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Intercellular Communication Network of CellChat Uncovers Mechanisms of Kidney Fibrosis Based on Single-Cell RNA Sequencing

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Objectives : Anti-renal fibrosis and the postponement of renal function are global challenges in treating chronic kidney disease (CKD). The study aimed to investigate the potential benefits of SGLT2 inhibitors in non-diabetic CKD.

Methods : We established a CKD model using 5/6 nephrectomy (5/6 Nx) rats and divided them into three groups: placebo-treated sham surgery rats, placebo-treated 5/6 Nx rats, and Empagliflozin (Empa)-treated 5/6 Nx rats. We conducted single-cell RNA sequencing on kidney tissues to analyze intercellular communication networks.

Results : Intercellular analysis revealed that the probability and intensity of universal communications were higher in the kidneys of 5/6 Nx rats treated with placebo than in rats treated with sham surgery and placebo. We observed that MIF and GRN were up-regulated in tubular epithelial cells of 5/6 Nx rats, which were activated by paracrine signaling from M2 macrophages. And these up-regulated fibrogenic genes were enriched in TGF- β pathway of endothelial, mesangial, and fibroblast cells. This process promotes collagen synthesis and extracellular matrix deposition by activating the COLLAGEN, FN1, LAMNIN, and THBS pathways. In addition, Empa treatment improves renal morphology in 5/6 Nx rats by inhibiting MIF and GRN expression in tubular epithelial cells and down-regulating the COLLAGEN, FN1, THBS, and LAMNIN pathways associated with kidney fibrosis.

Conclusions : We identified ligand-receptor pairs and signaling pathways involved in CKD fibrosis by intercellular communication network of CellChat. Moreover, Empa reduce renal fibrosis in CKD by modulating the intercellular communication network.

机制图.jpg

