

# The effects of type VI collagen on the bone formation

Abstract of Doctoral Thesis

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Type VI collagen (Col VI), a component of the extracellular matrix in the periosteum, is thought to regulate osteoblast behaviors. However, the detailed functions of Col VI on the bone formation have not been elucidated. To clarify the functions of Col VI on the bone formation, I examined the distribution of Col VI and osteoblast lineages expressing Neural/Glial Antigen 2 (NG2), a major cell-surface receptor for Col VI, in the rat long bones during postnatal growing periods. I also investigated the effects of Col VI on the cellular behaviors using cultured osteoblasts. Immunohistochemical results revealed that Col VI accumulated in the osteonal cavity in the primary osteon of rat long bone diaphysis during postnatal growing periods. Additionally, in the perichondrium of growth plate (Groove of Ranvier), Col VI accumulated in the middle layer. Osteoblast-lineages were under differentiation process in these Col VI-accumulated areas and express NG2. These findings indicate that interactions between NG2 and Col VI may regulate osteoblast behavior. The investigation of Col VI functions on cultured osteoblasts revealed that proliferation, differentiation, bone matrix production, and matrix mineralization were reduced in the osteoblast lineage cultured on Col VI-coated dish. Interestingly, Osterix expression was decreased in the osteoblasts on Col VI-coated dish, whereas Osteopontin expression and Notch signaling were increased. Taken together, these findings indicate that Col VI may suppress osteoblast differentiation via inhibition of Osterix expression and induction of Osteopontin expression and Notch signaling, leading to regulation of the ossification of the cortical bone in the primary osteon and the Groove of Ranvier.