

### **C112. The Role Of Human Cathelicidin Antimicrobial Peptide LL-37 In Calcific Aortic Valve Disease**

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**OBJECTIVES:** Calcific aortic valve stenosis is a complex disease, resembling both atheroinflammatory processes and skeletal mineralization. Human cathelicidin antimicrobial peptide LL-37 is a multifunctional mediator in the complex network of immune responses and inflammatory diseases. The objective of this study was to explore the potential role of LL-37 in the pathogenesis of calcific aortic valve stenosis.

**METHODS:** We investigated the presence and cell origin of LL-37 in human calcified and noncalcified aortic valves using immunohistochemistry. The pro-apoptotic effects of LL-37 on cultured pig aortic valve interstitial cells (PAVICs) were examined by cell viability with MTT assay and annexin V expression by FACS analysis. The bone differentiation effects of LL-37 on cultured PAVICs were also examined, using nodule formation and alkaline phosphatase (ALP) activity analysis.

**RESULTS:** LL-37 was present in calcified human aortic valves, and was expressed by CD68 positive multinuclear giant cells. LL-37 did not increase ALP activity, or nodule formation, indicating that LL 37 did not cause differentiation of PAVICs into osteoblast-like cells. However, LL37 reduced the viability of PAVICs by MTT assay and increased the expression of annexin-V on the cells, suggesting LL37 induced apoptosis in PAVICs at higher concentrations.

**CONCLUSIONS:** Our findings suggest that human cathelicidin antimicrobial peptide LL-37 is involved in the pathogenesis of calcific aortic stenosis, possibly by inducing VIC apoptosis. These effects may represent an early event in the calcification processes that may subsequently be followed by mineralisation of the apoptotic bodies. In addition, the antimicrobial function of LL-37 in valve calcification warrants further investigation.