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GENOMIC AND PROTEOMIC ANALYSES REVEAL A RELATIONSHIP BETWEEN WNT PATHWAY GENES, OXIDATIVE STRESS METABOLISM AND VASCULAR CALCIFICATION

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Introduction and Aims: Vascular calcification (VC) is a highly prevalent condition and one important cause of mortality in chronic kidney disease (CKD) patients. The aim of this study was to analyze the change of expression of genes and proteins that occurs in the development of VC.

Methods: Rats with 7/8 nephrectomy fed with high (0.9%) or normal (0.6%) phosphorus diet were used. Rats were sacrificed after 8, 16 and 20 weeks after surgery (5 animals per group). Serum biochemical parameters and bone mineral density in tibia were measured. Von Kossa staining of the aorta was carried out to detect the presence of VC. Differential gene and protein expression in aortas were assessed by gene expression microarrays and DIGE followed by MS and LC/MS-MS, respectively.

Results: Only the animals fed with high phosphorus during 20 weeks developed VC. Moreover, this group showed a significant decrease in renal function and bone mass, and a significant increase in serum P, iPTH and mortality. In the calcified aortas; at gene level, 3 secreted related frizzled proteins genes (SFRPs), inhibitors of the wnt pathway, involved in bone formation, were up-regulated. At protein level, 40% of the proteins with significant changes in their expression belong to the oxidative stress metabolism. Muscle related proteins were down regulated.

Conclusions: The SFRPs and the oxidative stress metabolism seem to play a role in the development of VC and it may play also a role in the reduction of bone mass.