



PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 65098

Title: Methods to produce induced pluripotent stem cell-derived mesenchymal stem cells: Mesenchymal stem cells from induced pluripotent stem cells

Reviewer's code: 05405722

Position: Peer Reviewer

Academic degree: PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Lebanon

Author's Country/Territory: Spain

Manuscript submission date: 2021-02-28

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-02-28 18:41

Reviewer performed review: 2021-03-06 12:58

Review time: 5 Days and 18 Hours

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 Grade E: Do not publish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 type="checkbox"/> Grade B: Minor language polishing <input checked="" 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



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

SPECIFIC COMMENTS TO AUTHORS

This manuscript provides a review about the different methods used to differentiate iPSCs into MSCs. this is an interesting topic to the scientific community given the therapeutic potential of MSCs. However, there are some aspects that need to be addressed by the authors before this work can be accepted. 1. Cite appropriately the latest, important and authoritative references in the introduction and discussion sections. there are hardly any citations in the introduction as well as the discussion section which is unacceptable. 2. the English needs extensive editing. herein some examples , the paragraph (lines 327-line 330) should be rewritten. no need for line 41 (you can delete it); paragraph (line 100-line 103) should be rewritten. line 116: cells rapidly senesce not senescence, line 120: subject to ethical concerns. line 122: adult MSCs face for clinical . Line 128-130: the paragraph is not clear, rewrite. line 132: describes ; line 149, consists of ; line 209: to replace FBS and therefore produce .. line 229: media not mediums 3. no explanation is provided for the MSC switch strategy as well as EB formation. Provide examples from papers and elaborate. 4. try to draw comparison between the different strategies by stating the limitation and strength of each. 4. all figures , delete the word evaluates



PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 65098

Title: Methods to produce induced pluripotent stem cell-derived mesenchymal stem cells: Mesenchymal stem cells from induced pluripotent stem cells

Reviewer's code: 05818921

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Italy

Author's Country/Territory: Spain

Manuscript submission date: 2021-02-28

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2021-03-09 14:58

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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 type="checkbox"/> Grade B: Minor language polishing <input checked="" 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 checked="" type="checkbox"/> Minor revision <input 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



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SPECIFIC COMMENTS TO AUTHORS

In this review, the authors summarize the current protocols used to obtain Mesenchymal Stem Cells (MSCs) from induced pluripotent stem cells (iPSCs) and describe the markers commonly used to identify them. The paper contains useful information regarding the topic, but the English language should be revised. Some sentences are not well written, such as lines 102-105 ("Among the Indoleamine 2,3-dioxygenase (IDO), prostaglandin E2 (PGE2), transforming growth factor beta (TGF- β), sHLA-G5, interleukin-10 (IL-10) and interleukin-6 (IL-6) are a few of these soluble factors allowing MSCs and immune cells cross-talk"), lines 256-258 ("The only other uncommon supplement worth mentioning for EB protocols being ITS and SB431542, with 2 studies out of the 13 (15%) each"), lines 306-311 ("In addition to the thirty-two studies selected as the main representatives for the five categories to produce iMSCs by non-commercial methods, twelve additional studies, using the protocols described by these thirty-two original studies, were included in our analysis, as they described characterization of the obtained iMSCs (Table 6 and Supplementary Table S4) by the evaluated protocols") and others. I suggest having a native English speaker proofread the text. Moreover, I have some comments for the authors: 1) in the background, I would suggest citing the articles that reported the concepts described in the original contexts rather than review, so that the reader can identify the topic presented in the original scientific article. For example, in the sentence in line 95-96 ("but later have been found in many other tissues: adipose tissue, umbilical cord, neural crest cells, dental tissues") I would suggest inserting the references regarding the identification of MSCs in each of the tissue cited. Moreover, I think that the background section should be enriched explaining the potential uses of MSCs in clinic (regenerative medicine? How these cells could practically be used to treat inflammatory disease?) 2) Line 41 and line 122: it is not totally correct to affirm that



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iPSCs have no ethical issue. Indeed, they have their own ethical issue, that are different from those of ESCs. 3) Lines 117-118: I suggest correcting the sentence “it was shown that during in vitro culture expansion MSC cells rapidly senescence, limiting the amounts obtained from donors”, senescence is not a verb. 4) Lines 143-150: I would suggest expressing the number of studies that used a particular method only as a fraction. The sum of percentages is not 100% (because some papers described more than one method) and, in my opinion, this could be confusing. 5) Tables 1-2-3-4-5: I would add a caption for the tables. For example, what represent the “Time” column? The required days to reach the MSCs state from induction of differentiation? I can not understand why some “time” have a plus and other not, please explain. Moreover, what is the meaning of “NA” in “iPSC origin” column? 6) Figure 1-2: The sum of percentage of some pie charts is not 100 because some media and coating have been used in more than one article. I think that the pie chart is not the best to graphically represent these data. I would suggest using bar charts. 7) Lines 398-400: I would suggest correcting the sentence “Their relationship with iMSCs properties is yet another underexplored sector of high priority to set protocols in accordance to therapeutic demands” because it is not clear.



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Title: Methods to produce induced pluripotent stem cell-derived mesenchymal stem cells: Mesenchymal stem cells from induced pluripotent stem cells

Reviewer's code: 05818581

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Oman

Author's Country/Territory: Spain

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input 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
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
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SPECIFIC COMMENTS TO AUTHORS

The authors reviewed different papers that were dealing with the generation of MSCs from iPSCs and compared different techniques. The paper may be considered as one of the references for those who are working in the field or would like to start producing MSCs from iPSCs. However, there was not much information about limitations and advantages of each technique. Moreover, although the isolation of MSCs from different tissues has limitations, the generation of iMSCs from iPSCs has also different complications which limit their use in clinical practice.



RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Title: Methods to produce induced pluripotent stem cell-derived mesenchymal stem cells: Mesenchymal stem cells from induced pluripotent stem cells

Reviewer's code: 05405722

Position: Peer Reviewer

Academic degree: PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Lebanon

Author's Country/Territory: Spain

Manuscript submission date: 2021-02-28

Reviewer chosen by: Chen-Chen Gao

Reviewer accepted review: 2021-05-07 10:04

Reviewer performed review: 2021-05-07 10:14

Review time: 1 Hour

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
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E-mail: bpgoffice@wjgnet.com
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All comments were replied to