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Kinetics of Phosphate Induced Calcification and Osteoblast Differentiation in Rat Aortic Valve Cells

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Objectives: Calcific aortic stenosis is a common disease in renal failure patients. The mechanisms leading to this disorder remain unclear. We have previously demonstrated osteoblast-like cell transformation in an in vivo rat model of uremia. In the present study, we used an in vitro system to dissect the mechanisms playing a role in aortic valve interstitial cells (AVICs) calcification in the uremic model.

Methods and results: We identified phosphate as the most efficient inducer of AVICs calcification. This was evident by analyses of mineralization and expression of osteoblast related genes. The mineralization was accompanied by decreased cell viability.
Consistently, increased apoptosis was observed by TUNEL staining and activated caspase-3 expression. Comparisons of the kinetics of mineralization (evident at 3 days), osteoblastic gene induction (evident within hours) and apoptotic markers (evident at 6 days) indicate that apoptosis cannot be the trigger of the calcification. The effect of phosphate was abolished by inhibition of its uptake.

Conclusions: Our findings suggest that phosphate is a major determinant in AVICs calcification, furthermore, the induction of osteochondrogenic genes started as early as 2 hours post phosphate treatment, preceding the apoptosis markers and the mineralized nodules. Key words: Aortic valve, calcification, phosphate, apoptosis, renal failure.