Stimulation of NCAM1-14.3.3.ζδ-derived Peptide Interaction Fuels Angiogenesis and Osteogenesis in Ageing

Authors : Taha Kadir Yesin, Hanyu Liu, Zhangfan Ding, Amit Singh, Qi Tian, Yuheng Zhang, Biswajyoti Borah, Junyu Chen, Anjali P. Kusumbe

Abstract : The skeletal structure and bone marrow endothelium collectively form a critical functional unit essential for bone development, health, and aging. At the core of osteogenesis and bone formation lies the dynamic process of angiogenesis. In this study, we reveal a potent endogenous anabolic NCAM1-14.3.3. ζ 6-derived- Peptide interaction, which stimulates bone angiogenesis and osteogenesis during homeostasis, aging, and age-related bone diseases. Employing high-resolution imaging and inducible cell-specific mouse genetics, our results elucidate the pivotal role of the NCAM1-14.3.3. ζ 6-derived-Peptide interaction in driving the expansion of Clec14a+ angiogenic endothelial cells. Notably, Clec14a+ endothelial cells express key osteogenic factors. The NCAM1-14.3.3. ζ 6-derived-Peptide interaction in osteoblasts drives osteoblast differentiation, ultimately contributing to the genesis of bone. Moreover, the NCAM1-14.3.3. ζ 6-derived-Peptide interaction leads to a reduction in bone resorption. In age-associated vascular and bone loss diseases, stimulating the NCAM1-14.3.3. ζ 6-derived-Peptide interaction not only promotes angiogenesis but also reverses bone loss. Consequently, harnessing the endogenous anabolic potential of the NCAM1-14.3.3. ζ 6-derived-Peptide interaction modality for managing age-related bone diseases.

Keywords : endothelial cell, NCAM1, Clec14a, 14.3.3.ζδ

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