

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Stem Cells*

**Manuscript NO:** 78512

**Title:** IFN- $\gamma$  and TNF- $\alpha$  synergistically enhance the immunosuppressive capacity of hUC-MSCs by increasing PD- Y expression

**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 04861666

**Position:** Peer Reviewer

**Academic degree:** BSc, MSc, PhD

**Professional title:** Assistant Professor

**Reviewer's Country/Territory:** India

**Author's Country/Territory:** China

**Manuscript submission date:** 2023-03-13

**Reviewer chosen by:** Geng-Long Liu

**Reviewer accepted review:** 2023-05-12 03:00

**Reviewer performed review:** 2023-05-22 06:34

**Review time:** 10 Days and 3 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 Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<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
<b>Conclusion</b>	<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
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

The expression of immunosuppressive molecules, such as PD-L1, in MSCs, poses limitations on the effectiveness of MSCT therapy. Nonetheless, the precise mechanism through which IFN- $\gamma$  alone or in combination with TNF- $\alpha$  induces a significant increase in PD-L1 expression in hUC-MSCs has not been fully elucidated. In the current research authors have answered this research question. They demonstrated that the expression of PD-L1 in hUC-MSCs was increased by IFN- $\gamma$ , leading to an enhancement of their immunosuppressive abilities through the JAK/STAT1/IRF1 pathway. Moreover, TNF- $\alpha$  acted in synergy with IFN- $\gamma$  to further elevate PD-L1 expression in hUC-MSCs by upregulating the Nuclear Factor kappa-B (NF- $\kappa$ B)-mediated expression of IFN- $\gamma$  receptor 1 (IFNGR1), which subsequently activated the JAK/STAT1/IRF1 signaling pathway. In my opinion manuscript is well planned and all the experiments are executed nicely. So it is suitable for publication after addressing following queries; 1. Discuss about the future transnational potential of the current study. 2. Include some of the limitations of the current study before translating it.

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**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05816287

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** Italy

**Author's Country/Territory:** China

**Manuscript submission date:** 2023-03-13

**Reviewer chosen by:** Geng-Long Liu

**Reviewer accepted review:** 2023-06-01 18:08

**Reviewer performed review:** 2023-06-01 18:20

**Review time:** 1 Hour

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
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<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
<b>Conclusion</b>	<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
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	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 study developed in this work is very interesting. It is an excellent starting point for future studies. I would prolong the time associated with the expression of TNF $\alpha$  to better validate the results and repeat them in more biological replicates to be sure of reproducibility. Congratulations to the authors.