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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36006

Title: Mesenchymal stem cells rescue acute hepatic failure by polarizing M2 macrophages

Reviewer's code: 03478635

Reviewer's country: Japan

Science editor: Ze-Mao Gong

Date sent for review: 2017-09-03

Date reviewed: 2017-09-04

Review time: 18 Hours

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This study describes about the possibility of MSCs to promote hepatic regeneration. The definition of M1 markers to select TNF alpha and INF gamma may be described more in detail. It seems like polarization in the manuscript means differentiation. Please check the whole manuscript carefully. Proofreading is needed.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36006

Title: Mesenchymal stem cells rescue acute hepatic failure by polarizing M2 macrophages

Reviewer's code: 00054465

Reviewer's country: United States

Science editor: Ze-Mao Gong

Date sent for review: 2017-09-03

Date reviewed: 2017-09-10

Review time: 7 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This is a very well carried out bench study that provides greater insight to the role of MSCs in acute liver failure. M2 polarization contributes to the therapeutic effects of MSCs in AHF by altering levels of anti-inflammatory and pro-inflammatory factors. This is a major finding and does offer a potential therapeutic application. It will need to be followed up by more bench studies but this is potentially an opportunity for a new clinical approach.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36006

Title: Mesenchymal stem cells rescue acute hepatic failure by polarizing M2 macrophages

Reviewer's code: 00182114

Reviewer's country: Japan

Science editor: Ze-Mao Gong

Date sent for review: 2017-09-03

Date reviewed: 2017-09-12

Review time: 8 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

Author concluded that MSCs transfused into rats were recruited and increased the survival rate by inhibiting apoptotic hepatocytes and promoting hepatocyte regeneration. I ask some questions to author. 1. Please tell me the detail etiology which MSCs transfused into rats inhibit apoptotic hepatocytes and promote hepatocyte regeneration. According to Fig 2, Ki 67 was much higher in experimental group compared to control and Tunnel was much lower in experimental group compared to control group.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36006

Title: Mesenchymal stem cells rescue acute hepatic failure by polarizing M2 macrophages

Reviewer's code: 02462687

Reviewer's country: Japan

Science editor: Ze-Mao Gong

Date sent for review: 2017-09-03

Date reviewed: 2017-09-12

Review time: 8 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input checked="" type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This is a experimental study to evaluate the effect of MSCs on rat with acute hepatic failure. The authors concluded that MSCs polarize macrophage to M2 by altering anti-inflammatory cytokines levels. This was well written, but there were several points to be clarified. Major 1. The authors compare the immunohistochemistry and real-time PCR of liver between dead and survival group. I wonder how to get liver tissue and in the dead group. Does this mean that liver tissue was obtained after dead? Please provide how and when you get the liver tissue in dead group. You should also provide the number of each group in dead and survival group in Figure 3,4,5 and 6. 2. In AHF animal models, rats were divided into group A (D-GaIN ip, N=16) and Group B (PBS ip, N=10). In MSC transplantation, rat were also divided into two groups (MSC group, N=16, and DPBS group, N=10). I recognized this as two-by-two method, which resulted



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into 4 groups. Please revise about this points as understandable. 3. CD68 was a pan-macrophage marker, not a M1 macrophage marker. CD68 positive macrophage did not mean M1 macrophage. The other marker for M1 macrophage was necessary to assess macrophage polarization. Minor 1. Please spell out D-GaIN and DPBS. 2. In results 1 and figure 1, please provide the histology of the PBS group after 5 days. 3. Please provide more precise explanation of HE histology. 4. In the second paragraph of Discussion, CD68+ macrophages and levels of TNF-A and INOS were significantly down-regulated in the death group. I think this was a typo. "Up-regulated" was correct.