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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Pathophysiology*

Manuscript NO: 84756

Title: The role of p53 suppression in the pathogenesis of hepatocellular carcinoma

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02860506
Position: Peer Reviewer
Academic degree: MD, PhD

Professional title: Chief Doctor, Professor, Surgeon

Reviewer's Country/Territory: China

Author's Country/Territory: India

Manuscript submission date: 2023-03-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-03-27 13:09

Reviewer performed review: 2023-04-03 08:11

Review time: 6 Days and 19 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors systematically reviewed the role and mechanism of p53 in the pathogenesis of HCC and therapeutic strategy targeting p53. There are several comments: 1. The role of p53 in carcinogenesis and its regulation with MDM2 has already been reported. Several reviews have summarized similar content (PMID: 25477334, 32595984). In addition, references about p53 and HCC in recent years are rarely cited and presented in your article. It should be updated. 2. In the section of 'Roles of p53 in extrinsic factor-induced liver carcinogenesis', alcohol and cirrhosis are very important factors promoting carcinogenesis, which should not be omitted. Please add it. 3. In the section of 'Therapeutic products with p53 as a target', studies of therapeutic approaches targeting p53 are presented. However, these studies only stay at the cellular or animal model level. Is there any clinical trial of therapeutic agent targeting p53? 4. The author summarized the role of p53 in resistance to several chemotherapeutic agents, cisplatin and doxorubicin. However, several important related studies in recent years (PMID: 31244936, 21660965, etc.) were not presented. 5. Molecular targeted drugs, such as sorafenib and regorafenib, are vital treatments for advanced HCC. Many studies have

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reported the role of p53 in resistance to molecular targeted drugs, please add them.

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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Pathophysiology*

Manuscript NO: 84756

Title: The role of p53 suppression in the pathogenesis of hepatocellular carcinoma

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03727494
Position: Peer Reviewer
Academic degree: MD
Professional title: Doctor
Reviewer's Country/Territory: China
Author's Country/Territory: India

Manuscript submission date: 2023-03-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-03-29 09:04

Reviewer performed review: 2023-04-06 09:32

Review time: 8 Days

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

In this study, The authors conducted a large number of literature research, not only analyzing the molecular mechanism of P53 on the development and progression of hepatocellular carcinoma, but also listing how P53 is involved in cancer formation under multifactorial conditions (aflatoxin, vinyl chloride, nonalcoholic fatty liver, iron overloading, hepatitis B virus, hepatitis C virus, etc.). In addition, the authors summarize P53 as a therapeutic target and what is said about drug resistance. Finally, it is proposed that future research directions should focus on the malfunction of the MDM2-P53 axis. In conclusion, the authors made a detailed review of the tumor suppressor gene P53. Although P53-related research has taken many years, its signal transduction pathway is complex and highly correlated with cancer occurrence, and it still has great research value. Therefore, this article has certain reference significance for guiding basic research. However, there are still some parts of the manuscript that need to be improved. 1.

Language needs further improvement. There are still some statements that are difficult to understand. In the "Tumour Suppressor p53" section, the authors mentioned that “A variety of stress signals are detected by p53”, such statements are obviously

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confusing. Moreover, there is no source of documentary evidence for this statement. 2. The penultimate line in the "Tumour Suppressor p53" section, "RINg finger domain" should be "RING finger domain". There are similar problems in the text, for example, in the "Non-alcoholic fatty liver disease (NAFLD)" section, there are some spelling mistakes, such as "percent" with a space in between, "NFk-B" should be written as "NF-κB". 3. The figure notes in this manuscript have too little descriptive text to introduce the content of the figures specifically. 4. The authors have already described the location of p53 in the chromosome and the size of its encoded in the first paragraph of "Tumour Suppressor p53" section, but then repeated this description in the last sentence of the first paragraph of "Role of p53 in mechanisms of hepatocarcinogenesis". 5. The pathogenesis of P53-associated HCC still needs to be elaborated in the context of specific biological phenomena and given an appropriate explanation. The connection and special features of P53 as a tumor target with other related biological targets need to be highlighted. 6. The therapeutic and drug resistance mechanisms of hepatocellular carcinoma-associated P53 are insufficiently described, and the association of MDM2-P53 axis dysfunction with the mechanisms involved is not clear. Whether MDM2 and p53 are a major direct pathway for hepatocarcinogenesis should be added to the description of the pathway mechanism.

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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Pathophysiology*

Manuscript NO: 84756

Title: The role of p53 suppression in the pathogenesis of hepatocellular carcinoma

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02904354
Position: Peer Reviewer
Academic degree: MD
Professional title: Academic Editor, Associate Chief Physician, Associate Professor, Deputy Director
Reviewer's Country/Territory: China
Author's Country/Territory: India

Manuscript submission date: 2023-03-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-03-28 14:15

Reviewer performed review: 2023-04-10 07:53

Review time: 12 Days and 17 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No

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Peer-reviewer statements	Peer-Review: [ ] Anonymous [Y] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The primary issue of this manuscript is that the authors focused on describing the content of the references, but they had few summary from their own perspectives.

When quoting the original text, the authors should refine and summarize the content of the article rather than directly quoting the original sentence. According to the guideline, immunotherapy and targeted therapy are main pharmacological treatment for HCC, but chemotherapy is not the standard conservative treatment for HCC. In this setting, p53 for resistance of chemotherapeutic agents should be of limited value. In the "Conclusion" section, the authors said that they intended to offer some guidance for techniques to cure pre-HCC. Considering that HCC patients with different etiologies had different molecular mechanism, the authors can simply add some suggestions for treatment according to the various etiologies. The authors should carefully check the use of abbreviations in the manuscript. Use the full name at its first occurrence, and then use its abbreviation. For example, in the "Conclusion" section, the authors said "...in this axis during the progression of hepatocellular carcinoma (HCC) are intricate", where the words "hepatocellular carcinoma (HCC)" should be revised as "HCC". The same mistakes can be easily seen. Language and grammar should be improved. For example, in the "Introduction" section, the authors said "As transplantation, ablation and resection can only be used for the treatment of early-stage HCC patients and since diagnosis of the majority of patients is diagnosed with severe stages...", where the words "diagnosis of" should be deleted. The same mistakes can be easily seen. In the "p53 alterations and hepatocarcinogenesis" section, the authors said "Aflatoxin B1, which contaminates foods in regions where it is endemic, clearly plays a part in the

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development of ss...", what's the meaning of "ss"? In the "Aflatoxin B1 (AFB1)" part of "Roles of p53 in extrinsic factor-induced liver carcinogenesis" section, the authors said "As a result, the p53 mutation caused by AFB1 is critical for the development of HCC, pIt's interesting to note that HepG2 cell viability and proliferation are reduced when IGF-2 is silencedresumably through increased IGF-2 signalling.", where the words "pIt's" and "silencedresumably" were wrong. In the "Non-alcoholic fatty liver disease (NAFLD)" part of "Roles of p53 in extrinsic factor-induced liver carcinogenesis" section, the authors said "Just 11.5 per cent of individuals...", where the word "per cent" should be revised as "percent".