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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 43045

Title: Similarities and differences between mesenchymal stem/progenitor cells derived from various human tissues

Reviewer's code: 03773730

Reviewer's country: China

Science editor: Ying Dou

Date sent for review: 2018-10-27

Date reviewed: 2018-10-28

Review time: 13 Hours

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[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[ ] Accept (High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

SPECIFIC COMMENTS TO AUTHORS

The author of this manuscript attempted to investigate the biological properties of mesenchymal stromal/ stem cells in long-term cultured. However, at present, the paper can not be accepted unless you make a major revision. The comments are as below:

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Major concern: 1. The aim and conclusion in the Abstract of this manuscript is too big to demonstrate, here, only gene expression and cytokines were detected, so, these descriptions should be narrow down to the examination you done in this manuscript. 2. Is it possible to characterize MSC with different phenotype by double immunostaining and flow cytometry analysis, such as CD73/CD146, CD90/PDGFR, or CD105/PW1, so that we can clearly know the percentage of MSC with different phenotype. 3. Was it possible of the MSC phenotype changed during the passage, or after some passages. Can you examine the percentage of MSC with different phenotype during the passage? 4. Quantification of osteogenic, adipogenic and chondrogenic potentials changes during passage. So that you can give us enough information that MSC still have differentiation ability after some passages. 5. How do you know the spontaneous fusion happened, two dye merged with yellow color is not enough to demonstrate, CLSM should be used to check the colocalization of these two dyes in one cell, moreover, you also can us flow cytometry analysis to check the DNA content after coculture, and then based on the quantification, you can know how many cells infusion happened spontaneously. 6.From the discussion, biological properties evaluation should be clearly described, or can you clearly answer how long we can culture the MSC which still keep the differentiation potential. Minor concern: 1. The figure 5 have 8 histograms, you'd better label them using different letter. 2. Y axis in figure 5 should be amending to fit the value of all groups in the graph shown, such as BM-MSC (IL-5, IL-6 and MIP1) AT-MSC (MCP-1, IL8 and VEGF), no need to keep all the maximum same in different groups.

INITIAL REVIEW OF THE MANUSCRIPT

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[Y] No

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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 43045

Title: Similarities and differences between mesenchymal stem/progenitor cells derived from various human tissues

Reviewer's code: 02492656

Reviewer's country: United States

Science editor: Ying Dou

Date sent for review: 2018-10-27

Date reviewed: 2018-11-01

Review time: 5 Days

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

SPECIFIC COMMENTS TO AUTHORS

This is an interesting, well written paper in a highly significant area of research. The authors have provided very extensive data on stem cells derived from a variety of tissue types, and it appears that much useful information has been expertly obtained and

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provided with excellent graphs and legends. This reviewer is having a problem getting my head around all of the data which are extensive. I was looking for a table that allows cross referencing among all (or at least many) of the variables. In other words if one could run down a column that includes a stem cell from adipose tissue and wants to know if that cell type releases IL-8 or expresses P53, the reader could go directly to the IL column or the gene expression column and quickly know what the AT-Stem cells can do. Much time and effort was spent on cell fusion, but it is not clear what the significance of "fusion" may be when stem cells are used experimentally or in therapeutic trials. A brief introduction to this topic before the data are presented would be helpful.

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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 43045

Title: Similarities and differences between mesenchymal stem/progenitor cells derived from various human tissues

Reviewer's code: 00504800

Reviewer's country: United States

Science editor: Ying Dou

Date sent for review: 2018-10-27

Date reviewed: 2018-11-03

Review time: 7 Days

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

SPECIFIC COMMENTS TO AUTHORS

This manuscript is a descriptive study comparing MSC isolated from various human tissues. The value is that the authors have performed a comprehensive study of a number of biological factors from multiple isolates of MSC. The stability of MSC

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phenotype in this comprehensive study, for example, is useful data for the field. The problem is that some of data show significant variability, such that trends and conclusions are difficult to draw, and the authors sometimes don't clearly express their opinions as to why the variability exists and why this is significant. Specific comments: 1. The manuscript is very long/wordy, and could be shortened considerably without altering the conclusions. 2. Introduction, page 5: The authors should at least briefly mention teeth (dental pulp, periodontal ligament) as another source of MSC, as there is an extensive literature on dental-derived MSC. Furthermore, there are several papers comparing dental MSC to MSC from other tissues (e.g., Alge DL, et al., J Tissue Eng Regen Med. 2010; Yamada Y et al., Tissue Eng Part A 2010; Kunimatsu R, et al., Biochem Biophys Res Commun. 2018) which should be referenced and considered in the Discussion. 3. Methods, page 7: What were the ages and age range of the donors for each type of tissue? Do the authors think donor age could have impacted some of their findings/caused variability? Same with the timing of death to when tissues were obtained for culture. 4. Methods, page 8: Why was immunohistochemistry chosen to analyze expression of CD146 and PDGFRa instead of flow? This would allow easier quantitation for the reader in Figure 1. I understand this may not be feasible for PW1. 5. Results, page 11: More explanation is needed on HOW expression of CD146 and PDGFRa is different between the cell types, and why the authors consider this to be significant. 6. Results, page 12, paragraph 4: The potential role of naive MSC markers in myogenesis needs to be explained more in the Discussion. 7. Results, page 13 and 14: The presentation of the data on mRNA is expression is very lengthy and somewhat confusing. More importantly, the authors need to better explain (here or in the Discussion) whether these statistically significant increases and decreases in mRNA expression are thought to be real or artifact; how they compare to other MSC studies; and if true, what the biological significance might be. For example, c-Myc expression in

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AT-MSCs declined in P5, but went up again in P10 - why? What does this mean - something significant biologically, or simply variability in the samples studied? 8. Discussion, page 17: Same comment for the lengthy discussion of CD146 variability - what does this mean? The finding that CD146 expression is most stable in BM-MSC, and that they may be the most useful cells for impacting angiogenesis is notable; what does the low and/or variable expression in the other MSC types mean, if anything? 9. Discussion, pages 18-20: The background on Sox2 and Oct4 could be shortened considerably by just citing others' work, allowing for better discussion of the authors' findings. In particular, I am still unclear as to the potential role of PW1 in the MSC from these tissue types. Its expression seems very variable as well; can a conclusion be drawn? 10. Discussion, pages 20-21: Again, the cytokine expression data and discussion is lengthy and could be improved by more concisely summarizing which families of cytokines are produced by which MSC types, why these differences exist biologically, and how this may be exploited clinically. 11. Discussion, page 21: The fusion data is interesting, and its potential application in DMD therapy is intriguing. Of all the items in the Discussion, this subject would benefit from a more extensive discussion. 12. Discussion, page 22: It is really true that BM is more difficult to access than adipose for a given patient? It's simply a different procedure for procuring marrow than adipose. 13: Discussion, page 22: Were cells from later passages (P6-P8) used for any fusion experiments, especially P6-P8 SK-MSC when they express higher levels of CD146? 14: Summary, page 22, first paragraph: The authors use the term "different" or "different role" for stemness marker expression in several places, including the Summary, when I think a statement that expression is variable is more appropriate.

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 43045

Title: Similarities and differences between mesenchymal stem/progenitor cells derived from various human tissues

Reviewer's code: 02446319

Reviewer's country: South Korea

Science editor: Ying Dou

Date sent for review: 2018-10-27

Date reviewed: 2018-11-12

Review time: 16 Days

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

SPECIFIC COMMENTS TO AUTHORS

Thank you for your great manuscript about Similarities and differences between mesenchymal stem/progenitor cells derived from various human tissues. It's very valuable to readers.

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