306f Development of a Bioactive Polysaccharide-Based Tissue Engineered Aortic Valve

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Valvular heart disease is a significant cause of morbidity and mortality with valve replacement being the favored solution in most cases. Current replacement options (mechanical valves and decellularized porcine valves) lack the ability to grow or remodel in response to patient needs. This limitation is a major problem for pediatric patients who may require multiple surgical procedures before reaching adulthood. In this ongoing study, we are exploring the feasibility of tissue engineering an aortic valve for pediatric applications, using polysaccharide biomaterials. Specifically, our scaffold design is based on the use of chitosan as the main structural biopolymer, with cell adhesion and protein binding characteristics provided by grafting various glycosaminoglycans (GAGs). GAGs (most notably hyaluronan and dermatan sulfate) are significant components of the valvular extracellular matrix and modulate many cell-matrix and cell-growth factor interactions. In order to compare the cell-interaction properties of various GAGs, valvular interstitial cells (VIC) and valvular endocardial cells (VEC) were isolated from lamb heart valve leaflets and cultured on various GAG-derivatized chitosan membranes. VIC proliferation rates and morphological characteristics indicated that dermatan sulfate-modified surfaces produced the highest growth rates and were excellent substrates for VIC colonization. To generate the valve scaffold, a prototype aortic valve mold was first designed and optimized with CAD software. The mold was then fabricated in nylon using rapid prototyping techniques. Using this mold, porous chitosan valve scaffolds were prepared by controlled freezing and lyophilization of 2% (w/v) chitosan solutions. This process generated scaffold pores sizes in the range 75-300 microns. The scaffolds were then derivatized with dermatan sulfate (0.2 g GAG/g chitosan) using carbodiimide chemistry to form amide linkages between the GAG carboxyls and chitosan amines. VICs were seeded into the scaffold under static conditions (1.2 million/day for 4 consecutive days) followed by VECs (1 million on day 5). On day 6 the construct was transferred to a pulsatile flow, perfusion bioreactor. Results on cellular organization, proliferation and matrix deposition during long-term culture will be reported.