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On Demand

Endothelial to Mesenchymal Transformation-derived Activated Fibroblast Behavior in a 3D Culture Environment

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Abstract

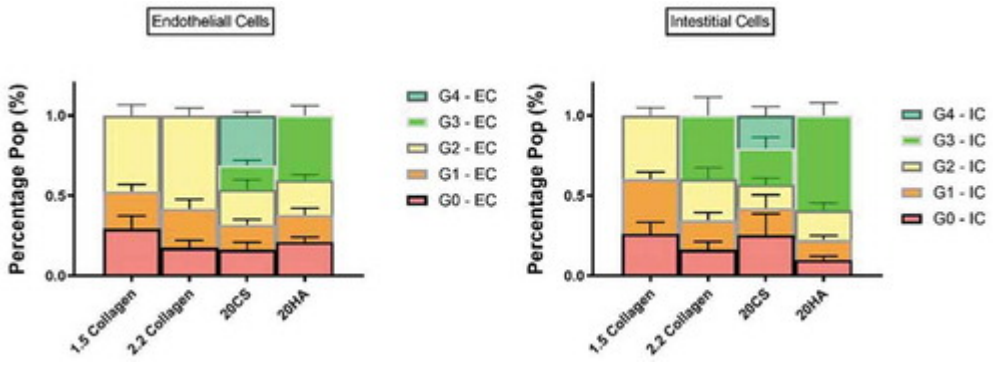
Objective: In calcific aortic valve disease (CAVD), glycosaminoglycans (GAGs) such as chondroitin sulfate (CS) and hyaluronic acid (HA) are present in the normally collagen-rich aortic valve fibrosa near calcified nodules. Previous work using a 3D in vitro model has shown that GAGs can also promote endothelial to mesenchymal transformation (EndMT). The role of mesenchymal transformation in the progression of CAVD remains unclear. The goal of this study is to investigate the role of GAGs and EndMT on valve cell behavior in a 3D, in vitro model of healthy and diseased valves.

Methods: Three dimensional in-vitro cultures, representing healthy (collagen 1 hydrogels) or diseased (collagen 1 hydrogels + GAGs) valve tissue, were seeded with Porcine Aortic Valve Endothelial Cells (PAVEC) and Porcine Aortic Valve Interstitial Cells (PAVIC). Cell cultures were grown for 14 days in regular medium and then evaluated for calcified nodule formation, alkaline phosphatase activity, proliferation and protein expression relating to EndMT activity

Results: Introduction of GAGs into the in vitro model resulted in decreased alkaline phosphatase activity. Hydrogels containing CS conditions induced the greatest calcification, as measured with Alzarin Red quantification, while gels containing HA conditions did not have calcification that was significantly different than controls. Proliferation results suggest high levels of cell division activity, for both PAVEC and PAVIC in CS conditions. Protein expression analysis indicated increased EndMT in hydrogels containing GAGs.

Conclusions: 3D, in vitro models of the aortic valve simulated progression toward late stage CAVD. Further investigation of the downstream role of EndMT within the aortic

valve microenvironment is critical to subsequent improvement in treatment options.



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Previous article **View** issue table of contents **Next** article

Disclosure Statement

The authors do not declare any conflict of interest.