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3D micro-patterned co-culture of mesenchymal and endothelial stem cells for concurrent induction of vasculogenesis and osteogenesis

Osteogenesis and vascularization during development are coupled by spatiotemporal regulation of paracrine signaling in which the invading vascular endothelial progenitor cells secrete osteogenic morphogens to stimulate cell differentiation and bone formation. Conversely, the committed mesenchymal stem cells (MSCs) in the vicinity of the vascular endothelial cells release vasculogenic morphogens to further stimulate vasculogenesis for the metabolically highly active osteoblasts. The objective of this work was to investigate the effect of micro-patterning of mesenchymal stem cells (MSCs) and endothelial colony forming cells (ECFCs) within a 3D hydrogel matrix combined with localized delivery of osteogenic and vasculogenic morphogens BMP-2 and VEGF on synergistic expression of paracrine signaling factors and coupling of osteogenesis and vasculogenesis. Human MSCs and sustained release BMP-2 nanogels were encapsulated in a slow-resorbing polyethylene glycol-based hydrogel matrix containing micro-channels. Next, a combination of human MSCs, human ECFCs, and on-time release VEGF nanogels were delivered to the micro-channels of the matrix in a fast-resorbing galatin-based hydrogel. This approach resulted in spatial patterning of MSCs and ECFCs and spatiotemporal delivery of BMP-2 and VEGF morphogens. The effect of cell and morphogen patterning on vascularized osteogenesis and paracrine signaling was assessed by biochemical, mRNA, protein analysis, and immunofluorescent staining. The localization of MSCs to the matrix and MSCs+ECFCs to the microchannels combined with temporal release of BMP-2 in the matrix and VEGF in the channels sharply increased the expression of paracrine signaling factors basic fibroblast growth factor (bFGF, vasculogenic and osteogenic), platelet-derived growth factor (PDGF, vasculogenic), and transforming growth factor-beta (TGF- β , osteogenic) by the encapsulated human MSCs and ECFCs. These results suggest that osteogenesis and vascularization are coupled by localized secretion of paracrine signaling factors by the differentiating MSCs and ECFCs.

Biography

Esmail Jabbari has completed his PhD at Purdue University and Post-doctoral studies at Monsanto, Rice University, and Mayo Clinic. He is the Director of Tissue Engineering and Drug Delivery Laboratory and Full Professor of Chemical and Biomedical Engineering at University of South Carolina. He received the Berton Rahn Award from AO Foundation in 2012 and the Stephen Milam Award from Oral and Maxillofacial Surgery Foundation in 2008. He was elected to the College of Fellows of AIMBE in 2013. He has published >250 peer-reviewed articles and presented >260 conference lectures. He serves as Academic Editor of PLOS ONE.

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