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July 11th 2016

Dear Editor,

Please find attached a revised version of the manuscript No. 26818 by Taro Tsujimura *et al.*, entitled "Roles and regulation of BMP7 in kidney development and diseases".

We were extremely pleased to see that the reviewer expressed very positive views on our work. We have modified the manuscript in accordance with the requests they made, as listed in the point-by-point response to the comments below.

In addition, we asked Filipodia Publishing, LLC to perform proofreading of the manuscript. Following their suggestions, we have corrected words and phrases so that they become more comprehensible to readers.

None of the changes that we have made affects the contents and the messages that the original version of the manuscript carried.

We are confident that this revised version addresses all the points raised by the initial review, and now you will be able to accept it for World Journal of Stem Cells.

Sincerely yours,

Keiichi Hishikawa, MD, PhD.
Department of Advanced Nephrology and Regenerative Medicine,
Division of Tissue Engineering,
The University of Tokyo Hospital

Point-by-point responses to reviewers' comments.

Reviewer's code: 00503292

COMMENTS TO AUTHORS

See attached file

-We appreciate the reviewer's suggestions, which were mostly related to the English language usage. We corrected phrases following the suggestions.

Reviewer's code: 00607640

COMMENTS TO AUTHORS

The authors reviewed the related findings in the regulation of BMP7 expression in the kidney development and disease and discussed the possibility of the future application of hyper-activation of the endogenous action of BMP7 for the treatment of kidney disease. Overall, this article is interesting, and provides insight in the therapy of kidney diseases.

-We thank the reviewer for her/his very positive comments on the interest and quality of our work.

Reviewer's code: 02446027

COMMENTS TO AUTHORS

The authors review the roles and regulation of BMP7 in kidney development and diseases. The authors also review the several regulatory mechanism of the Bmp7 expression. The topic is of considerable interest since BMP7 plays an important role in both the development and regeneration of the kidney. Acute and chronic kidney diseases such as kidney inflammation and fibrosis are affecting millions of people worldwide and the prevalence of these diseases is increasing and it is a serious health problem. Administration of BMP7 to injured kidneys prevent inflammation and fibrosis. Therefore, review on the roles and regulation of BMP7 in kidney development and diseases and use of BMP7 as therapies intervention is a beneficial. Overall the review is complete, and contains most important information about the roles and regulation of BMP7 in kidney. However, there are several concerns about the manuscript which need to be improved. Therefore, I cannot recommend acceptance of the manuscript in its present form. The manuscript needs minor revision.

Comments: 1. The manuscript is long, and there are some spelling, grammar and syntax errors that require attention.

-We removed the following sentence on the page 15 for the sake of simplicity:

"However, it has not been assessed well whether the regulation is direct or indirect: it might be possible that cellular changes as a result of the action of TGF β 1 pathway or MyoR lead to regulatory alteration impinging on the *Bmp7* expression. "

-We checked our manuscript for spelling, grammar and syntax errors. We also utilized an English language editing service by Filipodia Publishing, LLC and obtained a certificate from them for the language usage of our manuscript.

2. The manuscript as written is somewhat difficult and needs revision.

-As noted in the response to the comment 1, we have extensively revised the manuscript. We believe that the manuscript is now comprehensible to broad readers.

3. Some of the references were old. For example, reference number 1, 5, ext. The authors need to add new, up-to-date references to the reference section.

-We added the following references that should guide readers to the up-to-date knowledge:

2 Salazar VS, Gamer LW, Rosen V. Bmp signalling in skeletal development, disease and repair. *Nature reviews Endocrinology* 2016; 12: 203-221 [PMID: 26893264 DOI: 10.1038/nrendo.2016.12]

5 Zouvelou V, Luder HU, Mitsiadis TA, Graf D. Deletion of bmp7 affects the development of bones, teeth, and other ectodermal appendages of the orofacial complex. *Journal of experimental zoology Part B, Molecular and developmental evolution* 2009; 312B: 361-374 [PMID: 19127565 DOI: 10.1002/jez.b.21262]

9 Yanagita M. Inhibitors/antagonists of tgf-beta system in kidney fibrosis. *Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association* 2012; 27: 3686-3691 [PMID: 23114895 DOI: 10.1093/ndt/gfs381]

10 Tampe D, Zeisberg M. Potential approaches to reverse or repair renal fibrosis. *Nature reviews Nephrology* 2014; 10: 226-237 [PMID: 24514753 DOI: 10.1038/nrneph.2014.14]

16 Nishinakamura R, Sakaguchi M. Bmp signaling and its modifiers in kidney development. *Pediatric nephrology* 2014; 29: 681-686 [PMID: 24217785 DOI: 10.1007/s00467-013-2671-9]