THE SEMILUNAR HEART VALVE INTERSTITIAL CELL CYTOSKELETON: ROLE IN CELL STIFFNESS, CONTRACTION, AND TISSUE REMODELING

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Phenotypically, heart valve interstitial cells (VICs) appear to be plastic and reversible, with this attribute speculated to be necessary for tissue remodeling during times of development and repair, but may also be a contributor to degenerative valve disease. Therefore, we hypothesized that the cytoskeletal (CSK) remodeling capability of the porcine aortic and pulmonary VICs (AVICs and PVICs, respectively), which is dominated by smooth muscle α-actin, would exhibit unique contractility when seeded on collagen gels. Moreover, we speculated that this response would be further explained by comparing AVIC and PVIC stiffness with atomic force microscopy to reveal any mechanical influence of the underlying CSK prior to seeding. AVICs were not only significantly stiffer ($p<0.001$) than the PVICs but also contracted the gels significantly more at 24 and 48 hours ($p<0.001$). Neither VIC population contracted the gels at early time points (2 and 4 hours) as dermal fibroblasts did, but formed a central cluster of cells prior to contraction. After clustering, VICs appeared to radiate out from the center of the gels; fibroblasts did not migrate but contracted the gels locally. VIC gels treated with TGF-β1 contracted the gels rapidly, revealing similar sensitivity to the cytokine. These findings suggest that the AVIC is capable of greater contraction, and as has been shown previously, greater biosynthetic output. Results form this study serve to compare the mechanobiological aspect of the AVIC and PVIC and are believed to have implications for understanding possible etiologies of VIC mediated pathologies.