Design of in vitro model of fibrotic cardiac tissue

Fibrotic cardiac tissue *in vitro* models based on bioartificial scaffolds

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Myocardial infarction causes massive cardiomyocytes loss, and the remodelling of local extracellular matrix. This in turn leads to the progressive formation of a stiff fibrotic tissue, mainly populated by cardiac fibroblasts. In vitro models of human pathological cardiac tissue able to precisely reproduce post-infarct microenvironment could greatly improve preclinical experimentation, helping in the selection of potential therapies for human heart regeneration.

In this work, adult human cardiac fibroblasts (AHCFs) were cultured on bioartificial 2D and 3D scaffolds designed to mimic different extensions of early stage cardiac fibrosis.

2D and 3D polycaprolactone (PCL)-based scaffolds were prepared by electrospinning and fused deposition modelling, respectively. Type A Gelatin was grafted on scaffolds. Physicochemical, morphological, and mechanical characterisations were performed at each functionalisation step. AHCFs isolated from ventricle (PromoCell) were seeded on scaffolds, and their adhesion, proliferation and extracellular matrix (ECM) deposition were analysed after long culture times (up to 21 days).

Random electrospun nanofibrous 2D scaffolds and grid interconnected 3D scaffolds with different pore size (150 and 350 μm) were prepared. Efficient gelatin grafting was demonstrated by QCM-D, ATR-FTIR, contact angle analyses and colorimetric assay. Gelatin coating improved attachment and proliferation of AHCFs. Fibroblast markers expression (α-SMA) and cardiac ECM proteins (Fibronectin, Laminin, Tenascin and Collagen IV) secretion were confirmed by immunofluorescence analysis.

2D and 3D bioartificial scaffolds sustained long-term AHCFs culture. Analysis of deposited ECM as a function of scaffold geometry and infarction extension is in progress.