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Phenotype of VICs from Normal and Pathological Pediatric Valves: Implications for a Tissue Engineered Heart Valve

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Objectives:

While the need for a tissue-engineered heart valve (TEHV) for treatment of pediatric valve disease is well established, there has been limited characterization of the pediatric valve cell phenotype.

Method:

Cells from surgically removed pediatric aortic valves (AV, n=18) and pulmonic valves (PV, n=11) were cultured and categorized as normal (n=15), pathological (n=12), or neoaortic (NAV, PV placed in AV position, n=2). Pathological cells were further divided into bicuspid aortic (BAV, n=7) and general pathological (GP, n=5). Flow cytometry was used to detect phenotypic markers and assess cell morphology based on complexity and size. Mean fluorescence intensities were compared using ANOVA.

Results:

Compared to normal PV cells, normal AV cells expressed more vimentin, smooth muscle myosin (SMM), and smooth muscle alpha-actin (SMaA), and demonstrated greater cell complexity. BAV, GP, and NAV cells demonstrated less SMM, fibronectin, and CD44 than normal AV cells. Pathological PV cells expressed less vimentin than normal PV cells. Overall, pathological cells had greater complexity and size than normal cells. Compared to normal PV cells, NAV cells were similar to AV with less fibronectin and greater CD44 and SMaA. These results suggest that hemodynamics are important, but are not the sole determinant of valve cell phenotype.

Conclusions:

The significantly higher levels of muscle-related markers in normal AV cells compared to PV cells correlate to increased stresses on AV, and suggest distinct design goals for AV and PV TEHVs. Unique protein expression profiles in specific valve pathologies could give insight into pathogenesis and possible treatments for each of these diseases.