Constitutive aryl hydrocarbon receptor facilitates regenerative potential of mouse bone marrow mesenchymal stromal cells

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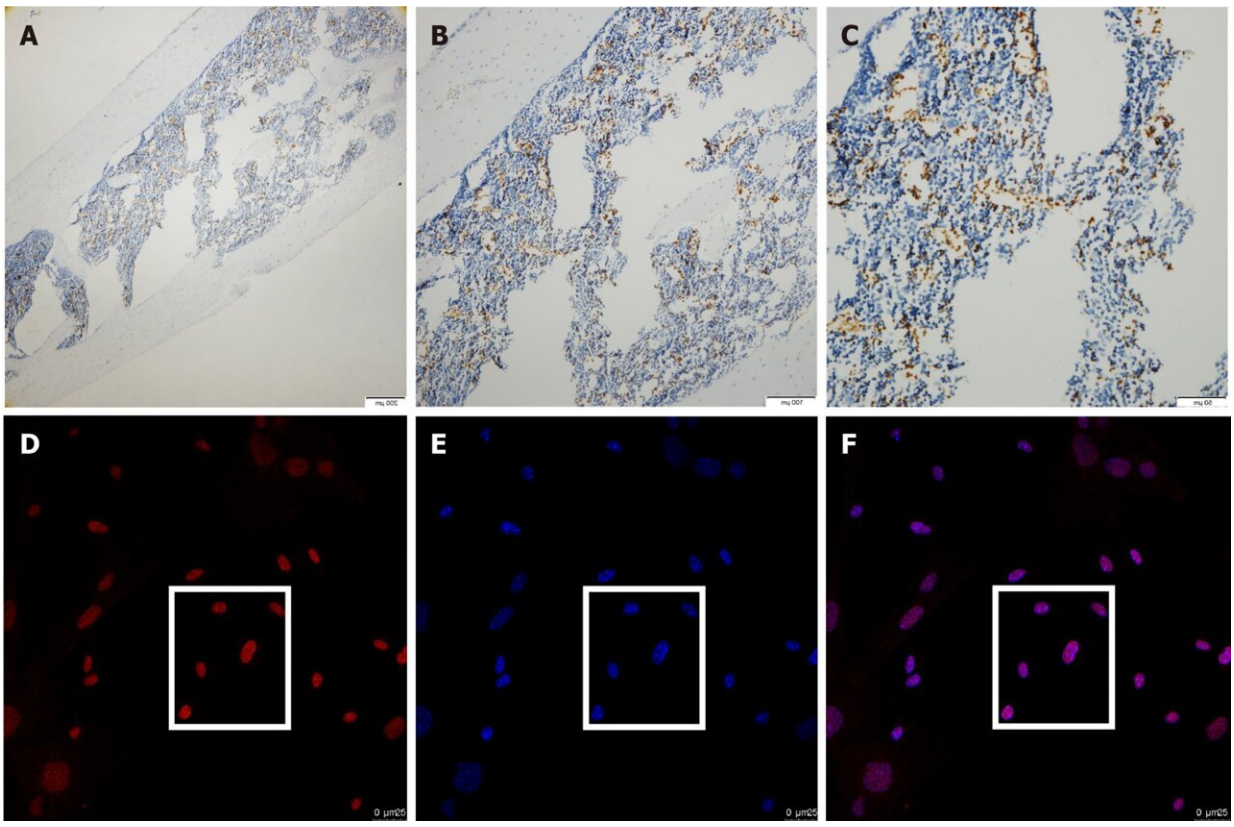

The expression of aryl hydrocarbon receptor in bone marrow tissue of mouse femur and isolated bone marrow mesenchymal stromal cells. A-C: Immunochemistry staining showed positive aryl hydrocarbon receptor (AhR) expression in bone marrow tissue [bar: 200 mm (left), 100 mm (middle) and 50 mm (right)]. D-I: Immunofluorescence staining of AhR in mouse bone marrow mesenchymal stromal cells via confocal microscopy (red: AhR; blue:

4,"6-diamidino-2-phenylindole; pink: Merge) [bar: 25mm (D-F) and 10mm (G-I)]. Credit: *World Journal of Stem Cells* (2023). DOI: 10.4252/wjsc.v15.i8.807

Bone marrow mesenchymal stromal cells (BMSCs) are the commonly used seed cells in tissue engineering. Aryl hydrocarbon receptor (AhR) is a transcription factor involved in various cellular processes. However, the function of constitutive AhR in BMSCs remains unclear.

Researchers have now investigated the role of AhR in the osteogenic and macrophage-modulating potential of mouse BMSCs (mBMSCs) and the underlying mechanism. Their findings are published in the *World Journal of Stem Cells*.

Immunochemistry and immunofluorescent staining were used to observe the expression of AhR in mouse bone marrow tissue and mBMSCs. The overexpression or knockdown of AhR was achieved by lentivirus-mediated plasmid. The osteogenic potential was observed by alkaline phosphatase and alizarin red staining. The mRNA and protein levels of osteogenic markers were detected by quantitative polymerase chain reaction (qPCR) and western blot.

After coculture with different mBMSCs, the cluster of differentiation (CD) 86 and CD206 expressions levels in RAW 264.7 cells were analyzed by flow cytometry. To explore the underlying molecular mechanism, the interaction of AhR with signal transducer and activator of transcription 3 (STAT3) was observed by co-immunoprecipitation and phosphorylation of STAT3 was detected by western blot.

AhR expressions in mouse bone marrow tissue and isolated mBMSCs were detected. AhR overexpression enhanced the osteogenic potential of mBMSCs while AhR knockdown suppressed it. The ratio of CD86+

RAW 264.7 cells cocultured with AhR-overexpressed mBMSCs was reduced and that of CD206+ cells was increased. AhR directly interacted with STAT3. AhR overexpression increased the phosphorylation of STAT3. After inhibition of STAT3 via stattic, the promotive effects of AhR overexpression on the osteogenic differentiation and macrophage-modulating were partially counteracted.

Therefore, AhR plays a beneficial role in the regenerative potential of mBMSCs partially by increasing phosphorylation of STAT3.

Aryl hydrocarbon receptor (AhR) was positively expressed in murine bone marrow tissue and bone marrow mesenchymal stromal cells (BMSCs). In vitro, overexpression of AhR enhanced the osteogenic potential of mouse BMSCs. Additionally, AhR-overexpressed BMSCs had an increased ability to polarize macrophages to an anti-inflammatory phenotype.

While knockdown of AhR showed the opposite effects. Mechanistically, the beneficial effects of AhR were partially dependent on increased phosphorylation of signal transducer and activator of transcription 3. This study suggests that AhR might be a target for achieving optimal bone regeneration in mouse BMSCs-based tissue engineering.

More information: Jing Huang et al, Constitutive aryl hydrocarbon receptor facilitates the regenerative potential of mouse bone marrow mesenchymal stromal cells, *World Journal of Stem Cells* (2023). DOI: 10.4252/wjsc.v15.i8.807

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