

## **C25**

### **Growth factor modulation of extracellular matrix gene expression in aortic valve tissue engineering**

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#### **Objectives:**

Vascular smooth muscle cells are a potential autologous cell source for aortic valve tissue engineering. We hypothesized that combining basic fibroblast growth factor (bFGF), epidermal growth factor (EGF) and platelet derived growth factor (PDGF) with transforming growth factor beta-1 (TGF- $\beta$ 1) treatment would allow temporal control of rat aortic smooth muscle cell (RASMC) proliferation and ECM production.

#### **Method:**

The ability of various combinations of growth factors to induce myofibroblast-like phenotype in RASMCs in monolayer culture was assessed by confocal microscopy and western blot analysis. Cell proliferation was measured by MTT assay following treatment with growth factor combinations. Total RNA was isolated to assess ECM gene expression by real-time PCR.

#### **Results:**

Combinations of growth factors which included PDGF showed the greatest increases in proliferation. Immunofluorescence and western blot analysis for alpha-smooth muscle actin ( $\alpha$ -SMA) in conditioned cultures demonstrated an inverse correlation between proliferation and myofibroblast phenotype, with the combination of TGF- $\beta$ 1+bFGF+EGF showing significantly greater quantity of  $\alpha$ -SMA protein compared to untreated control. Finally, TGF- $\beta$ 1+EGF+PDGF treatment showed a significant increase in versican, fibronectin and type I collagen mRNA expression, while decreasing aggrecan, type III collagen, and matrix metalloproteinase 1 expression.

#### **Conclusions:**

A combination of TGF- $\beta$ 1+EGF+PDGF can increase RASMC proliferation and induce ECM gene expression profiles of components that resemble those found in the native aortic valve. bFGF treatment has an inhibitory effect on attaining the desired ECM expression profile.