

We appreciate the reviewers for the interest in our manuscript and helpful comments. As indicated below, we addressed each of their concerns as outlined below.

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

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 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.

Answer: The Discussion is improved by deleting the overlapped part with Results, and proposing the future research direction.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: The study demonstrates the mechanisms of constitutive AhR in osteogenic and macrophage-modulating potential of mouse BMSCs.

Answer: Thanks.

Reviewer #3:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

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.

Answer: The language is checked and revised again.

Reviewer #4:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

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.

Answer: The concentration of STAT3 inhibitor stattic is supplemented in the manuscript and figure legend.