

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Nephrology

**ESPS manuscript NO:** 15412

**Title:** Species differences in the regulation of renal proximal tubule transport

**Reviewer's code:** 00502999

**Reviewer's country:** Argentina

**Science editor:** Yue-Li Tian

**Date sent for review:** 2014-11-26 17:21

**Date reviewed:** 2014-11-30 05:28

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

The manuscript by G Seki et al about certain species differences in the regulation of renal PCT transport is well-written and interesting. Minor changes: As the paper refers to only 3 molecules, I suggest the title be modified: Maybe "Species differences in the transport (or handling) of certain molecules in the renal proximal tubule" could be more suitable. When talking about TZDs, authors explain that these drugs have no effect at the distal tubule (pages 4 and 5). However, at the end of that section they state that ENaC maybe involved in the mechanisms of salt and water retention caused by these drugs (last sentence page 6). Please conciliate and clarify this contradiction. Page 9: Main paragraph. From "However, renal NO production...." until "However, such an adaptive...humans" needs to be rewritten. It is repetitive.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Nephrology

**ESPS manuscript NO:** 15412

**Title:** Species differences in the regulation of renal proximal tubule transport

**Reviewer's code:** 00503043

**Reviewer's country:** Canada

**Science editor:** Yue-Li Tian

**Date sent for review:** 2014-11-26 17:21

**Date reviewed:** 2014-11-30 17:37

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

In the study, it was aimed to review the "Species differences in the regulation of renal proximal tubule transport" (ESPS Manuscript NO: 15412. The subject is interesting and has certain clinical significance. However, the paper has some important limits stated as follows: 1) Title " Maybe Species differeces in the transport of certain molecules in the renal proximal tubule" could be more suitable 2) I suggest add content of "WNK kinases regulates the balance between renal NaCl reabsorption and K<sup>+</sup> secretion"some references are following 2.1 Yang CL, Angell J, Mitchell R, Ellison DH. WNK kinases regulate thiazide- sensitive Na-Cl cotransport. J Clin Invest, 2003, 111(7):1039-1045. 2.2 Kahle KT, Wilsom FH, Leng Q, Lalioti MD, O'Connell AD, Dong K, Rapson AK, MacGregor GG, Giebisch G, Hebert SC, Lifton RP. WNK4 regulates the balance between renal NaCl reabsorption and K<sup>+</sup> secretion. Nat Genet, 2003, 35(4):372-376. 2.3 Kahle KT, Gimenez I, Hassan H, Wilson FH, Wong RD, Forbush B, Aronson PS, Lifton RP. WNK4 regulates apical and basolateral Cl<sup>-</sup> flux in extrarenal epithelia. Proc Natl Acad Sci U S A, 2004,101(7):2064-2069 In conclusion, This manuscript should be subjected to revision to be deemed for publication.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Nephrology

**ESPS manuscript NO:** 15412

**Title:** Species differences in the regulation of renal proximal tubule transport

**Reviewer's code:** 00503339

**Reviewer's country:** United States

**Science editor:** Yue-Li Tian

**Date sent for review:** 2014-11-26 17:21

**Date reviewed:** 2014-11-26 21:59

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D: Fair		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

Topic is important and studies cited in review are meaningful. The Reader is left without a clear grasp of what points have been made and how the information transmitted may lead to clinical advances in using proximal tubular transport for the benefit of patients with diabetes or other disorders that effect electrolyte and fluid balance. The Authors would strengthen their case that species differences in renal physiologic response may impact both the presentation of diseases and response to therapy. Clear examples include the recognition of the importance of advanced glycosylated endproducts in the deleterious effect of induced diabetes in rodents as well as the marvelous blockage of progression of induced diabetic nephropathy by aminoguanidine and a series of other drugs including Alagebrium, Pyridoxamine, and Ruboxistaurin which were not found effective in initial human trials in diabetic patients. The point being made is that the Authors would add to the meaning of their Review by proffering several examples of how metabolic species differences have thus far created substantive problems to the extent that several well known investigators have turned away from using rodents in favor of canines and primates for their important trials. It would also increase the meaning of this Review if the Authors added several summaries within the paper of what is being discussed and which derivative studies might prove productive. Lastly, one or two diagrams centering on the Proximal Tubule and the inferences drawn from the studies cited would help Reader understanding. In its present form, there is minimal enthusiasm generated for



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