Dear Editor,

please find enclosed the edited manuscript in word format（file name：51858-Manuscript File.doc）.

Name of Journal: World Journal of Clinical Cases

Manuscript NO.: 51858

Column: Review

Title: Overview of OATs and OATPs and their roles in the liver.

Authors: Tingting Li, Jiaxing An, Jing-Yu Xu and Biguang Tuo

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

The first reviewer

(1) Fig 1 is referred to in the text only after Fig 2. It is suggested to reference Fig 1 already in the introduction chapter.

Already made revisions.

(2) Chapter 4 largely discusses OAT and OTATP in HCC and provides less information on HB/HCV and other causes of chronic liver diseases. It would be good to include more aspects of e.g. PBC, PSC, alcoholic liver diseas and especially NAFLD and NASH as the latter two are rapidly increasing in prevalence and importance for endstage liver disease

worldwide.

There are few studies on OAT/OATP in chronic liver diseases. We add some information about OAT/OATP in NAFLD.

The second reviewer

(1) Extensive language editing is needed. For example, in lines 4 of the abstract, what does it mean “normal”. In addition, in the line of third to the last, it should be “… OAT and OATP structures…”. Moreover, the first sentence of Introduction section (the third word), it should be “…are…”. There are other places.

Already made revisions by professional translation sevice.

(2) HNF1a was defined on page 22/50. However, it was defined again on page 24/50. Please use abbreviation when you defined an abbreviation.

Already made revisions.

(3) The value of the current view can be improved if the chromosome loci of those transporters in human are summarized in if data are available.

The chromosome loci of those transporters have been added in Table1 and Table2.

(4) In addition, in those tables, it will be very helpful if the Km of these transporters to those substrates are shown.

The Km of these transporters to those substrates have been added in

Table1 and Table2.

(5) Figure 2 should have more figure legend to describe the content.

Already made revisions.

The third reviewer

(1) Page 15, line 1-7: The authors indicate that changes in OAT2 expression may help explain the pharmacokinetic changes in patients with cirrhosis who have high plasma hepatocyte growth factor HGF levels. However, the quoted references only mentioned about the function and changes of HGF levels in patients with liver decompensation. Although Le et al found that HGF treatment downregulated OAT2 mRNA levels, this is not necessarily linked to the pharmacokinetic changes in cirrhotic patients, because OAT2 are multifunctioning.

OAT2 acts as a liver uptake transporter, and its down-regulation leads to prolonged plasma retention of the drug, potentially increasing drug toxicity. Therefore, the expression of OAT2 may affect the clearance of drugs in patients with cirrhosis with high HGF levels, but further research is needed.

(2) Page 16, line 13-14: ……”It has been hypothesized that these

microenvironmental changes may occur in patients with early chronic HCV.” The reference is suggested to be quoted.

Already made revisions.

3.References and typesetting were corrected.

Thank you again for publishing our manuscript in the World Journal of Clinical Cases.

Sincerely yours,

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