Mural cells of Distinct Phenotypes Differentiated from Human Pluripotent Stem Cells: Generation of 3D Vascular Units for Tissue Engineering.

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ABSTRACT

Mural cells (MCs), such as the pericytes (PCs) that reside at the capillary walls and the smooth muscle cells (SMCs) that exist in larger arterioles are essential components of blood vessels. They interact with endothelial cells (ECs), which form the inner lining of the vessel wall, and are essential for vascular maturation and stability. Lack of MCs leads to embryonic lethality, whereas alterations in MC density and phenotype is associated with several human diseases such as diabetic retinopathy. However, the molecular mechanisms underlying their phenotypic plasticity and their interaction with ECs have not been studied extensively, partially due to limitations concerning their isolation and expansion.

We developed a simple, efficient and quick method, using feeder free and low serum conditions to induce the differentiation of human Pluripotent Stem Cells-hPSCs (human embryonic stem cells-hESCs and human induced Pluripotent Stem Cells-hiPSCs) to defined MC populations (human pluripotent stem cell derived MCs/hPSCs-MCs). Cells were extensively characterised regarding their phenotypic plasticity (contractile, synthetic) and function. hPSC-MCs stabilised vascular tube formation, when co-cultured with ECs. In order to confirm their functionality in vivo, we carried out co-implantation of distinct populations of hPSCs-MCs with ECs on an in vivo matrigel assay. We implanted the co-implants as 3D spheroids, which allow complex interactions between the co-implanted cells reconstituting in a superior manner the physiological situation providing valuable information with regard to regulation of cell growth, migration, differentiation and survival being also adaptable for multiple applications in cell-based angiogenic therapeutic strategies.