

Prof. Lian-Sheng Ma,  
President and Company Editor-in-Chief  
Editor-in-Chief,  
World Journal of Gastroenterology  
E-mail: l.s.ma@wjgnet.com

Dr. Ze-Mao Gong  
Senior Editor, World Journal of Gastroenterology  
Science Editor, Editorial Office  
Baishideng Publishing Group Inc

Please find enclosed the edited manuscript in Word format (file name: Revised-38962-Edited.docx).

**Title:** Apoptosis and non-alcoholic fatty liver diseases (Topical review)

**Authors:** Tatsuo Kanda, Shunichi Matsuoka, Motomi Yamazaki, Toshikatsu Shibata, Kazushige Nirei, Hiroshi Takahashi, Tomohiro Kaneko, Mariko Fujisawa, Teruhisa Higuchi, Hitomi Nakamura, Naoki Matsumoto, Hiroaki Yamagami, Masahiro Ogawa, Hiroo Imazu, Kazumichi Kuroda, Mitsuhiko Moriyama

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

**ESPS Manuscript NO: 38962**

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

1 The format has been updated.

2 The revisions have been implemented according to the suggestions of the reviewers:

(1) The comment from reviewer **03646639**

*Response to your comment: "Kanda et al reviewed the importance of cell death in NAFLD and NASH. Clinical trials for the treatment of NASH targeting apoptosis are being performed. This is well written paper, No seriously grammar mistakes were found and no statistical methods were observed. I think this article can be accepted."*

Thank you for your encouraging comments.

(2) The comment from reviewer **02447091**

*Response to your major comment 1: "Page 6, lines 2-4. Apoptosis in the pathogenesis of alcoholic hepatitis is also important in some literatures, an example of those is listed below.*

*Thus, the authors should cite such a reference and change the sentences in this part. Takahashi T, So-Wan T, Kamimura T, Asakura. Infiltrating polymorphonuclear leukocytes and apoptotic bodies derived from hepatocytes but not from ballooning hepatocytes containing Mallory bodies show nuclear DNA fragmentation in alcoholic hepatitis. Alcoholism: Clin Exp Res 2000; 24: 68S-73S."*

Thank you for your valuable comments. We agree with you. According to your suggestions, we added a new reference [3] and revised our manuscript as follows.

In page 6, lines 8-11,

....of liver transplants in the USA<sup>[2]</sup>. Accordingly, there is increasing evidence that HCC can develop in the NASH<sup>[2]</sup>. **In the liver of patients with alcoholic hepatitis, infiltrating polymorphonuclear leukocytes and apoptotic bodies derived from hepatocytes are observed<sup>[3]</sup>.** A combination of....

*Response to your minor comment 1: "Page 5, lines 8. ... and NAFLD-HCC are ... should be ... and NAFLD-HCC (hepatocellular carcinoma) are..."*

Thank you for your valuable comments. We agree with you. Accordingly, we revised our manuscript with red color.

*Response to your minor comment 2: "Page 5, lines 9. ... that hepatocellular carcinoma (HCC) should be ... that HCC can..."*

Thank you for your valuable comments. We agree with you. Accordingly, we revised our manuscript with red color.

*Response to your minor comment 3: "Page 9, lines 21. ...Spl, which results in ... should be ...Spl, which results in ..."*

Thank you for your valuable comments. We agree with you. Accordingly, we revised our manuscript with red color.

*Response to your minor comment 4: "Page 16, lines 2. It has also been reported ... should be It has also been reported ..."*

Thank you for your valuable comments. We agree with you. Accordingly, we revised our manuscript with red color.

*Response to your minor comment 5: "Page 16, lines 6. ... apoptosis[67]. should be ... apoptosis [67]"*

Thank you for your valuable comments. We agree with you. Accordingly, we revised our manuscript with red color.

*Response to your minor comment 6: "Page 18, lines 12. ... to cell autophagy may inhibit ... should be ... to cell autophagy and may inhibit ..."*

Thank you for your valuable comments. We agree with you. Accordingly, we revised our manuscript with red color.

*Response to your minor comment 7: "Page 18, lines 24. ... SIRT3 negative regulates ... should be ... SIRT3 negatively regulates ..."*

Thank you for your valuable comments. We agree with you. Accordingly, we revised our manuscript with red color.

*Response to your minor comment 8: "Page 20, lines 8. ... FGF-21 were founded to be ... should be ... FGF-21 were found to be."*

Thank you for your valuable comments. We agree with you. Accordingly, we revised our manuscript with red color.

*Response to your minor comment 9: "Page 20, lines 10. ... study founded that... should be ... study found that."*

Thank you for your valuable comments. We agree with you. Accordingly, we revised our manuscript with red color.

*Response to your minor comment 10: "Page 21, lines 24. These complex liquids are ..."*

should be These complex lipids are."

Thank you for your valuable comments. We agree with you. Accordingly, we revised our manuscript with red color.

*Response to your minor comment 11: "Page 23, lines 6. ... (LPC)-induced ... should be ... (LPC) induced ..."*

Thank you for your valuable comments. We agree with you. Accordingly, we revised our manuscript with red color.

*Response to your minor comment 12: "Page 47. Table 1, lines 30. (MMO should be (MMO). "*

Thank you for your valuable comments. We agree with you. Accordingly, we revised our manuscript with red color.

(3) The comment from reviewer **00503536**

*Response to your comment: "The only one point that need to be addressed is the differences between NAFLD and NASH, which is an important issue for the management of those patients, and for the understanding of the mechanism critically related to the progression to NASH."*

Thank you for your valuable comments. We agree with you. According to your suggestions, we revised our manuscript as follows.

In page 24, lines 15-16,

....in NASH patients. Increased hepatocyte apoptosis may distinguish NASH from NAFLD<sup>[126]</sup>. Repair responses may play an important role in controlling the disease severities of NASH<sup>[126]</sup>. We reviewed....