

PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 40480

Title: Hematopoietic stem cell transplantation for Crohn's disease: Gaps, doubts and perspectives

Reviewer's code: 00609371

Reviewer's country: United States

Science editor: Fang-Fang Ji

Date sent for review: 2018-06-30

Date reviewed: 2018-06-30

Review time: 4 Hours

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

SPECIFIC COMMENTS TO AUTHORS

The topic of this editorial is of interest it helps us to put a right Perspective on the Stem cell therapy for Crohn's disease. However, 1) the title doesn't match the content of the article, i.e., Stem cell therapy is a very broad term, which should include all kinds of



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stem cell, but in the article, the authors focused only on HSCT, even though they also mentioned another kind of stem cells (MSC). The authors need to either change the title or addition more content to the text. 2) Editorial is supposed to highlight the main points in the broad-brush style; therefore the first subtitle “the Definition and location of disease” seems in appropriate for this editorial.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
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- ☐ [Y] No

BPG Search:

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- ☐ [Y] No

PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 40480

Title: Hematopoietic stem cell transplantation for Crohn's disease: Gaps, doubts and perspectives

Reviewer's code: 00573611

Reviewer's country: Taiwan

Science editor: Fang-Fang Ji

Date sent for review: 2018-06-30

Date reviewed: 2018-06-30

Review time: 6 Hours

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

SPECIFIC COMMENTS TO AUTHORS

In this editorial paper, the author described and discussed the aspects and the future of cell therapy in Crohn's disease. This is an interesting editorial paper. The manuscript is well-written. The reviewer has no further comments.



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INITIAL REVIEW OF THE MANUSCRIPT

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- ☐ [Y] No

PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 40480

Title: Hematopoietic stem cell transplantation for Crohn's disease: Gaps, doubts and perspectives

Reviewer's code: 03370303

Reviewer's country: Japan

Science editor: Fang-Fang Ji

Date sent for review: 2018-06-30

Date reviewed: 2018-06-30

Review time: 17 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
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publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This Editorial is valuable, raising an alarm at an easy decision of taking autologous HSCT as a measure for the treatment of Chron's disease. Showing the unsatisfactory points in the evaluation of efficacy of HSCT and explaining the adverse effects regarding

HSCT, authors illustrate the important points that we must consider when deciding which therapeutics we should take. Nevertheless, the evaluation of mesenchymal stem cell transplantation (MSCT) seems rather unclear. I speculate that authors have a positive thought for MSCT since it has no adverse effects due to lack of need to use chemotherapeutic and immunosuppressive agents. While HSCT aims a reconstitution (or initialization) of the hematopoietic system, MSCT aims the modulation of immune system (ref S1, S2). One of the important factors that mediate immunosuppressive effects of MSC is prostaglandin E2 (PGE2) (ref S1, S2), which is also known as a mediator for the effect of G-CSF (ref S3). In this sense, it is interesting that G-CSF alone has provided successful outcome for the treatment of Chron's disease as authors mentioned (ref 18). I think that the message of this article would become clearer if authors could add certain comments regarding the evaluation or mechanistic insight for MSCT.

Supplemental Reference: S1. Zhao Q, Ren H, Han Z. Mesenchymal stem cells: Immunomodulatory capability and clinical potential in immune diseases. *Journal of Cellular Immunotherapy* 2: 3-20, 2016. S2. F Gao, S M Chiu, D A L Motan, Z Zhang, L Chen, H-L Ji, H-F Tse, Q-L Fu, Q Lian. Mesenchymal stem cells and immunomodulation: current status and future prospects. *Cell Death Dis.* 7: e2062, 2016. S3. Kawano Y, Fukui C, Shinohara M, Wakahashi K, Ishii S, Suzuki T, Sato M, Asada N, Kawano H, Minagawa K, Sada A, Furuyashiki T, Uematsu S, Akira S, Uede T, Narumiya S, Matsui T, Katayama Y. G-CSF-induced sympathetic tone provokes fever and primes antimobilizing functions of neutrophils via PGE2. *Blood* 129:587-597, 2017. A minor point to be corrected: The term "stromal mesenchymal cells" in Abstract in page 2 and in line 13 in page 5 should be corrected as "mesenchymal stromal cells".

INITIAL REVIEW OF THE MANUSCRIPT

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