

Dear Editor and Reviewers,

I am glad to receive your letter. Thank you very much for your hard work and kind suggestions. I have read the comments carefully and revised the manuscript according to your suggestions. Thanks again for your excellent work.

The main corrections in the paper and the responds to the reviewer's comments are as following:

Response to Reviewer:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Reply: Many thanks for your kind comments.

Conclusion: Major revision

Reply: Many thanks for your kind comments. The manuscript has been revised following your comments. Thank you again.

Specific Comments to Authors:

Qingqing Liang and Lei Liu uncovered vascular endothelial cells in stem cell to be relevant in permeability, angiogenesis, blood pressure regulation, immunity, and pathological development, such as atherosclerosis and malignant tumor. The manuscript is of interest.

Reply: Many thanks for your kind comments.

Point to be considered:

1) The rationale of why the authors came up with this review.

Reply: Thanks for your kind comments. We are very sorry for the ambiguity caused by our misleading expression. We have modified the revised manuscript to highlight its rationale following your suggestion.

2) What is the information that is not exactly available that motivated the authors to come up with this information. What are the current caveats and how do the authors highlight the current research in answering them? If not they need to address in future directions.

Reply: Thanks for your kind comments. The opinion is extremely important to us. We add some information to expound what motivated us to come up with this information. Following your suggestion, a section on the current problems and solutions for VECs application has been added in the revised manuscript.

3) This reviewer personally misses some important consequences of the data

reviewed by the authors, especially in the oncology field: VEGF receptors play a pivotal role in cancer, indeed, neo-angiogenesis constitutes a crucial event for cancer progression (i.e. For prostate cancer (PCa), abundant angiogenic signalling has been associated with aggressive courses of disease). Specifically, VEGFR2, which is one of the main therapeutic targets of tyrosine kinase inhibitors (TKI), was reported to be upregulated in aggressive PCa. While TKI-based regimens do not appear promising for unselected PCa patients at first sight, distinct patient subgroups could benefit from such a treatment (please refer to PMID: 32131507 and expand accordingly).

Reply: Thanks for your kind advices. These advices are of great help to improve the quality of manuscript. We have revised the manuscript according to your advices. In addition, we have read Krebs's article[68], whose research is of significant reference value to us. We have revised the manuscript according to its content and cited it. Thanks again for your help.

4) Does this role of endothelial cells in angiogenesis in a tumor micro-environment involve hypoxia? Since hypoxia is a key factor for angiogenesis, the authors need to substantiate.

Reply: Thanks for your valuable advice. The opinion is extremely important to us. Following your suggestion, a section on the role of hypoxia in a tumor micro-environment for angiogenesis has been added in the revised manuscript.

5) The authors need to come up with a table to show the role of endothelial cells as Checkpoint For Immunological Patrolling in solid and hematological cancers to highlight their exact role in light of the stem cell role.

Reply: Thanks for your valuable advice. Following your suggestion, a table on the the role of endothelial cells as Checkpoint For Immunological Patrolling has been added in the revised manuscript.

6) The authors need to highlight what new information the review is providing to enhance the research in progress.

Reply: Thanks for your valuable advice. Following your suggestion, the manuscript has been revised to highlight the new information to enhance the research in progress.

Reviewer:

The authors have clarified several of the questions I raised in my previous review. Most of the major problems have been addressed by this revision.

Reply: Thanks for your comments.

Response to Science editor:

1 Scientific quality: The manuscript is a review about the use of vascular endothelial cells in stem cell medicine. The topic is within the scope of the WJSC.

(1) Classification: Check and list the scientific quality classification of the manuscript provided within the peer-review report; (2) Summarization of the Peer-Review Report: Grade C (Good) (3) Format: There manuscript does not contains any figures or tables; (4) References: There is a total of 96 references, including 59 references published in last 3 years; (5) Self-cited references: There are not self-cited references. (6) References recommendations: The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially those published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately.

2 Language evaluation: Grade B (Minor language polishing). A certificate of editing Certificate issued by Koji Yamashita (Managing Director and CEO, www.liwenbianji.cn/) was provided

3 Academic norms and rules: No academic misconduct was found by the Google/Bing search.

4 Supplementary comments: It is an invited manuscript. The topic of the manuscript was previously published in the journal.

Reply: Many thanks for your excellent work.

5 Issues raised: 1) The rationale of why the authors came up with this review. 2) What is the information that is not exactly available that motivated the authors to come up with this information. What are the current caveats and how do the authors highlight the current research in answering them? If not they need to address in future directions. 3) This reviewer personally misses some important consequences of the data reviewed by the authors, especially in the oncology field: VEGF receptors play a pivotal role in cancer, indeed, neo-angiogenesis constitutes a crucial event for cancer progression (i.e. For prostate cancer (PCa), abundant angiogenic signalling has been associated with aggressive courses of disease). Specifically, VEGFR2, which is one of the main therapeutic targets of tyrosine kinase inhibitors (TKI), was reported to be upregulated in aggressive PCa. While TKI-based regimens do not appear promising for unselected PCa patients at first sight, distinct patient subgroups could benefit from such a treatment (please refer to PMID: 32131507 and expand accordingly). 4) Does this role of endothelial cells in angiogenesis in a tumor micro-environment involve hypoxia? Since hypoxia is a key factor for angiogenesis, the authors need to substantiate. 5) The authors need to come up with a table to show the role of endothelial cells as Checkpoint For Immunological Patrolling in solid and hematological cancers to highlight their exact role in light of the stem cell role. 6) The authors need to highlight what new information the review is providing to enhance the research in progress. 6

Re-Review: Major revision 7 Recommendation: Conditional acceptance.

Reply: Many thanks for your excellent work. The manuscript has been revised following your comments. Thank you again.

Response to Company editor-in-chief:

I recommend the manuscript to be published in the World Journal of Clinical Cases. Before final acceptance, the author(s) must add a table/figure to the manuscript.

Reply: Thank you. The manuscript has been revised and a table has been added.

If you have any question, please don't hesitate to contact me.

With best regards,

Yours Sincerely

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