

ANSWERING REVIEWERS



February 10, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 6262-review.doc).

Title: The inhibitory Effects of Rapamycin on the Different Stages of Hepatic Fibrosis

Author: Yun Jeung Kim, Eaum Seok Lee, Seok Hyun Kim, HeonYoung Lee, Seung Moo Noh, Dae Young Kang, Byung Seok Lee

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 6262

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) The language has been edited by the American Journal Experts service mentioned in –“ The Revision Policies of BPG for Article.”

(2) Answers are provided according to ‘Reviewed by 00070577.’

1) Serum data (TB, AST) got worse. How the author explain this discrepancies?

The AST and TB discrepancies may be associated with hemolysis or fasting time.

2) The CK 19 staining is not positive in the RAP+ and RAP ++ groups except in the BDL-no treatment group as shown in Figure 1.

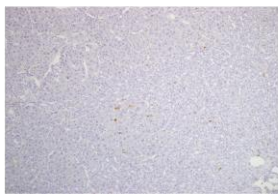
3) The authors intend to reveal that rapamycin can inhibit hepatic fibrosis and has a different effect in the different stages of fibrosis. The target cells of rapamycin may be myofibroblasts, which serve an important role. So we thus examined α -SMA, which is a marker of activated hepatic stellate cells (HSCs) and myofibroblasts, and found that this marker increases following chronic liver damages.

4) Our lab used semiquantitative-PCR instead of real-time PCR due to our experimental conditions.

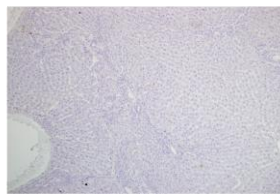
(3) Answered according to ‘Reviewed by 005033398.’

- 1) The authors used a-SMA and CK-19 liver staining which are indirect measures. In future studies, the authors will attempt to utilize direct approaches, such as picroserious red staining or biochemical estimation of liver hydroxyproline.
- 2) Our lab used semiquantitative-PCR instead of real -time PCR dut to our experimental conditions.
- 3) The study revealed that BDL+/Rapa++ showed decreased expression level compared with BDL+/Rapa+ but the difference was not significant (Figures 2A and 2B). However, the P70s6k and p-p70s6k protein expression patterns were significantly different.
- 4) We performed TUNEL staining as apoptosis marker but, there was no difference in experimental groups. We guess that our results are not due to apoptosis of hepatic stellate cell. We did not add these results in the results and discussion.

BDL⁺/Rapa⁻



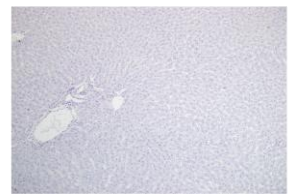
BDL⁺/Rapa⁺



BDL⁺/Rapa⁺⁺



BDL⁻/Rapa⁻



- 5) A discussion of differences between this study and the work of Bicker et al. has been added to the discussion.
- 6) References on human studies should be included in the discussion.

3 References and typesetting were corrected

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

Sincerely yours,



Peter Laszlo LAKATOS, MD, PhD
1st Dept. of Medicine
Semmelweis University
Budapest, Koranyi 2A
H-1083-Hungary
Fax: +36-1-313-0250
E-mail: kislakpet@bell.sote.hu

