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315-321 Lockhart Road,
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ESPS Peer-review Report
Name of Journal: World Journal of Hypertension
ESPS Manuscript NO: 4196
Title: Tissue angiotensin II-forming activity in two-kidney, one-clip (2K1C) hypertensive hamster model
Reviewer code: 00504359
Science editor: Wen, Ling-Ling
Date sent for review: 2013-06-21 16:37
Date reviewed: 2013-06-27 02:42

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[Y] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

The paper by Uehara et al investigates the contribution of tissue chymase and ACE to AngII formation and blood pressure regulation in a RAS-dependent hypertension model in hamsters. The design of the study is good. However, the style in writing requires some improvement as the information presented does not flow and appears out of focus. Some sentences should be differently placed to avoid interruption of ideas. A few examples: Introduction paragraph 3: The paragraph should be re-written as such: "Chymase is a chymotrypsin-like serine protease found in human heart (9), blood vessels (12), and several other tissues (10), but not in plasma (11). Chymase is stored in a complex with heparin proteoglycan in the secretary granules of mast cells. It remains in this complex, which binds to the extracellular matrix, and remains active for several weeks after it is released from these granules." The last sentence is repetitive. Note re-organization of reference numbers. p.5: line 5: delete the "physiological role of chymase is not known". The following sentence would read: "Interestingly, human 'and hamster' chymase primarily form……" Delete the first 2 sentences of paragraph 2, which starts : "Because of species…." . Instead write: "In these studies, we compared …… Methods: Have the studies been approved by the Institutional Ethics Committee following animal handling guidelines? Please add the information. Results: Fig 1A: What is the basis for blood pressure measurement at these time points: 18 and 34 weeks? BP could have been elevated earlier? Paragraph 1: Move the sentence "At the end of the experimental protocol, hamster hearts 'and kidneys' were removed and weighed" to experimental protocol. Re-write the paragraph to include results only. Paragraph 2: "low levels of pulmonary chymase mRNA expressions were detected". Because the increased chymase mRNA levels in the heart and aorta "peaked at 16

weeks". The word peaked is misleading. We do not know what the levels were at an earlier time point. The sentence could be re-written as: "Because the increased chymase mRNA levels in the heart and aorta were high at 16 weeks…." Discussion Paragraph 2: The sentence "Human chymase appears to be involved in clinical disorders such as atherosclerotic lesions (19), acute coronary syndrome (20), disorders in the metabolism of apolipoprotein (21), and extracellular matrix degradation (22-25)" must be taken out from this paragraph as it interrupts the flow of information. Paragraph 3: After this sentence "Some remarkable differences in Ang II-forming pathways have been reported among various species (13)" we would expect differences in various species. However, these species-differences are not presented. And so on…The Discussion must be shortened and re-written with more focus.

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ESPS Peer-review Report
Name of Journal: World Journal of Hypertension
ESPS Manuscript NO: 4196
Title: Tissue angiotensin II-forming activity in two-kidney, one-clip (2K1C) hypertensive hamster model
Reviewer code: 00070389
Science editor: Wen, Ling-Ling
Date sent for review: 2013-06-21 16:37
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
The authors have found that after renal artery clipping, systolic blood pressure increased in parallel with chymase-dependent Ang II-forming activities in the heart and aorta tissues. Although there is some scientific merits in this manuscript, the paper will be significantly strengthened if the authors consider to address following issues: major concerns: (1) Despite aorta and cardiac tissue Ang II was found to have changed, what are possible changes in the circulating Ang II or brain Ang II after renal artery clipping? Please discuss this in the Discussion. (2) Figs 3-4, what the statistical significance for $p<0.1$? Please remove it if it does not mean anything. (3) Change in the mast cell number: it's better to show the data. (4) Discuss possible pathophysiological mechanisms underlying the changes in heart weight proportion following renal artery clipping.

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ESPS Peer-review Report
Name of Journal: World Journal of Hypertension
ESPS Manuscript NO: 4196
Title: Tissue angiotensin II-forming activity in two-kidney, one-clip (2K1C) hypertensive hamster model
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Science editor: Wen, Ling-Ling
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
This manuscript reports an interesting study concerning the regulation of tissue Ang II-forming enzymes ACE and chymase in 2K1C hypertensive hamsters. It was found that tissue ACE and chymase were regulated in a tissue-dependent manner, and the both enzymes were independently regulated. The experiments were well-designed, and results presented in a clear manner. The data supports the conclusions reached by the authors, and this study will add to our current knowledge on RAS. However, I have a few minor concerns and recommendations for improving the manuscript. 1. The discussion on the difference of Ang II forming pathways existing among various species is not antiquate (paragraph 3 on page 11) 2. The biological and pathological significances of tissue-dependent regulation on ACE and chymase were not well discussed.

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ESPS Peer-review Report
Name of Journal: World Journal of Hypertension
ESPS Manuscript NO: 4196
Title: Tissue angiotensin II-forming activity in two-kidney, one-clip (2K1C) hypertensive hamster model
Reviewer code: 00070411
Science editor: Wen, Ling-Ling
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[ ] Accept
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COMMENTS TO AUTHORS
GENERAL COMMENTS MAY CONSIST OF FOUR MAJOR POINTS The authors of the study evaluated the role of chymase in blood pressure regulation and its actions on tissue RAS in 2K1C hypertensive hamsters. The methods of the study were novel to analyze the same problem. SPECIFIC COMMENTS MAY CONSIST OF THE FOLLOWING POINTS 1. For the title, it mostly accurately reflects the major topic and contents of the study. Additionally, the more concise, the better. 2. "Each drug was used at its maximum dosage" must be given the reference information and the evidences. 3. The results didn't refer to the protein expression levels (for example" western blotting"). However, the discussion also didn't give more interpretation. 4. Most of the references in this manuscript were senior, which cannot represent the updated information. 5. Parts of the pathology pictures should be presented for more direct information. 6. Did the experiment have consented by the animal ethics committees? 7. Figures are excellent.