

August 8, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word 2010 format (file name: Uehara\_WJH\_2ndSubmit.docx).

**Title:** Induction of tissue angiotensin II-forming activity in two-kidney, one-clip (2K1C) hypertensive hamster model

**Author:** Yoshinari Uehara, Kanta Fujimi, Eiji Yahiro, Satomi Abe, Sankar Devarajan, Keijiro Saku, Hidenori Urata

**Name of Journal:** *World Journal of Hypertension*

**ESPS Manuscript NO:** 4196

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

1 Format has been updated

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

1. For the title, it mostly accurately reflects the major topic and contents of the study. Additionally, the more concise, the better.

As reviewer suggested, we changed the title more accurately.

2. "Each drug was used at its maximum dosage" must be given the reference information and the evidences.

We agree with the reviewer. Page 13, line 5; “maximum dosage” feels discomfort. We have changed the word from “maximum dosage” to “sufficient dosage”, and we have cited 3 references (Ref #18, #19, #20) for information of the dosage.

3. The results didn't refer to the protein expression levels (for example" western blotting"). However, the discussion also didn't give more interpretation.

It is a very important question. We tried to detect hamster chymase by western blot analysis, however it was not possible to detect a specific band for hamster chymase protein, although the antibodies could detect a human chymase protein. In addition, finally 3 kinds of commercially available chymase antibodies were tried to be analyzed for western blot, but all of them did not recognize it.

4. Most of the references in this manuscript were senior, which cannot represent the updated information.

We agree with the reviewer. We have added 2 updated references (Ref #32, #33).

5. Parts of the pathology pictures should be presented for more direct information.

Thank you very much for this comment; Immunohistochemical study against hamster chymase did not success because antibody problem as described above. Therefore, we have added histological study to detect mast cell which is main source of chymase by using toluidine blue staining. We have added histological pictures in Figure 2G-2J.

6. Did the experiment have consented by the animal ethics committees?

Thank you very much for this comment; All of the study protocol were approved by the Animal Care and Use Committee of Fukuoka University. Therefore, we have added the sentence about it in Page6, line4.

7. Figures are excellent.

Figure 2 was modified to add the histological results.

Thank you again for considered for publication our manuscript in the *World Journal of Hypertension*.

Sincerely yours,

A handwritten signature in black ink, appearing to read 'Y. uehara' with a stylized flourish at the end.

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