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Negative regulation of BMP signaling by Tob

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Keywords

BMP, osteoblast, SMAD, Tob

Context

The mechanisms of bone remodeling have been studied for years, but the molecular control of osteoblast differentiation and function is much less understood than that of osteoclasts because no adequate murine models exist. The aim of this study was to analyze the role of *tob* in osteoblast proliferation and differentiation by generatig *tob*-/- mice.

Tob protein interacts with the ERBB2 gene product p185; its amino terminus is homologous to the antiproliferative gene product BTG1. Overexpressed Tob has been shown to suppress the growth of NIH3T3 cells. The expression of *tob*has been observed in various cells, but this is the first about expression in osteoblasts.

Significant findings

The *tob*-/- mice showed an increased bone mass due to increased numbers of osteoblasts, with no changes in the number and function of osteoclasts. Bone morphogenetic protein (BMP)-2 induced osteoblast maturation, and bone formation was enhanced in *tob*-/- mice. Furthermore, Tob repressed, but BMP induced, Smad-dependent transcription by ligand-dependent association with R-Smads (Smads 1, 5, and 8). The authors suggest that Tob plays a critical role as a Smad inhibitor in BMP-2/Smad-regulated gene expression in osteoblasts.

Comments

BMPs are known to control osteoblast proliferation and differentiation via Smad signaling pathways. In this paper, the authors demonstrate by using *tob*-deficient mice that Tob regulates the function of osteoblasts via Smads. Some years ago, Cbfa1 was identified as an osteoblast-specific transcription

regulator that can also form complexes with Smads. As mentioned by the authors, further studies on the functional link between Tob and Cbfa1 in the control of BMP signaling will help to understand the process of bone formation and may contribute to therapy for osteoporosis and healing of bone fractures.

Methods

Tob-deficient mice, transient transfection, reporter gene assays, immunoprecipitation, immunofluorescence

References

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