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Effect of flow on BOECs capture and alignment on TPS-modified nanofibrous Polycaprolactone tissue engineering scaffolds

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Introductions: Endothelial progenitor cells (EPCs) are a promising source for the in situ endothelialisation of tissue engineering scaffolds. TPS (TPSLEQRTVYAK) is a specific peptide synthesised to induce the adhesion and proliferation of blood outgrowth endothelial cells (BOECs) expanded from EPCs[1]. In a previous study, we were able to design a biofunctionalised TPS-nanofibrous-PCL scaffold, and have shown its ability to capture BOECs in vitro under static conditions[2]. In this abstract, we test the biocomposite's ability to capture BOECs under flow conditions, and study their subsequent alignment.

Methods: BOECs were isolated from the blood of healthy donors using selective plating. PCL nanofibrous scaffolds were prepared by jet spraying technique[3]. Scaffolds were biofunctionalised by maleimide crosslinking of cysteine-containing-TPS as we have previously described[2], and modification stability was confirmed by visualising the fluorescence intensity of FITC-tagged-TPS. Cell capturing ability under flow conditions was tested by incubating the scaffolds with 30ml suspension of BOECs in a tube rotator at 15RPM. Number of adhered cells and percentage of infiltration were calculated at 1,7and 14days in cross sections. The effect of shear was studied by exposing the seeded scaffolds to oscillatory or uni-directional flow for 24 hours using a Cone and Plate Bioreactor. Nuclear orientation of DAPI stained nucleus was estimated through the quantification of Feret angle.

Results: Crosslinking efficiency was not affected by incubating the biofunctionalised scaffolds at 37ºC under flow for 7 and 14 days, as indicated by fluorescent intensity ($P=0.75, n=3$ compared to day 1). BOECs were able to infiltrate both untreated and TPS modified PCL, but the number of infiltrating cells was significantly higher in TPS-modified-scaffolds ($P<0.05, n=3$; 3.1±0.9, 2.1±0.9, and 2.7±1.0 folds increase at 1,7, and 14 days respectively). BOECs cultured on modified PCL grew in the direction of the fibres. Exposing seeded scaffolds to shear stress in a cone and plate bioreactor resulted in the elongation of the nucleus, while the cells were still aligned with the direction of the underlying fibres under both types of shear.

Conclusion: The results showed the biocomposite's ability to attract BOECs under flow conditions, and their adhesion stability and ability to response to flow. We are currently investigating the ability of this material to capture endothelial cells directly from blood mononuclear cells, to confirm its potential as an instructive implant for in situ endothelialization of tissue engineered scaffolds.

References:

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3- Sohier J *et al.*(2014).Biomaterials.**35(6)**:1833-44.