A 3D in vitro bone organ model using human progenitor cells

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Three-dimensional (3D) organotypic culture models based on human cells may reduce the use of complex and costly animal models, while gaining clinical relevance. This study aimed at developing a 3D osteoblastic-osteoclastic-endothelial cell co-culture system, as an in vitro model to mimic the process of bone turnover. Osteoprogenitor and endothelial lineage cells were isolated from the stromal vascular fraction (SVF) of human adipose tissue, whereas CD14+ osteoclast progenitors were derived from human peripheral blood. Cells were co-cultured within 3D porous ceramic scaffolds using a perfusion-based bioreactor device, in the presence of typical osteoclastogenic factors. After 3 weeks, the scaffolds contained cells with endothelial (2.0+/-0.3%), pre/osteoclastic (14.0+/-1.4%) and mesenchymal/osteoblastic (44.0+/-8.4%) phenotypes, along with tartrate-resistant acid phosphatase-positive (TRAP+) osteoclastic cells in contact with deposited bone-like matrix. Supernatant analysis demonstrated sustained matrix deposition (by C-terminus procollagen-I propeptides), resorption (by N-terminus collagen-I telopeptides and phosphate levels) and osteoclastic activity (by TRAP-5b) only when SVF and CD14+ cells were co-cultured. Scanning electron microscopy and magnetic resonance imaging confirmed the pattern of matrix deposition and resorption. The effectiveness of Vitamin D in replacing osteoclastogenic factors indicated a functional osteoblast-osteoclast coupling in the system. The formation of human-origin bone-like tissue, blood vessels and osteoclasts upon ectopic implantation validated the functionality of the developed cell types. The 3D co-culture system and the associated non-invasive analytical tools can be used as an advanced model to capture some aspects of the functional coupling of bone-like matrix deposition and resorption and could be exploited toward the engineering of multifunctional bone substitute implants.
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