarified (PMID 25987665). HIF-1 involved-renal fibrosis induced by Ang II has been also reported. Therefore, in vivo findings of this study lack novelty.

2. Similar in vitro results have been also reported (PMID 22555025). Ang II increased HIF-1α transcriptional activity was demonstrated in podocytes, mesangial cells and proximal tubular cells. Interestingly, in the previous paper, HIF-1α transcriptional activity was decreased after 9 hours of Ang II treatment, and increased 24 hours. The authors should measure HIF-1α expression in several time-points. Thus, the in vivo findings of this study also lack novelty.

3. Blood pressure should be evaluated. Rats were treated with Ang II (400 ng/kg/min) for 28 days. Did Ang II treatment increase blood pressure? Did Ang II induce renal injury via high blood pressure or direct Ang II effect?

4. Figure 1: There is a typo (MPC-1).

5. Figures 1 and 2: Pictures of immunohistochemistry were poor, especially TNF-α. Where is positive area? Glomerulus and/or tubules? The positive stains should be indicated with arrowheads.

6. Figures 2, 3 and 4: There was no indication of statistical analysis in Figures 2 and 4. In addition, statistical analysis should be performed in Figure 3.

7. Figure 4: How long were cells treated with Ang II for measurement of TNF-α and MCP-1?
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

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