

ANSWERING REVIEWERS



May 30, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 8506-revised-review.doc).

Title: Necroptosis; An Emerging type of cell death in liver diseases

Author: Waqar Khalid Saeed and Dae Won Jun

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 8506

The manuscript has been improved according to the suggestions of reviewers and changes made are highlighted.

1. English has been revised and re-checked to meet the standards.
2. Revision has been made according to the suggestions of the reviewers

Reviewer 1

1. English language must be improved along the manuscript.
 - As reviewer pointed, English of the manuscript has been re-checked and improved accordingly.
2. For scientists no familiar with necroptosis, it would be most useful to include liver histologies of cases showing necroptosis, in comparison with apoptosis and necrosis.
 - Morphologically, accidental necrosis and necroptosis (programmed necrosis) are quite the same. It is the molecular and signaling machinery, which is said to be different. Although, necroptosis has been extensively studied now a day, there is no clear consensus on specified necroptosis markers. Most of studies evaluated the presence of molecular machinery of necroptosis (RIPK1, RIPK3) in their studies to confirm the existence of necroptosis.
3. Are there studies showing liver necroptosis in humans? If the answer is yes, include a brief description and relevance.
 - To best of our knowledge, only Roychowdhury *et al.* (Page 7), documented an increased expression of RIP3 in human liver biopsies of alcoholic liver disease. The text is highlighted and relevance has been mentioned.
4. In page 9, the authors should give some information regarding pyroptosis and ferroptosis.
 - As reviewer suggested, we have briefly described about pyroptosis and ferroptosis (Page 9).
5. FIGURE 2 should be cited in the text of the manuscript.
 - As reviewer pointed out, Figure 2, has been renamed and cited as Figure 1 (Page 5) has been mentioned in the text of the manuscript.

Reviewer 2

1. A brief explanation for figure 2 (figure legend) is needed. In the text, figure 2 is cited before figure 1.
 - We have re-arranged the figures order as reviewer suggested and a brief explanation of figure 1 is also added.

Sincerely yours,

Waqar Khalid Saeed and Dae Won Jun