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# MicroRNA expression signature for Satb2-induced osteogenic differentiation in bone marrow stromal cells

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**Abstract** Satb2 acts as a potent transcription factor to promote osteoblast differentiation and bone regeneration. Recently, microRNAs (miRNA) have been identified as critical regulators of osteogenic differentiation. This study aimed to identify specific miRNAs and their regulatory roles in the process of Satb2-induced osteogenic differentiation. We studied the differentially expressed miRNAs by Satb2 overexpression in murine bone marrow stromal cells using miRNA microarray. Ten down-regulated miRNAs including miR-27a, miR-125a-5p, and miR-466f-3p, and 18 up-regulated miRNAs including miR-17, miR-20a and miR-210 were found to be differentially expressed and their expression were verified by quantitative real time PCR. The differentially expressed miRNAs were further subjected to gene ontology and KEGG analysis. The highly enriched GOs and KEGG pathway showed target genes of these miRNAs were significantly involved in multiple biological processes (mesenchymal cell differentiation, bone formation, and skeletal development), and several osteogenic pathways (TGF-β/BMP, MAPK, and Wnt signaling pathway). Finally, miR-27a was selected for target verification and function analysis. BMP2, BMPR1A, and Smad9, members of the TGF-β/BMP superfamily, which were predicted to be target genes of miR-27a, were confirmed to be significantly up-regulated in Satb2-over-expressing cells by quantitative real time PCR. Overexpression of miR-27a significantly inhibited osteogenesis and repressed BMP2, BMPR1A, and Smad9 expression. In this study, we identified that a number of differentially regulated miRNAs, whose target genes involved in the TGF-β/BMP signaling pathway, play an important role in the early stage of Satb2-induced osteogenic differentiation.

**Keywords** Osteogenic differentiation · MicroRNA · Satb2 · Bone marrow stromal cell · Transforming growth factor β · BMP

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## Introduction

Bone marrow stromal cells (BMSCs), a potential cell source capable of differentiating into several mesenchymal cell types including osteoblasts and chondrocytes, are considered ideal seed cells in bone tissue engineering approach [1]. To maximize the capacity of BMSCs to regenerate bone, the combination of gene therapies and BMSCs could be an optimal clinic strategy for tissue repair, where BMSCs are genetically modified to express higher levels of some specific factors that have the potential to accelerate osteogenesis in bone defects; these factors include growth factors such as bone morphogenic proteins (BMP) and transcription factors such as Runx2 and Osterix [2–4].

Satb2 is a member of the special family of AT-rich binding transcription factors that play a pivotal role in craniofacial patterning and osteoblast differentiation [5–7].

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