

ENGINEERING A GRAFT FOR CORONARY BYPASS SURGERY: ROLE OF CHEMICAL COATINGS TO ENHANCE ATTACHMENT OF SMOOTH MUSCLE CELLS TO COMPLIANT POLY(CARBONATE- UREA)URETHANE MATRICES

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INTRODUCTION: Obstructive atherosclerotic vascular disease in the form of cardiovascular and cerebrovascular disease is the largest cause of mortality in the USA and Europe¹. When angioplasty or stenting of the occluded vessels is not possible or unsuccessful then the surgical remedy for coronary artery ischaemia requires the use of bypass grafts. Normally this uses the patient's own blood vessels: principally the Internal Mammary Artery and the Long Saphenous Vein. However, in a third of patient's there is insufficient blood vessel available. The use of synthetic materials has largely been abandoned due to their poor patency and higher infection rates. Endothelial cell seeding of synthetic materials like expanded polytetrafluoroethylene (ePTFE) have shown higher patency rates in clinical trials.

To further improve this our group has been working on the development of a biological 4mm graft with both endothelial and smooth muscle cells incorporating an elastin and collagen matrix. The engineering of functional smooth muscle cells is critical in the development of such an engineered conduit. This study reports on the effects chemical coatings have in enhancing attachment and subsequent proliferation on matrices made of compliant poly(carbonate-urea)urethane (Myolink).

METHODS: Myolink was coated with: RGD - ARG-GLY-ASP – (633mcg/ml); Superfibronection (42mcg/ml); Fibronectin (118mcg/ml); Fibronectin-Like Engineered Polymer Protein (118mcg/ml); Fibronectin-Like Engineered Polymer Protein Plus (133mcg/ml); Type 1 collagen (1mg/ml) or Native (no coating) overnight.

Small bioreactors were developed into which the coated Myolink was inserted, onto which was seeded smooth muscle cells (SMC) at a density of 2.27×10^5 SMCs/ml, radiolabelled with ¹¹¹In-Oxine as per our previous protocol².

After around 48 hours seeding, the solution was aspirated off and the Myolink sections were then washed with sterile PBS. The initial aspirate and then the washings were collected in separate tubes.

The Myolink, aspirate and washings were then counted in a gamma counter to give the percentage attachment of SMCs to the Myolink. The radioactivity reflected the number of SMCs.

RESULTS: FEPP+ was significantly better than the native Myolink in terms of attachment of the SMCs, with a mean of 31.45% cell attachment compared to 20.71% for the Native graft ($p < 0.01$) – see Figure 1 below.

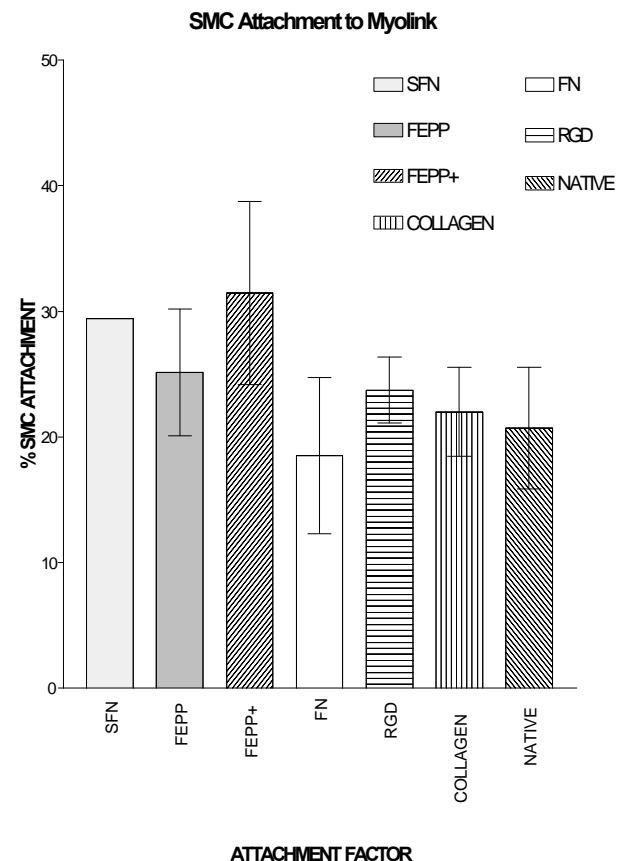


Figure 1: % SMC Attachment to Myolink using different Attachment Factors.

CONCLUSION: We report a new radiolabelling method for assessing attachment of SMCs to graft material. It has been validated by assessing the attachment of SMCs with different extra-cellular matrix materials. FEPP+ was found to have the most significant effect because it is positively

charged and thus attracts the negatively charged cells and has repeating sequences of RGD. This tissue-engineered material may find a clinical application and provide a tool to study molecular mechanisms in coronary graft development.

REFERENCES ¹World Health Organization. World Health Organization: The World Health Report 1999. 1-1-1999. Ref Type: Report. ²Giudiceandrea A, Seifalian AM, Krijgsman B, Hamilton G. Effect of prolonged pulsatile shear stress

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