

PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 65148

Title: Effects of immune cells on mesenchymal stem cells during fracture healing

Reviewer's code: 05821062

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Germany

Manuscript submission date: 2021-02-28

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2021-03-09 09:52

Reviewer performed review: 2021-03-09 11:51

Review time: 1 Hour

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 Grade E: Do not publish
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 type="checkbox"/> Yes <input checked="" 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

Comments The manuscript 65148 reviewed the effects of immune cells on mesenchymal stem cells during fracture healing. Some points in doubt proposed in my first review as follows. 1. All the gene name should be italic. 2. On this theme, the function and origins of immune cells should be elucidated. For example, immune cells, derived from hematopoietic stem cells arising from the mesoderm during embryonic development, are essential for the normal bone development and the proper fracture healing. 3. As we known, fracture repair is a well-orchestrated and complex regenerative process involving with numerous signaling pathways and cell types. In your review, which processes, primary (direct) fracture repair or secondary fracture repair, are immune cells for bone fracture healing? 4. Among the listed immune cells, would you like to make their lineage clear, for example, macrophages are phagocytic cells of the myeloid lineage. 5. How do immune cells receive mesenchymal signals? 6. Immune cells play the critical role in bone fracture healing. What is the conclusion for this review?

PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 65148

Title: Effects of immune cells on mesenchymal stem cells during fracture healing

Reviewer's code: 05323461

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Doctor, Research Scientist, Surgeon

Reviewer's Country/Territory: China

Author's Country/Territory: Germany

Manuscript submission date: 2021-02-28

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2021-03-09 13:21

Reviewer performed review: 2021-03-12 13:52

Review time: 3 Days

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 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
Re-review	<input type="checkbox"/> Yes <input checked="" 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

The article 'Effects of Immune Cells on Mesenchymal Stem Cells during Fracture Healing' by Sabrina Ehnert et al. introduces the effects of immune cells on mesenchymal stem cells during fracture healing based on the analysis of a large number of studies. In general, this review is very well written and organized. Methods are described carefully and a large quantity of data is presented. This article is worth being published in a scientific journal like 'World Journal of Stem Cells'.

PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 65148

Title: Effects of immune cells on mesenchymal stem cells during fracture healing

Reviewer's code: 05468066

Position: Peer Reviewer

Academic degree: PhD

Professional title: Senior Lecturer

Reviewer's Country/Territory: Bangladesh

Author's Country/Territory: Germany

Manuscript submission date: 2021-02-28

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2021-03-09 07:27

Reviewer performed review: 2021-03-18 03:13

Review time: 8 Days and 19 Hours

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 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 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

The manuscript has been written on an interesting topic. The manuscript covered all the important areas related to it. There are no major issues I can point to. However, there are a few minor issues need to be resolved to improve the readability of this manuscript.

1. Please provide a short description to each figure. Provide elaboration of the abbreviated terms used in the figures to make them stand-alone. 2. Please avoid abbreviation of any term being used first time in the text.

PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 65148

Title: Effects of immune cells on mesenchymal stem cells during fracture healing

Reviewer's code: 05246923

Position: Peer Reviewer

Academic degree: BPharm, MSc

Professional title: Academic Research, Pharmacist

Reviewer's Country/Territory: Japan

Author's Country/Territory: Germany

Manuscript submission date: 2021-02-28

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2021-03-11 02:32

Reviewer performed review: 2021-03-25 03:38

Review time: 14 Days and 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 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 type="checkbox"/> Yes <input checked="" 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

The review presented by authors is describing the effects of immune cells during fracture healing. The review is informative however, in my point of view the title is not reflect the main subject. The authors represent basic information about immune cells and their roles in fracture healing and a small paragraph are given for MSCs. In introduction no background about MSCs and their origin, roles and characteristics. - The introduction should give general view of the story or the topic. Instead of that, the authors are presenting specific examples in detail about role of different immune cells in healing process. And the introduction focus on detail of roles of immune cells and osteoblast cells in healing process rather than interaction between those cells and MSCs.

- The different between M1 and M2 macrophages should be explained - There are many minor English errors examples are giver below and many punctuation marks are missing. For example: - Comma in "In their pro-inflammatory state, T cells may act....." - "MSC application improved phagocytosis during a bacterial sepsis model in mice [59] and reduced infiltration of neutrophils into the liver could be observed [60], and consequently improved survival in both studies" This sentence should be corrected by removing second "and" - Rephrase following sentence to make it clearer "MSC application improved phagocytosis during a bacterial sepsis model in mice [59] and reduced infiltration of neutrophils into the liver could be observed [60], and consequently improved survival in both studies. Furthermore, in an injured gut model or a vasculitis model inflammation and neutrophil infiltration as well as the release of tissue-harming factors by neutrophils could be reduced by MSCs" - Add comma "Apart from strong induction of overall inflammation, neutrophils have another - Rephrase the sentence "There is evidence that NETs are formed in response to trauma [68, 69], however, if NET formation, in general, is pathologic for healing processes is not yet known." - "In their large number of secretory granules MCs store numerous preformed



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mediators" It should be "In their large number of secretory granules, MCs store numerous preformed mediators" - The link (<https://patents.google.com/patent/EP2623978A1/en>) should move to references - In T cells section , A long paragraph with lot of info about T cells with only two studies of MSCs. Bests