

### **C17. Effect Of Increasing In-vitro Cyclic Strain On Aortic Valve Interstitial Cell Phenotype And Subsequent Gene Expression Of Extracellular Matrix Constituents**

Christopher A. Carruthers<sup>1</sup>; Christina M. Alfieri<sup>2</sup>; Katherine E. Yutzey<sup>2</sup>; Michael S. Sacks<sup>1</sup>

<sup>1</sup>University of Pittsburgh, Pittsburgh, PA, United States; <sup>2</sup>University of Cincinnati, Cincinnati, OH, United States

**OBJECTIVES:** While clinical explant studies have implicated interstitial cells (VICs) in heart valve disease, the initiating mechanism of matrix degeneration is unknown. Cell activation by heightened valve tissue stress, potentially resulting from external factors such as increased hemodynamic loading, may be causal in matrix degeneration. We thus hypothesize that stress overload of valve tissue will result in an increase in VIC activation and collagen biosynthesis, resulting in detrimental fibrosis.

**METHODS:** Circumferentially oriented rectangular porcine aortic valve tissue strips were cultured for six days in a bioreactor at cyclic strain levels of 0%, 10%, and 30% at 1 Hz. Cell viability and extracellular matrix organization were assessed histologically. Phenotype and biosynthetic activity were assessed with immunohistochemistry and qRT-PCR examining the gene expression of alpha-smooth muscle actin, periostin, collagen type I and type III, MMP-1 and MMP-13 expression.

**RESULTS:** H&E stain demonstrated evenly dispersed nuclei throughout the tissue thickness. Movat's pentachrome stain demonstrated a trilaminar layer structure with a decrease in proteoglycans and elastin at 0% strain, and thickening of the ventricularis layer at 30% strain compared to day zero. Current results indicate that periostin expression was affected by strain level.

**CONCLUSIONS:** Current results indicate that cyclic mechanical stimulus maintains the in-vivo trilaminar layer structure while its absence leads to a decrease in organization. High strain level results suggest that this condition has a deleterious effect on VICs. The fact that periostin is critical to collagen fibrillogenesis supports our finding that maintenance of the trilaminar layer architecture is dependent on strain level.