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Crosstalk between ECs and VSMCs mediated vascular calcification in CKD by exosomal miRNA-299

Si-lie Chen

Southeast University, Nanjing, China

Chronic kidney disease (CKD) is often complicated by vascular calcification (VC). Stimulated endothelial cells (ECs) can promote vascular smooth muscle cells (VSMCs) to the osteogenic phenotype, leading to VC. However, the mechanism by which ECs promote phenotypic transformation of VSMCs is unclear. This research aimed to explore whether ECs can promote osteogenic transdifferentiation of VSMC and its related signaling pathways by releasing exosomes. EC-Exos was isolated, and VSMCs were detected. miRNA omics was applied to explore exosomal miRNA's differential levels. Osteogenic transcription factors' protein and mRNA levels were exploded. We found that ECs' high phosphate-induced exosomes (HP-Exos) were absorbed by VSMCs, promoting VS-

MCs' osteogenic transdifferentiation. Omics analysis showed that miRNA-299 expression in exosomes after ECs was up-regulated by high phosphorus. Specific knockout of miR299-3p could significantly inhibit VC in mice fed a high phosphate and adenine diet. The downstream target of miR299-3p was MARCH7. Knocking down MARCH7 expression with small interfering RNAs aggravated VSMCs' calcification and activated the PI3K/AKT signaling pathway. In sum, the HP-treated endothelium-derived exosome miR-299-3p can promote aortic calcification by targeting MARCH7. The PI3K/AKT pathway's activation may be a mechanism by which exosomes promote VSMC calcification, and MARCH7 may be a novel target for treating patients with VC with CKD.

Biography

Si-Jie Chen is a medical Doctor, currently studying nephrology at Southeast University School of Medicine. Her main research interest is the mechanism and treatment of vascular calcification regulated by exosomes in chronic kidney disease. She appears in the journal "cellproliferation, International Journal of Molecular Sciences" and other relevant papers. She has participated in a number of scientific studies on vascular calcification in chronic kidney disease and exosome-targeted drug therapy, and her research has found that endothelial mesenchymal transdifferentiation promotes the formation of osteoblast-like cells, leading to the occurrence and development of vascular calcification in chronic kidney disease. She is passionate about scientific research.