



**Baishideng
Publishing
Group**

7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
https:// www.wjgnet.com

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39751

Title: Carcinogenesis on the background of fibrosis: a major challenge in managing Hepatocellular Cancer

Reviewer's code: 00000663

Reviewer's country: Italy

Science editor: Xue-Jiao Wang

Date sent for review: 2018-05-16

Date reviewed: 2018-05-22

Review time: 6 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

A detailed analysis of the carcinogenic processes occurring in the liver in response to necroinflammation and fibrosis. The problem is expected to become of paramount importance, given the increase in the prevalence of NAFLD in the general population.



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The importance of microenvironment in the carcinogenic pathway is probably pivotal, as is the immune-response of the host. 1. I have no major reservations. In order to make the review more easily understandable, one or two pictures summarizing the whole process would be definitely important. 2. Not clear how the ALBI score may be calculated (in the same way as the Child-Pugh classification?). 3. The paragraph on sarcopenia must be better defined. A low muscle mass is definitely a risk factor for complications in cirrhosis, but its relation with cancer goes well beyond the scope of this review. As a matter of fact, there is no evidence that sarcopenia may be involved in creating the microenvironment for HCC, but simply remains a risk factor mortality.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

BPG Search:

- ☐ The same title
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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39751

Title: Carcinogenesis on the background of fibrosis: a major challenge in managing Hepatocellular Cancer

Reviewer's code: 02527528

Reviewer's country: China

Science editor: Xue-Jiao Wang

Date sent for review: 2018-05-25

Date reviewed: 2018-05-25

Review time: 20 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input checked="" type="checkbox"/> Grade D: Fair	<input checked="" type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

1 Primary liver cancer is not identical to hepatocellular carcinoma. 2 In the section of "Core tip", the phrase "development of cancer" should be specified as HCC or not. 3 HCC is resulted from various causes, not only cirrhosis. The authors are suggested to



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provide a table showing these causes and emphasizing the impact of cirrhosis. 4 Fibrosis is only an outside condition for carcinogenesis, genetic mutation must be stated. 5 The title is lack of sense, the word “challenge” is not clearly standed for. 6 Typo- and grammatical errors are found, including misuse of verb tense and sentence structure.

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BPG Search:

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39751

Title: Carcinogenesis on the background of fibrosis: a major challenge in managing Hepatocellular Cancer

Reviewer's code: 00467030

Reviewer's country: Taiwan

Science editor: Xue-Jiao Wang

Date sent for review: 2018-05-25

Date reviewed: 2018-05-29

Review time: 4 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This is a well-written review manuscript dealing with the issue of carcinogenesis of hepatocellular carcinoma on the background of fibrosis of liver. The following point is suggested. 1. The title of the subsection 'Discussion' is better to be modified as



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'Conclusion'.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

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BPG Search:

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39751

Title: Carcinogenesis on the background of fibrosis: a major challenge in managing Hepatocellular Cancer

Reviewer's code: 00053419

Reviewer's country: Spain

Science editor: Xue-Jiao Wang

Date sent for review: 2018-05-21

Date reviewed: 2018-05-29

Review time: 8 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The submitted study summarizes the state of the art of hepatocarcinogenesis under an inflammatory and fibrotic environment, emphasizing on the management of immunosuppression as a therapeutic option. The manuscript is clearly explained and the



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most relevant items have been comprehensively highlighted. To further detail the hepatocarcinogenic process some additional references might be of use: Sia d et al, Gastroenterology 2017; Loved JM et al Nat Rev Dis Primers, 2016; Marquardt Ju et al Nat Rev Cancer, 2015. Moreover, some references to illustrate the role of microbiota in liver cancer progression would be of interest (see, for instance, Yu LX and Schwabe RF, Nat Rev Gastroenterol Hepatol, 2017). Finally, a graphical schema to summarize the most relevant factors involved in the development of liver cancer, as described in the text, would be of great help to have an integrative view of such a complex process.

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BPG Search:

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- ☐ No

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39751

Title: Carcinogenesis on the background of fibrosis: a major challenge in managing Hepatocellular Cancer

Reviewer's code: 00225294

Reviewer's country: Spain

Science editor: Xue-Jiao Wang

Date sent for review: 2018-05-25

Date reviewed: 2018-05-31

Review time: 6 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
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<input type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
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		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This is an update on the interplay between fibrosis and HCC, with specific comments on secured mechanisms and outcomes. The title is appropriate for the content of the minireview, with an appropriate update of therapeutics, clinical trials and issues and



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mechanisms. This is also covered in the abstract. I only suggest two improvements: 1. An in-depth critical analysis of the current therapeutic interventions in preventing fibrosis and HCC (based on clinical trials). This is only marginally covered. 2. To provide a positive note on the WHO on the Global health sector strategy on viral hepatitis 2016-2021 (<http://www.who.int/hepatitis/strategy2016-2001/ghss-hep/en/>), that is aiming a global effort on a significant reduction of HCC in the future.

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