

January 30, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 1387-review.docx).

Title: Pericytes synthesize renin

Author: Alison C Berg, Catalina Chernavvsky-Sequeira, Jennifer Lindsey, R Ariel Gomez, Maria Luisa S Sequeira-Lopez

Name of Journal: *World Journal of Nephrology*

ESPS Manuscript NO: 1387

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

1. Format has been updated
2. We want to thank reviewer 1 for his comments and suggestions that helped us improve the manuscript.
Revision has been made according to all the suggestions of reviewer 1.

- (1) Question: Abstract: The conclusion "Interstitial pericytes synthesize renin throughout development...." seems misleading since in WT mice the number of renin-expressing pericytes diminishes with age. Not sure what the authors meant by "Conclusion: in response to a homeostatic threat imposed early in life". Were the authors talking about the knockout condition?

Answer: We clarified our conclusion as follows: Interstitial pericytes synthesize renin during development and the number of renin-expressing pericytes increases in response to a homeostatic threat imposed early in life such as lack of angiotensinogen.

- (2) Question: Introduction: The authors need to make it clearer regarding the rationale and the significance of the study. The sentence "Recently, a lineage relationship between renin-expressing cells and pericytes has been suggested...." seems rather vague to provide a strong rationale why there is a need to conduct this study.

Answer: We added the reference of an extensive previous study that suggested a lineage relationship between renin cells and pericytes due to a high expression of typical pericyte markers such as Rgs5, Rgs2 and several smooth muscle genes.

- (3) Question: Results: The authors described the distribution of renin in the kidneys of AGT -/- mice vs. WT mice on E18, P1, P5, P10, etc. However, there was only one figure showing the immunostaining for renin in angiotensinogen deficient mice at 10 days of postnatal life. Where are the other data? The authors need to show all the data. In addition, the authors need to quantify the renin staining in order to demonstrate the results.

Answer: As suggested by the reviewer we are showing representative figures for all the ages studied from both genotypes at low magnification (Figure 1) and representative ages at higher magnification (Figure 2). The figures are at high resolution and can be zoomed. We also quantified and compared the number of renin-positive pericytes at each developmental stage. These new results are now included in the text and also illustrated in Figure 3.

- (4) Question Discussion: Without actually showing the data, the discussion seems futile.

Answer: We are now showing all the data making the discussion more fruitful.

We also want to thank reviewers 2, 3 and 4 for their encouraging and positive comments regarding our manuscript.

3. References and typesetting were corrected

4. Please note that there was a spelling error in one of the author's last name (should be **Lindsey** instead of Lindsay)

Thank you again for publishing our manuscript in the *World Journal of Nephrology*.

Sincerely yours,



Maria Luisa S Sequeira-Lopez, MD

Department of Pediatrics

University of Virginia School of Medicine

409 Lane Rd MR4 Bldg room 2001, Box 801334

Charlottesville, VA 22908

United States.

Msl7u@virginia.edu

Telephone: +1-434-9245065/1741

Fax: +1-434-9824328