

Format for ANSWERING REVIEWERS



September 14th, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 12178-review.doc).

Title: Roles of the (pro)renin receptor in the kidney

Author: Yoichi Oshima, Satoshi Morimoto, Atsuhiko Ichihara

Name of Journal: *World Journal of Nephrology*

ESPS Manuscript NO: 12178

The manuscript has been improved according to the suggestions of reviewers:

1 The language polishing has been updated with the native check.

2 Revision has been made according to the suggestions of the reviewer

(1) As suggested by reviewer 02446027, we added summary section to make the paper complete. Also, we have gone over conclusion section and provided expert opinions.

(2) As suggested by reviewer 00352837, the sentence "transgenic rats overexpressing human PRR showed high PRR mRNA expression in tissue including kidney (originally page 6 line 18)," would misinform about the natural PRR expression. Therefore we deleted the sentence.

(3) As suggested by reviewer 00352837, originally from page 6 line 15 to page 7 line 5, we discussed about the effect of increased PRR activity in podocyte, although some evidences were not focused on podocytes. Therefore, we rewrote our sentences to focus on podocytes. For example, we changed reference from original reference number 28 to newly selected reference number 27 (Durvasula RV, Shankland SJ. Activation of a local renin angiotensin system in podocytes by glucose. *Am J Physiol Renal Physiol*. 2008; 294: F830-839 [PMID: 18216149 DOI: 10.1152/ajprenal.00266.2007]) so that the evidence shows increased PRR expression in rat DM podocytes.

(4) As suggested by reviewer 00352837, originally from page 6 line 25, we stated all RAS components are expressed in podocytes. This is not in accordance with drift of an argument. Therefore, we deleted the sentence.

(5) As suggested by reviewer 00352837, we stated that PRR up-regulation in the kidney of DM rats was inhibited by ARB treatment (originally page 7 line 16). We also stated that regression of nephropathy was observed in HRP treatment, but not ACEi treated DM rats. This phenomenon is yet to be proven and needs to be experimentally shown. Also, it is difficult to present a hypothesis for an explanation. Therefore we deleted the sentence in originally page 7 line 16.

3 There were too many abbreviations in the manuscript. Therefore we reduced the number of abbreviations.

4 The figures were not clear. Therefore we uploaded the figure tiff file.

5 The figures are down-sized to be less than 4 Mbs for ESPS. If the figures are not clear, we are cable of providing original 300dpi tiff figure files via e-mail.

6 The title of the article has been modified slightly.

Thank you again for reviewing our manuscript and we hope that with these revisions you will consider our manuscript suitable for publication in the *World Journal of Nephrology*.

Sincerely yours,

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