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Depot-specific characteristics of visceral adipose-derived mesenchymal stem cells (ADMSCs) from patients with chronic kidney disease (CKD): A single-cell RNA sequencing study

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Objectives: Patients with CKD experience unique systemic conditions, such as chronic inflammation, oxidative stress, and protein-energy wasting. While many studies have attempted to understand these conditions through inter-organ communication, the changes in adipose tissue in a uremic environment are not well understood. This study aimed to investigate the characteristics of visceral adipose tissue of CKD patients focusing on ADMSCs.

Methods: We obtained retroperitoneal adipose tissue (RP) close to the kidney and omental adipose tissue (OM) from healthy kidney donors and patients with end-stage kidney disease who received kidney transplantation or peritoneal catheter insertion. We evaluated the characteristics of stromal vascular fraction in the adipose tissue using single–cell RNA sequencing.

Results: We harvested 66,668 cells. In the ADMSCs cluster of RP, antioxidant genes, such as metallothioneins, SOD2, and GPX3 were significantly upregulated in CKD. In addition, Gene Ontology and pathway analysis showed that differentially expressed genes (DEGs) upregulated in CKD were related to ribosomal biogenesis and ferroptosis. We also observed an increase in the S phase of the cell cycle in RP of CKD which was accompanied by increased FOXO signaling pathway and cellular senescence to prevent DNA damage. Meanwhile, DEGs specifically upregulated in OM of CKD were related to the process of ATP synthesis, such as fatty acid beta-oxidation, TCA cycle, and oxidative phosphorylation in mitochondria. Lastly, when we examined total OM, median cell size of adipocytes from CKD patients was significantly smaller than that of healthy controls, and expression of UCP-1 was significantly increased in adipocytes of CKD.

Conclusions: We found depot-specific unique characteristics of ADMSCs in the adipose tissue of CKD patients. Further studies are needed to determine if these alterations in adipose tissue may mediate some of systemic conditions accompanied by CKD.