

## PEER-REVIEW REPORT

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

**Manuscript NO:** 84665

**Title:** Role and mechanism of constitutive aryl hydrocarbon receptor in the regenerative potential of mouse bone marrow mesenchymal stromal cells

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

**Peer-review model:** Single blind

**Reviewer's code:** 00532996

**Position:** Editorial Board

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

**Professional title:** Associate Professor, Senior Scientist

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

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

**Manuscript submission date:** 2023-03-28

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

**Reviewer accepted review:** 2023-05-15 03:57

**Reviewer performed review:** 2023-05-20 15:57

**Review time:** 5 Days and 12 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 Grade E: Do not publish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 checked="" type="checkbox"/> Grade A: Priority publishing <input 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 checked="" type="checkbox"/> Yes <input 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

Study is well designed. Experiments are conducted properly and data well represented.  
 Wherever use of inhibitor concentration used may be mentioned in figure legend as well.  
 Discussion well covered.

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**Peer-review model:** Single blind

**Reviewer's code:** 03067229

**Position:** Peer Reviewer

**Academic degree:** DSc

**Professional title:** Research Scientist

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

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

**Manuscript submission date:** 2023-03-28

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

**Reviewer accepted review:** 2023-06-12 11:55

**Reviewer performed review:** 2023-06-17 07:23

**Review time:** 4 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
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
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<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 data presented in the article is quite interesting. The research is complex. The research methodology corresponds to the modern level. There are no notes on content.

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

**Peer-review model:** Single blind

**Reviewer's code:** 03478635

**Position:** Editorial Board

**Academic degree:** PhD

**Professional title:** Senior Research Fellow

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

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

**Manuscript submission date:** 2023-03-28

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

**Reviewer accepted review:** 2023-06-22 00:26

**Reviewer performed review:** 2023-06-23 01:52

**Review time:** 1 Day and 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
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<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 demonstrates the mechanisms of constitutive AhR in osteogenic and macrophage-modulating potential of mouse BMSCs.

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**Peer-review model:** Single blind

**Reviewer's code:** 00415501

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Professor

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

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

**Manuscript submission date:** 2023-03-28

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

**Reviewer accepted review:** 2023-06-21 00:58

**Reviewer performed review:** 2023-06-24 05:50

**Review time:** 3 Days and 4 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
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<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

Reviewer's Comments to Author: This manuscript focused on the animal model to study AhR (aryl hydrocarbon receptor). The model suggested that the AhR plays a beneficial role in the regenerative potential of MSCs in part by increasing the phosphorylation of STAT3. In the context of BMSCs, studies have shown that the constitutive activation of AhR has an impact on their osteogenic potential. Activation of AhR by its ligands leads to the upregulation of osteogenic markers and promotes the differentiation of BMSCs into osteoblasts, which are the cells responsible for bone formation. This suggests that the constitutive AhR activation in BMSCs enhances their ability to undergo osteogenesis. When AhR is activated, it can interact with STAT3, thereby increasing the phosphorylation level of STAT3. This phosphorylation can activate the transcriptional activity of STAT3, which in turn initiates the expression of specific genes for cell regeneration and repair processes. Therefore, the activation of AhR can promote the regenerative potential of MSCs by increasing the phosphorylation of STAT3. This has important implications for tissue regeneration, wound repair, and disease treatment, and provides new potential strategies for related research and





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treatment. The manuscript is well-written but not sure what to think. Some text is repetitive and there tends to be a bit of Discussion creeping into the Results. A very large amount of work was involved in the study, and as far as I can determine, the work is solid. The results are not always new or interesting. The precise molecular mechanisms underlying the AhR-STAT3 interaction are still being elucidated, and further research is needed to fully understand the intricacies of this relationship. However, the AhR and STAT3 signaling pathways can interact and cross-regulate each other, highlighting their significance in various physiological and pathological processes.