



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Hepatology

**Manuscript NO:** 45419

**Title:** Angiogenesis of hepatocellular carcinoma: an immunohistochemistry study

**Reviewer’s code:** 00006459

**Reviewer’s country:** Australia

**Science editor:** Ruo-Yu Ma

**Date sent for review:** 2018-12-29

**Date reviewed:** 2019-01-03

**Review time:** 2 Hours, 5 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 type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input checked="" 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 work is interesting and done well. There are very few photomicrographs for a paper that relies totally on immunohistochemistry data. Please add more photomicrographs . Please show examples of lower power views of regions of note. Also, show examples of : 1. VEGF-A in small tumors without vascular invasion Versus HCC



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with low levels of VEGF-A. 2. COX-2 in dedifferentiated tumors in non-cirrhotic liver Vs HCC in the absence of premalignant lesions. 3. CD31 in HCC in patients with cirrhosis Versus no cirrhosis. 4. CD105 in tumors without associated hepatitis Versus HCC with low levels of CD105. I made about 20 minor edits to the English and will try to attach that edited file. ; if I cannot, please improve the English.

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

- The same title
- Duplicate publication
- Plagiarism
- No

##### ***BPG Search:***

- The same title
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- No



**PEER-REVIEW REPORT**

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

**Manuscript NO:** 45419

**Title:** Angiogenesis of hepatocellular carcinoma: an immunohistochemistry study

**Reviewer’s code:** 03478254

**Reviewer’s country:** China

**Science editor:** Ruo-Yu Ma

**Date sent for review:** 2018-12-29

**Date reviewed:** 2019-01-07

**Review time:** 2 Hours, 9 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 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 type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input checked="" 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**

In this article, Dr. Gurzu’ group has investigated the immunohistochemical aspects of angiogenesis in hepatocellular carcinoma (HCC) through a retrospective cohort study of 50 randomly selected HCC patients. This study provides valuable information in the individualized anti-angiogenesis therapy of HCC. It is a worthy study done by Dr.



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Gurzu's group, however, some concerns need to be sufficiently addressed before consideration for publication. Major Comments: 1. The purpose of this investigation, based on the title and main part of Introduction, is to retrospectively gather and analyze information on immunohistochemical aspects of angiogenesis in HCC; however, the information in the article on these selected cases is too vague such as the source of the cases, the criteria for inclusion and so on. 2. The article only mentioned that 50 out of 113 cases were randomly selected for analysis, but it did not explain why the sample size was 50. Why they did the random sampling other than using all cases? 3. Based on the small sample size, it is not surprise that most variables have no significance which P value more than 0.05. Still, because the small sample size, it should use Fisher's Exact Test other than Chi Square Test. 4. When authors did the Immunohistochemistry assessment, it should review and score by two pathologist and assess the consistency between them.

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**PEER-REVIEW REPORT**

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

**Manuscript NO:** 45419

**Title:** Angiogenesis of hepatocellular carcinoma: an immunohistochemistry study

**Reviewer's code:** 02439215

**Reviewer's country:** China

**Science editor:** Ruo-Yu Ma

**Date sent for review:** 2018-12-29

**Date reviewed:** 2019-01-09

**Review time:** 13 Hours, 11 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 checked="" type="checkbox"/> Grade B: Very good	<input checked="" 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 checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
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			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

1、 It did not mention its limitations and the question which remains to be solved. 2、 Showing the data in the form of table is not so intuitive. 3、 The originality of this manuscript is not cleared stated with the lack of efficient literature review. 4、 The results presented are too weak to support authors' stating of" it seems that dedifferentiated



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HCCs developed in non-cirrhotic liver may benefit by anti-COX-2 therapy. The anti-VEGF-A drugs might be used in patients with HCCs developed in patients with cirrhosis, before occurrence of vascular invasion." 5、Flaws exist in authors' writing in terms of grammar and typo. 6、The final conclusion of this study is only for patients with non-cirrhosis, but most of hepatocellular carcinoma is secondary to hepatitis and cirrhosis.

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**PEER-REVIEW REPORT**

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

**Manuscript NO:** 45419

**Title:** Angiogenesis of hepatocellular carcinoma: an immunohistochemistry study

**Reviewer's code:** 01437833

**Reviewer's country:** United States

**Science editor:** Ruo-Yu Ma

**Date sent for review:** 2018-12-29

**Date reviewed:** 2019-01-10

**Review time:** 7 Hours, 12 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 type="checkbox"/> Grade B: Minor language	(High priority)	<input 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 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 type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
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			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

In this paper, the authors proposed that COX-2 could be used as angiogenesis marker and predict benefit from anti-COX-2 therapy. The rational should be addressed for using anti-COX-2 treatment for HCC in Introduction or Discussion. Images in Fig 1 are not representative enough, IHC pictures from low power field should be shown beside the



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high power images.

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