



Rosario, June 18th 2015.

Jing Yu

Science Editor, Editorial Office

Baishideng Publishing Group Inc

Re: **Manuscript NO: 16533**

Authors: Anabel BRANDONI and Adriana TORRES

Name of Journal: **World Journal of Gastroenterology**

Column: **Basic Study**

Dear Editor,

We submit the revised version of the manuscript entitled "**EXPRESSION OF RENAL Oat5 AND NaDC1 TRANSPORTERS IN RATS WITH ACUTE BILIARY OBSTRUCTION**", according to the reviewer's comments. We took into account all the valuable comments made by the referee and modified our manuscript accordingly. We have also updated the manuscript according to the Format for Basic Study. We attach a revised manuscript with indications of changes in red and a revised manuscript without indications of changes. We feel that we satisfactorily responded to all the issues raised and are looking forward to your reconsideration of our manuscript.

We thank to the referee for the helpful suggestions which contributed substantially to improve the quality of our manuscript.

In the following, we briefly cite the comments made by the referee and give a statement on how we responded to them.

Sincerely yours,

Prof. Dr. Adriana M. Torres

Answers to Referee

First of all, we thank to the referee for evaluating this manuscript and for the helpful comments and suggestions which contributed substantially to improve the quality of our manuscript.

Comments to the author:

In this manuscript, the authors intended to characterize the urine excretion of organic anions and the expression of Oat5 and NaDC1 in bile duct ligated rat kidneys. This can be an interesting study, but need much more work before its publication.

1.- *Need to show samples from all animals in Figure 1 and 2 since there were only 4 in each group. Reference proteins also need to be included.*

ANSWER: The samples from all animals have been included in Figure 1 and Figure 2 (Figure 3 in the revised manuscript). β actin has been included as a reference protein in Western-blotting studies in order to follow the Reviewer's suggestion.

2.- *Were the altered expression of these two genes at mRNA level or at protein level only?*

ANSWER: the altered expression of these two genes was only at protein level. Nevertheless, we included mRNA levels in the revised manuscript.

3.- *Is there any immunofluorescence or immunohistochemistry labeling confirming increased membrane expression of kidney NaDC1 after BDL?*

ANSWER: we have included Immunohistochemistry labeling confirming the increased membrane expression of both renal NaDC1 and Oat5 after BDL in order to follow the Reviewer's request.

4.- *Most importantly, what causes the expression alteration of these genes? This will need some in vitro experiments.*

ANSWER: These genes are not altered. The possible causes of proteins expression alteration are discussed in the manuscript. We have not performed experiments in isolated proximal tubule cells since the available cell lines from renal cortical tubules do not express these proteins (Oat5 and NaDC1) and primary culture of renal proximal tubular cells lose the expression of these transporters, at least to our knowledge. Hering-Smith et al. (*Urolithiasis* 2014; 42: 209–219) have reported that OK cells express NaDC1 in submembrane vesicles, so these cells are not suitable for performing some experiments of our interest.

5.-*The results were not well illustrated and the Discussion is too lengthy.*

ANSWER: The results have been better illustrated and additional data have been included. Some paragraphs of the old Discussion have been deleted in the revised manuscript according to the Reviewer's suggestion. Nevertheless, we could not avoid including some short sentences to discuss the new data included in the revised manuscript.

6.-*Gene symbols of Oat5 and NaDC1 need to be included when they first appear in the text.*

ANSWER: Gene symbols of Oat5 and NaDC1 have been included in the revised manuscript.