KSN 2021
FULLY VIRTUAL MEETING
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The ubiquitin-specific protease USP47 is implicated in chronic kidney disease-related vascular calcification by regulating vascular smooth muscle cell phenotype

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Objectives: The aim of this study was to explore the underlying pathogenesis of vascular calcification (VC) and investigate effective therapeutic targets for VC in chronic kidney disease (CKD).

Methods: We have established the calcification model of rat aortic vascular smooth muscle cells (RASMCs) of high phosphorus environment and identified 37 significant proteins by the label-free quantification (LFQ) analysis. Furthermore, increased expression of USP47 was detected in high phosphate-induced calcification in RASMCs, in arteries of CKD subjects and Rats.

Results: We have established the calcification model of RASMCs in vitro of high phosphorus environment and identify 37 significant proteins by the label-free quantification (LFQ) to find the potential biomarkers for VC. In calcification （CAL） group 18 proteins were up-regulated while 19 proteins were down-regulated. Among them， USP47 showed the most significant difference. Furthermore, expression of USP47 was increased in high phosphate-induced calcification in RASMCs，in arteries of CKD subjects and Rats. USP47 had been knocked down successfully in RASMCs and all these data indicate that USP47 has an effective ability to induce VSMCs calcification activation and knockdown of USP47 proteins inhibits the level of calcification. STRING database were used to find that USP47 interacts with β-transducin repeat-containing protein (BTRC) directly to act on the AKT kinases 1 (AKT1) to regulate the calcification associated RUNX2, Klotho, fibroblast growth factor (FGF23) and matrix Gla protein (MGP). Although there was no statistical difference，the clinical serum sample results showed that the expression of USP47 was up-regulated in ESRD patients group （n=54）.

Conclusions: USP47 would be a potential promoting factor involved in regulatory mechanism in CKD-related VC. USP47 may promote VSMCs trans-differentiation to osteoblast phenotype probably through the activation of the BTRC-AKT1 signaling axis. Our observation has the potential to provide a novel therapeutic target for progression of VC after CKD.

Figure 1. Clustering heatmap of the principal significant proteins of the LFQ intensities obtained from RASMCs in comparison of CAL and Control. No protein names were drawn when exceeding a specific value and missed values were shown with '–'. Repeat the experiment three times with group of Control and CAL. Calculations were performed with Perseus.

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