

P13. Creation Of Engineered 3-D In Vitro Models Of Valvular Disease

Karien J. Rodriguez; Laura M. Piechura; Kristyn S. Masters
University of Wisconsin, Madison, WI, United States

OBJECTIVES: End-point analyses of explanted calcified valves have yielded much information about the characteristics of valvular disease. However, the development of 3-D in vitro models of valvular disease would provide a unique window into observing the initiation and intermediate stages of valvular calcification that cannot be easily observed in vivo.

METHODS: Porcine aortic valve leaflets were explanted and cultured as in vitro organ cultures for six days. To induce disease conditions, leaflets were treated with pro-calcific cytokines (TGF- β 1, BMP-7, or TNF- α) or subjected to extracellular matrix (ECM) disruption via targeted, enzymatic depletion of select ECM components. Leaflet cultures were analyzed for ECM composition, cellularity, phenotype, and mineralization.

RESULTS: Administration of the different growth factors or removal of individual matrix components yielded a wide variety of disease expression profiles. For instance, treatment of whole, cultured leaflets with TGF- β 1 resulted in only moderate elevation of myofibroblast markers, but strong elevation of osteogenic activity, and high amounts of mineralization. Meanwhile, leaflets that were selectively depleted of hyaluronic acid (HA) displayed high levels of myofibroblast activity, but little osteogenesis. The ECM depletion method was executed such that, at Day 0, both control and depleted valves had the same cellularity and amounts of other ECM components.

CONCLUSIONS: Mineralization can be induced in 3-D leaflet structures in vitro via administration of certain growth factors and/or disruption of the leaflet ECM. Creation of such 3-D in vitro disease conditions may enable a better understanding of the etiology of valvular disease or serve as platforms for identifying and testing anti-calcific therapies.

Figure 1

