

P20. Inflammation Induces Mesenchymal Transformation In Adult And Embryonic Valve Endothelial Cells Which May Be Further Modulated By Hemodynamics

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OBJECTIVES: Our goal is to uncover common mechanisms between early embryonic valve development and adult valve disease. In this study we investigated the roles of IL-6 and shear stress in mediating EMT events in adult porcine aortic valve endothelial cells (PAVECs) and quail embryonic endocardial explants. IL-6 levels in valve tissue have been shown to increase with progressing heart valve disease. The role of IL-6 in valve development is currently unknown, but recent work has shown that leptin, a member of the IL-6 superfamily, regulates EMT during valvulogenesis. Abnormal shear has been shown to induce developmental valve defects and is thought to contribute to adult valve disease.

METHODS: PAVECs or quail HH14- explants were plated onto three dimensional collagen gels. After exposure to IL-6 (1-100 ng/mL) or steady shear stress in a novel shear stress bioreactor for 48-72 hours, cell invasion, α -SMA, and CD31 or QH1 expression were monitored.

RESULTS: IL-6 has been shown to upregulate α -SMA expression in both quail embryonic endocardial explants and adult PAVECs. IL-6 also increases cell invasion in quail HH14- explants. Preliminary results in the shear stress bioreactor have shown that PAVECs exposed to steady shear stress do not invade the collagen matrix or express α -SMA.

CONCLUSIONS: Inflammatory agonists stimulate a recapitulation of embryonic-like phenotypes in the adult valve endothelium, which may be further modulated by alterations in local hemodynamics. Studying both embryonic and adult valve environments in parallel may provide a powerful paradigm for elucidating mechanisms of disease and identifying therapeutic strategies.