Phosphate is a Major Mediator of Aortic Valve Calcification

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Background: Calcific aortic valve stenosis is a common disease in the elderly. The molecular and cellular mechanisms leading to this disorder remain unclear because of the absence of appropriate experimental models. In patients undergoing dialysis, aortic valve calcification (AVC) is frequently found and progress rapidly. We have previously demonstrated osteoblast transformation in a rat model of uremia.

In the present study, we explored the molecular mechanism of the differentiation of valve interstitial cells (ICs) into osteoblasts.

Methods: Primary cultures of rat aortic valve ICs were treated with phosphate (7mM) and {phosphate (7mM) +Foscarnet (0.5mM)}. Osteopontin (a major osteoblast protein) and RUNX-2 (transcription factor regulating osteoblast differentiation and function) expression was analyzed by real time PCR and western blot after 14 days. Mineralization of the cells was analyzed by Von Kossa staining.

Results: Phosphate augmented RUNX-2 and osteopontin expression after 14 days. Intense mineralization was noted (by Von Kossa staining). Foscarnet (Phosphate receptor inhibitror) reduced Osteopontin and Runx-2 expression after 14 days and there were no findings of any mineralized nodules.

Conclusions: Our findings suggest that phosphate is a major determinant of the differentiation of valve interstitial cells into osteoblasts. Additional studies are required in order to investigate the cellular and molecular mechanism involving AVC *in vivo*.