

PEER-REVIEW REPORT

Name of journal: *World Journal of Hepatology*

Manuscript NO: 90648

Title: Multifaceted roles of lymphatic and blood endothelial cells in the tumor microenvironment of hepatocellular carcinoma: A comprehensive review

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05769914

Position: Peer Reviewer

Academic degree: PhD, MD

Professional title: Professor, Researcher, Doctor

Reviewer's Country/Territory: Mexico

Author's Country/Territory: China

Manuscript submission date: 2023-12-10

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-12-11 04:06

Reviewer performed review: 2023-12-15 04:50

Review time: 4 Days

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

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

SPECIFIC COMMENTS TO AUTHORS

In this paper entitled "Exploring the Multifaceted Roles of Lymphatic and Blood Endothelial Cells in the Tumor Microenvironment of Hepatocellular Carcinoma: A Comprehensive Review", Li and colleagues discussed lymphatic endothelial cells (LECs), blood endothelial cells (BECs), angiogenesis, immune modulation, lymphangiogenesis, and metastasis in hepatocellular carcinoma. The manuscript is interesting, but I have several comments that should be addressed before its publication. -In the following paragraph related to the introduction, please add the prevalence of HCC in Asia: "Hepatocellular carcinoma (HCC) is a prevalent form of cancer worldwide, particularly in Asia where the majority of cases are reported." -In the following information, the authors should check if the data are correct because the percentage seems very high: "...with 72.5% occurring in Asia alone[1]." -In the next phrase the reference is missing: "Liver cancer accounts for a significant percentage (8.3%)is the primary cause of mortality in solid tumors." -There are several grammatical errors throughout the manuscript, such as tumor immune invasion, intertumoral lymphatic, HGF significantly enhanced the proliferation, among others. -With respect to the following phrase, please

give some names of tumors, including HCC with its reference, respectively. "While studies have extensively investigated the effects of immune cells like CD cells and regulatory T (Treg) cells on tumors[4-8]," -In the introduction section, the authors should add main functions of lymphatic endothelial cells (LECs), blood endothelial cells (BECs) in liver Injury and tumor development. -I recommend the next good reference (PMID: 36612019) for the introduction section of this interesting manuscript. -In figure 1, the effects of growth factors on lymphangiogenesis should be briefly described in figure legend. -It is important to describe the effects and the processes, focusing on HCC or give names of cancers according to information written in the manuscript, because it is confusing and could be considered as information related to HCC. For example, in the next phrases, indicate the type of cancer: "LECs, the process can be inhibited by c-Met, the receptor of HGF[26]." "Overexpression of ANGPTs promotes lymphangiogenesis in adult tissue in vivo, as observed in experimental tumor models[28,29]." -The following information should be reviewed in order to confirm if it is correct according to reference 36: "Folkman[36] proposed the hypothesis that angiogenesis is essential for the development and growth of solid tumors beyond a size of 1-2mm³." -In the legend of table 1, define all markers and clarify in the manuscript if these markers were reported in HCC or indicate in which type of cancers are expressed. -According to the next information in the phrase, the reference 44 is not related to it, please add the appropriate one: "PROX-1, a transcription factor, is regarded as a constitutive marker of LECs due to its pivotal role in lymphangiogenesis[44-47]." The same situation for the reference 39, which does not mention PROX-1: "It is consistently located in the nuclei of all LECs, regardless of their physiological or pathological state[39]." -The reference 60 is not related to the next phrase, please add the appropriate one: "When VEGF-C/D binds RAS-RAF-1-MEK-ERK signaling pathway and ultimately promoting lymphangiogenesis[60]." -The author's name in the following sentence is wrong:



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“Recently, Michael et al.[63] investigated EVT801, a novel selective VEGFR-3 inhibitor that specifically targets.....” -Figure 2 should contain a brief description in the figure legend. -Please add the references for the following phrases: “ Tie is the receptor for Ang, containing Tie1.....expressed only in BECs and acts on BECs in an autocrine form, is a partial competitive antagonist of Ang1 against Tie2.” -There is scarce information in the heading “Role of LECs and BECs in tumor metastasis” related to the role of BECs and BECs in tumor metastasis, especially related to HCC, please add more information. -The next heading is incomplete “SPECIAL FOCUS ON HCC” Is it related to LECs and BECs? -The references 44, 92 and 93 are not related to the liver, please add the appropriate ones: “Preliminary results have been found in liver cancer about the correlation between lymphangiogenesis and cancer prognosis[44,92,93].” -In the manuscript there is little information about immune modulation in HCC. Please add more information. In addition, it should include more information regarding theTME components in HCC, for example factors secreted and effects. -In the abstract section, the authors propose to shed light on future research directions and potential therapeutic targets for HCC treatment. However, there is scarce information, therefore it should be added.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2024-01-20 02:47

Reviewer performed review: 2024-01-20 03:18

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

I have no comments.