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Interaction between Mesenchymal Stem Cells and the Extracellular Matrix; Relevance to Tissue Engineering Heart Valves

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Objectives:

Successful tissue engineering of a heart valve depends upon the ability of the cells to populate and remodel the supporting scaffold. We have assessed the adhesion, morphology cell viability and gene regulation of mesenchymal stem cells (MSCs) on various ECM protein substrates.

Method:

MSCs cultured from human bone marrow were seeded (5×10^3 cells/well) onto 96-well plates coated with human vitronectin, human fibronectin or bovine or human type I collagen. Cell morphology, adhesion and viability (MTS Assay) were assessed using calcein green AM labelled cells. Antibodies against integrins were used to block cell adhesion. Cell proliferation in response to growth factors (PDGF-AB or TGF- β) on ECM coated plates (0, 1, 10, 25, 50 μ g/ml) was also assessed.

Results:

Viable cells adhered to the ECM proteins with maximal attachment achieved by 24 hours: fibronectin($83.3 \pm 18.8\%$) = vitronectin($81.2 \pm 12.6\%$) > collagen($62.7 \pm 20.1\%$). Blocking cellular adhesion with a combination of the integrin antibodies ($\alpha_5 + \alpha_2$; $\alpha_5 + \alpha_v\beta_3$; $\alpha_5 + \alpha_2 + \alpha_v\beta_3$) significantly inhibited adhesion to fibronectin but not vitronectin. Cells stimulated with growth factors proliferated on all ECM proteins however, only a significant difference in the presence of PDGF-AB was observed on fibronectin (25 and 50 μ g/ml) and on human type I collagen (10, 25 and 50 μ g/ml), resulting in a 3 to 4 fold increase.

Conclusions:

These results suggest that integrins may act synergistically to enhance cell attachment and facilitate cell proliferation on specific ECM proteins. Therefore, incorporation of preferred ECM proteins into a biodegradable scaffold such as collagen could enhance the development of the tissue engineered heart valve tissue.