Development of Janus Hydrogel Microcapsules as Novel Biomaterials-Stem Cells Construct for 3D Co-culture Applications

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Co-cultures of two or more cell types and biodegradable biomaterials of natural origin have been successfully combined to recreate tissue microenvironments. Segregated co-cultures are preferred over conventional mixed ones in order to better control the degree of homotypic and heterotypic interactions. Hydrogel-based systems in particular, have gained much attention to mimic tissue-specific microenvironments and they can be microengineered by innovative bottom-up approaches such as microfluidics. In this study, we developed bi-compartmentalized (Janus) hydrogel microcapsules of methacrylated hyaluronic acid (MeHA)/methacrylated-chitosan (MeCht) blended with marine-origin collagen by droplet-based microfluidics co-flow. Human adipose stem cells (hASCs) and microvascular endothelial cells (hMVECs) were co-encapsulated to create platforms of study relevant for vascularized bone tissue engineering. A specially designed Janus-droplet generator chip was used to fabricate the microcapsules (<250 μm units) and Janus-gradient co-cultures of hASCs: hMVECs were generated in various ratios (90:10; 75:25; 50:50; 25:75; 10:90), through an automated microfluidic flow controller (Elveflow microfluidics system). Such monodisperse 3D co-culture systems were optimized regarding cell number and culture media specific for concomitant maintenance of both phenotypes to establish effective cell-cell (homotypic and heterotypic) and cell-materials interactions. Cellular parameters such as viability, matrix deposition, mineralization and hMVECs re-organization in tube-like structures, were enhanced by blending MeHA/MeCht with marine-origin collagen and increasing hASCs: hMVECs co-culture gradient had significant impact on it. Such Janus hybrid hydrogel microcapsules can be used as a platform to investigate biomaterials interactions with distinct combined cell populations.

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