



# Synergistic effect of BMP9 and TGF- $\beta$ in the proliferation and differentiation of osteoblasts

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**ABSTRACT.** We investigated the synergistic effect of bone morphogenetic protein 9 (BMP9) and transforming growth factor (TGF)- $\beta$  in the transformation of mesenchymal stem cells into osteoblasts. We evaluated the effect of BMP9 and TGF- $\beta$  on the induction of osteoblast formation. Mitogen-activated protein kinase (MAPK) pathway-related proteins such as p38, extracellular receptor kinase 1/2, and c-Jun N-terminal kinase (JNK) were analyzed. The interactions between TGF-Smad and BMP-MAPK were also studied. BMP9 alone induced the differentiation of mesenchymal stem cells (MSCs) into osteoblasts and enhanced phosphorylation of p38, extracellular receptor kinase 1/2, and JNK. TGF- $\beta$  alone failed to induce transformation, but could increase the effect of

BMP9. In this process the activation of Smad resulted in activation of the JNK pathway in the MAPK pathway. BMP9 induced osteogenesis of MSC differentiation through the MAPK pathway, while TGF- $\beta$  contributed to BMP9 enhancement through the Smad-JNK pathway.

**Key words:** Bone morphogenetic protein 9; Cell differentiation; Mesenchymal stem cells; Mitogen activated protein kinase; Signal transduction pathway