

RESPONSE LETTER

Reviewer A

No.	Comments	Reply action taken	Line number
1.	General comment: There are some minor typos in the manuscript that need fixing.	We have revised the typo in our manuscript that marked by yellow highlight	[Write the related line number of the revised manuscript with your response, i.e. 150-165]
2.	The direction of the research is good, as the outcome can be used in many applications with relatively simple and straightforward preparation of conditioned medium. However, the control of treatment and profiling of the CM needs to be carefully conducted	We've added 1 figure about the HMSC-CM cytokine profile. We also added a cytokine profile analysis method	100-103 141-147 Figure 2
3.	Comment on Title: It can be misleading because the conditioned medium was not purified to have high purity of PDGF. It might contain other growth factor(s) that affects the result.	We used conditioned media that had measured the content of cytokines and growth factors. Results Based on the analysis, the conditioned media contained the highest concentration of PDGF compared to other growth factors.	Figure 2
4.	Comment on Materials and Methods: The methods have been described clearly. However, the authors should describe the treatments and reagents used in Sham and Control.	We have added the information of sham and control according to reviewer suggestion.	Line 112 - 115
	Comment on Results and Discussion: a. Results and Discussion have been properly connected. However, the missing part of the PDGF purity may	a. We have added the cytokine profile data contained in HMSC-CM, from the results of the cytokine profile analysis it was found that the highest level contained was PDGF. The effect of other growth factors such as TGF-B has not been further disclosed. This is the limitation of this research.	Figure 2

	<p>create bias and misleading conclusions. Therefore, proof of PDGF purity in the absence of other growth factors must be present.</p> <p>b. In order for good Acceptance, addition of experiment to show the level of PDGF purity (with the insignificant level of other contributing growth factors) needs to be demonstrated to justify the role of PDGF, as the title has stated.</p> <p>c. The authors can increase the purity of PDGF in conditioned medium by conducting protein purification technique such as antibody affinity chromatography</p>	<p>b. We agree with the reviewer's suggestion, we have added a cytokine factor profile contained in HMSC-CM</p> <p>c. Thank you for the advice. We will consider this suggestion for further research.</p>	Figure 2
	<p>Comment on Figures: Figure 3. missing legend in Y-axis (micron?)</p>	<p>We have added the Y-axis legend. The Y-axis legend is square millimeters.</p>	Figure 4

Reviewer B

No.	Comments	Reply action taken	Line number
1.	General comment: The author should rearranged their writing, how they cite reference, etc.	We have rearrabged the writing of cite reference	
2.	Comment on Title: abbreviation should be explained	We have corrected the title to “Increased serial levels of Platelet-derived Growth Factor by Hypoxic Mesenchymal Stem Cells-Conditioned Medium promote wound closure acceleration in a full-thickness wound”	Line 1-2
3.	Comment on Abstract: a. In general the background not create animal models, but developed.	We have corrected according to reviewer suggestion	Line 15-16 Line 109-110
	Comment on Introduction: the consistency of writing is poor. for example, TGF-β and TGF-beta	We have corrected according to reviewer suggestion. TGF beta to TGF-β MSCs to MSC	Line 40, 41, 50
	Comment on Materials and Methods: a. how alizarin red staining is performed was not explained b. the third sentence of section 2.3 should cite at least a reference. c. how anesthesize drug is applied is not explained	a. we have added analysis method with alizarin red b. We have added the reference to: “The full-thickness cutaneous wound rat model was developed as described in a previous study (Hamra et al., 2021).” c. We have added the information about anesthesize that used in methods. “the rats were anesthetized by isoflurane inhalation and the dorsal hairs were shaved off and sterilized using 10% of povidone iodine solution”	a. Line 94-98 b. Line 114 c. Line 114-115
	Comment on Results and Discussion: a. last sentence in section 3.1. if the author write express CD44, they should not include express CD44+, because the meaning is	a. We have corrected according to the reviewer suggestion b. Thank you for the correction, we corrected the magnification is 100x and we added the scale bar in the figure 1. c. We corrected to: Our study showed that the rat treated by HMSC-CM 400μl showed significantly increased	a. Line 138 – 139 b. Line 142 c. Line 156-158

	<p>same</p> <p>b. Figure 1 legend. Are the author sure that the magnification is 10x? because the size of the cell will be so big, and no scale bar in the figure.</p> <p>c. Section 3.2. second sentence, which dose give the PDGF level mentioned in the paragraph</p>	<p>of PDGF levels on day 3 and 6 in both groups</p>	
	<p>Comment on Figures: Figure legend, x and y axis should be written properly</p>	<p>We have added the legend x and y axis in figure 2-4</p>	<p>Figure 2-4</p>