S22_6

The Role of the Extra Cellular Matrix in the Development of Aortic Valve Calcification

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Background:
The hallmarks of calcific aortic valve disease (CAVD) are changes that occur in the organization, composition, and mechanical properties of the extracellular matrix (ECM), ultimately resulting in stiffened stenotic leaflets. Therefore Understanding the role of the ECM in AVICs calcification is highly important.

Methods:
Valve Interstitial cells (ICs) were isolated from valve leaflets of Sprague–Dawley rats. ICs were incubated with different coating – fibronectin or tenascin or uncoated surfaces. In each of the above coating, the cells were exposed to phosphate 3.5mM (a calcification inducer) or left without phosphate. Mineralization of the cells was evaluated using von Kossa staining, calcium quantification using cresophthalein method. The levels of osteocalcin (an osteoblast related protein) were measured by immunostaining.

Results:
Interestingly, fibronectin and tenascin coating even without induction of calcification by phosphate treatment induced AVICs calcification after one week. Furthermore, addition of phosphate increased calcification as seen in calcium quantification using cresophthalein method and von-Kossa stain. The cells cultured on fibronectin or tenascin coated plate showed higher level of osteocalcin compared with controls while phosphate addition increased the osteocalcin level in uncoated and fibronectin coated plate but not in the tenascin coated plates.

Conclusions:
Our findings suggest that fibronectin and tenascin play an important role in AVIC calcification. It seems that fibronectin and tenascin promote calcification even without the additive effect phosphate. Our results suggest that targeting ECM may be a potential strategy in preventing aortic valve calcification but further studies needed for the complete understanding of their specific role.