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Age-related Differences in Valve Interstitial Cell Phenotype: Implications for Tissue-Engineered Heart Valves

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Objectives:

To characterize the phenotype of valve interstitial cells (VICs) from aortic valves (AVs) and mitral valves (MVs) of various aged pigs, an animal model commonly used to investigate human valve disease.

Method:

VICs were isolated from 6-week-old, 6-month-old, and 6-year-old pigs. The 6-month-old mitral VICs were subdivided into those from the anterior center (MVAC) and free edge (MVF). VICs were fixed and examined using flow cytometry to characterize phenotypic markers including the muscle-related markers smooth muscle alpha-actin (SMaA), non-muscle myosin heavy chain (NMM), and vimentin; markers of active collagen synthesis prolyl 4-hydroxylase (P4H) and heat shock protein-47 (HSP47); and markers associated with hyaluronan turnover, the hyaluronan receptor for endocytosis (HARE) and CD44, and the matrix component fibronectin.

Results:

6-week-old VICs had higher expression of vimentin, HSP47 and P4H, but lower expression of HARE and CD44 compared to 6-year-old VICs (each $p < 0.001$). 6-month-old MVAC VICs showed increased expression of SMaA, NMM, vimentin, and CD44 compared to 6-month-old MVF VICs ($p = 0.005$). In the 6-week-old, the AV VICs showed higher expression of SMaA, NMM, vimentin, HARE, and CD44 compared to MV VICs ($p < 0.001$). Similarly, in the 6-year-old AV VICs showed higher expression of all markers except HARE and P4H compared to MV VICs ($p < 0.001$).

Conclusions:

VICs from different aged porcine AVs and MVs showed considerable differences in markers related to myofibroblast activation, hyaluronan turnover, and collagen synthesis, which could indicate different potential for a number of cell processes important to the successful creation of a tissue-engineered heart valve.