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Deletion of osteoblastic Wntless reduces osteogenic differentiation of bone marrow mesenchymal stem cells and delays bone regeneration in a femur defected animal model

Sher Bahadur Poudel, Sung-Ho Kook, Hyun-Jaung Sim, Govinda Bhattarai and **Jeong-Chae Lee**
National University, South Korea

Wnt signaling pathway is essential not only during the embryonic development but also for maintaining the homeostasis of adult stem cells. The Wnt signaling pathway also plays an important role in regulating osteoblastic differentiation of mesenchymal stem cells (MSCs) and in promoting bone formation. Wnt includes a family of secreted signaling proteins called Wnt ligands. They are sorted and secreted by cells with the aid of chaperone protein called Wntless (Wls)/Gpr177. Inactivation of Wls abolishes the secretion of Wnt proteins. Here, we examined the phenotypic consequences of osteoblastic Wls deletion on the osteogenic differentiation of bone marrow MSCs cultures and on the regeneration of defected femur using osteoblast-specific Wls-deficient (Col2.3-Cre, Wls-flox) mice. The Inhibition of canonical and non-canonical Wnt signaling pathway was confirmed by the reduced expression of various Wnt ligands and β-catenin in osteoblasts of the homozygous Wls conditional knockout mice. The bone marrow MSCs isolated from tibia and femur of the Wls knockout mice showed lower proliferation rates compared with that of the control group. Significantly lower expression of osteogenic markers including Runx2, osterix, osteopontin, and bone sialoprotein with the decreased mineralization was also found in the MSCs from the knockout mice. In addition, transcendent distribution of Wls into the zones of newly formed bone elucidated its critical roles for bone regeneration. Furthermore, micro-CT and histological analyses revealed a delayed bone regeneration in femur defects of the Wls knockout mice along with the reduced expression of osteoblast-specific marker molecules. Collectively, our results implicate that Wls plays a crucial role in bone regeneration by positively regulating osteogenic differentiation and mineralization of bone marrow MSCs via the activation of Wnt signaling pathway.

Biography

Sher Bahadur Poudel is a Ph.D student at Graduate School of Dentistry, Chonbuk National University, Republic of Korea. He has received his MS degree in Molecular and Human Genetics from Banaras Hindu University, India (2010) and worked as a Lecturer of Molecular Cell Biology at School of Health and Allied Sciences, Pokhara University, Nepal (2010-2014). His research interest includes the mesenchymal stem cell niche maintenance during the homeostasis and repair or regeneration of bone. His current research project focuses on regulatory mechanism of Wnt signaling pathway in the maintenance of bone marrow mesenchymal stem cells and bone regeneration in animal bone defect models.

poudelsb@jbnu.ac.kr

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