



PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 41507

Title: Protein factors in adipose-derived mesenchymal stem cell transplantation for liver cirrhosis

Reviewer’s code: 02540473

Reviewer’s country: China

Science editor: Fang-Fang Ji

Date sent for review: 2018-08-13

Date reviewed: 2018-08-14

Review time: 1 Day

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 checked="" 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
<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

Previous studies demonstrated that adipose-derived mesenchymal stem cells (ADSCs) are a treatment cell source for patients with chronic liver injury. The review described the various cytokines and chemokines produced by ADSCs promote the healing of liver



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disease.

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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 41507

Title: Protein factors in adipose-derived mesenchymal stem cell transplantation for liver cirrhosis

Reviewer's code: 03478635

Reviewer's country: Japan

Science editor: Fang-Fang Ji

Date sent for review: 2018-08-13

Date reviewed: 2018-08-16

Review time: 2 Days

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 checked="" 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 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 title as Main content may be revised to indicate the context of the contents. The symptoms of acute liver failure may be described more in detail in the first paragraph. The reason for selecting growth factors, inhibition of inflammation of hepatic stellate



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cells and angiogenic factors as important factors for improvement of chronic liver failure symptoms may be added briefly around line 200 in page 7. The abbreviations for POSTN, SAP, SEM7A and PTK7 etc. should be described at the first time described. In Conclusion, the description about CXCL5 as a component to promote hepatocyte proliferation in front of (3) ADSC-secreted VEGF, HGF, EGF, MMP2, POSTN and MFGM are,,, is quite confusing since CXCL5 is classified as (2) inhibitors of inflammation of hepatic stellate cells in the main text. The conclusion may be revised to be clearer. This manuscript can be accepted without figures 3 and 4, if it is a minireview as shown in the file. The materials and methods and more detailed description are needed, if it is basic study research article.

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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 41507

Title: Protein factors in adipose-derived mesenchymal stem cell transplantation for liver cirrhosis

Reviewer’s code: 02728252

Reviewer’s country: Egypt

Science editor: Fang-Fang Ji

Date sent for review: 2018-08-13

Date reviewed: 2018-08-16

Review time: 3 Days

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
<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 type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
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SPECIFIC COMMENTS TO AUTHORS

My comments included in the attached manuscript.

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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 41507

Title: Protein factors in adipose-derived mesenchymal stem cell transplantation for liver cirrhosis

Reviewer's code: 02566952

Reviewer's country: Romania

Science editor: Fang-Fang Ji

Date sent for review: 2018-08-13

Date reviewed: 2018-08-20

Review time: 6 Days

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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		<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

The manuscript has the merit of offering an expert review regarding a not yet well explored topic, the mechanism of action of stem cell, specifically adipose derived stem cells in treating liver cirrhosis. The text is well written and organized easy to follow and



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presents relevant information. Below are point by point comments Abstract informs with accuracy about the content of the manuscript , however in my opinion the core tip is only a brief repetition of it, maybe this point could be reformulated to be shorter , concise and inviting for the reader. The chapter “main content could be maybe named introduction or background . It is just a minor formal element but can affect the general impression on the work presented. In the introductory part , R 166-168 presents ADSCs but the phrase has, in my opinion a little bit of problem. ADSCs are indeed obtained usually by liposuction but this accounts for their easiness in procurement (as being obtainable in large quantities through a minimally invasive procedure). ADSCs claimed lack of immunogenicity is a story that has been challenged. MSCs (ADSCs included as a form of MSCs) might be only immune evasive not immune privileged therefore any form of allo-MSCTherapy should be regarded with caution and tested from this perspective (Ankrum, 2014, Berglund, 2017), Furthermore, ADSCs based therapies ARE NOT a mainstream procedure in any medical field (unfortunately in my opinion) therefore one should acknowledge only several clinics worldwide practice this form of science based therapy. The problem of using animal based supplements (such as FBS) in the culture media for expansion of clinical grade stem cell population is under debate. What is the author opinion in this respect? Does this influence the immunogenicity or any other aspect of cultivated cell biology? What about batch reproducibility when trying to scale up cell manufacturing (cell growth and even surface markers have been shown to be affected by FBS batch variability) . R 177 “Terms defined in GO are called GO terms tries to explain a notion using the same terminology, maybe this could be reformulated. GO is rather a classification than a description of biological phenomena which associates genes with their so far known (reported by the existent literature) biological role structured based on given criteria. Maybe the subtitle growth factors could be complemented with “ growth factors improving liver chrrhosis symptoms” or



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similar for enhance clarity Have the authors used ADSCs cell population as cell therapy in their in vivo studies, ADSC-CM or both, if it is the case when and how, maybe this should be summarized in a phrase or a table. It seems that the therapeutic effect on cirrhosis symptoms is based on ADSC released growth factors , on anti-inflammatory effect over the stellate cells, anti fibrotic and angiogenic effect of ADSCs released proteins. Do the authors consider this could be summarized in a phrase/table, for improving clarity? The manuscript has two tables presenting a crude relationship between two kind of potentially active elements but a summary with all ADSCs expressed proteins that are presumable active in liver cirrhosis eventually indication on which basis is made this presumption (reference) should be of a help. They are only summarized in the conclusion, a little bit to late for the reader to follow. Instead maybe the conclusion should orient what could be the practical importance and relevance of deschpering these factors as potential therapeutic ones. Can stem cells used as a therapy be selected based on the expression of these factors? Is ADSC CM enough to act as therapeutic agent and if yes what could be the formulation of a proposed therapeutic intervention ? CM from FBS treated cells definitely contain a large amount of xenogenic proteins, how this could be accommodated with the requirements of a clinical grade therapy? Regarding ADSCs released factors, maybe it would be good to advance an opinion is the symptoms improvement based on real liver parenchyma regeneration or is it a transient decrease in inflammation and functional improvement based on a transitory supply of growth factors?

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