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Collagen 3D matrix regulates osteoblastogenesis and osteoclastogenesis in bone: A novel model for bone homeostasis

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Collagen is the extracellular matrix protein in bone that regulates ossification and bone resorption through modulating the paracrine cues of bone cells, and has been used for the treatment of bone disorders due to its bio-mimic properties. However, the biological activity of collagen depends on the interactions with other biomolecules such as minerals and glycosaminoglycan in bone. Considering the above perceptions, collagen was crosslinked with calcium apatite (CA) and chondroitin sulphate (CS), to produce a natural bone like 3D-structure and evaluated its effect on bone homeostasis using bone marrow mesenchymal stem cells, osteoblast and bone marrow macrophages (BMM). The arrangement of CA crystallites in collagen-CA-CS (CCACS) 3D-matrix was confirmed by XRD spectra. Micro-CT hierarchical structure confirmed the three-dimensional structure of matrix and the structure resembles as trabecular bone. The stimulatory osteoblastogenic and exploitive osteoclastogenic activity of CCACS 3D-matrices were identified by the high level of bone biomarkers (collagen, ALP, and minerals) in differentiated-osteoblasts and decreased mCSF-RANKL or rPTHr11 induced TRAP+ osteoclasts from ovariectomized-mice-BMM, respectively. Besides, paracrine cues of osteogenic progenitors for BMM-derived osteoclastogenesis by CCACS 3D-matrix disclose that the differentiated osteoblast secreted higher level of RANKL to support osteoclastogenesis and the effect was down-regulated by CCACS 3D-matrix. The present empirical evidence proved the osteogenic stimulatory and osteoclastogenic inhibitory effect of CCACS 3D-matrix. From that we hypothesize, the morphological features of CCACS 3D-matrix resembles as a trabecular bone, enhances bone growth and limits bone resorption.

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