

## 論 文 要 旨

**Bone morphogenetic protein 9 (BMP9) directly induces  
Notch effector molecule Hes1 through  
the SMAD signaling pathway in osteoblasts**

氏 名

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Bone morphogenetic protein (BMP) 9 is one of the most osteogenic BMPs, but its mechanism of action has not been fully elucidated. Hes1, a transcriptional regulator with a basic helix - loop - helix domain, is a well - known effector of Notch signaling. Here, we find that BMP9 induces periodic increases of Hes1 mRNA and protein expression in osteoblasts, presumably through an autocrine negative feedback mechanism. BMP9 - mediated Hes1 induction is significantly inhibited by an ALK inhibitor and overexpression of Smad7, an inhibitory Smad. Luciferase and ChIP assays revealed that two Smad - binding sites in the 5' upstream region of the mouse Hes1 gene are essential for transcriptional activation by BMP9. Thus, our data indicate that BMP9 induces Hes1 expression in osteoblasts *via* the Smad signaling pathway.