Endothelialization of tissue engineered vascular grafts

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Introduction

In 2004, approximately 425,000 coronary bypass graft procedures were performed in the USA on patients suffering from cardiovascular disease.[1] Tissue engineering of small diameter (<5 mm) blood vessels is a promising approach to develop viable alternatives for autologous vascular grafts. Development of a functional, adherent, shear resisting endothelial cell (EC) layer (figure 1) is one of the major issues limiting the successful application of these tissue engineered grafts.[2] The goal of the present study was to seed and culture ECs in tissue engineered vascular grafts.

Material and methods

Tubular PGA/P4HB scaffolds were placed around a silicone tube and were seeded with human saphenous vein myofibroblasts (MFs) using fibrin as a cell carrier. After 4 weeks of culture, the silicone tube was removed and a human saphenous vein EC suspension was injected into the lumen of the graft. The bioreactor was rotated for 3 hours, (figure 2) to homogeneously seed the ECs.

After seeding, a flow was applied through the vessels (figure 2) using a rollerpump. After 1 and 7 days of culture, vessels were removed from the bioreactors and the seeded ECs were visualized with a CLSM using a EC specific FITC UEA-1 lectin staining.

Results

During the 4 week culture period, the MFs produce extracellular matrix and the vascular grafts developed. The grafts were open and not leaking, in this way enabling EC seeding and the application of flow. During the 7 day EC culture period, the grafts remained open (figure 3).

ECs were homogeneously distributed in the graft 1 day after seeding (figure 4). After one week of culture, ECs were present throughout the whole vessel. In some parts confluent monolayers were found, while in other parts the cells were round and not connected (figure 5).

Summary

A method was developed to seed ECs in tissue engineered vascular grafts. Although the seeding protocol worked, the ECs did not always grow into a confluent monolayer.

Future

- Create full confluent EC monolayer
- Investigate influence of shear on EC layer
- Investigate thrombogenicity of EC layer

References: