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The role of resident renal fibroblast on renal fibrosis and crosstalk with tubular epithelial cells

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Objectives: Renal fibroblasts are the core cells that deposit the extracellular matrix and play a direct role in renal fibrosis. Understanding the process of myofibroblast transition and fibrotic deposition by renal resident fibroblast will provide important clues to understanding the mechanism of renal fibrosis.

Methods: A unilateral ureteral obstruction (UUO) model was constructed in 7-week-old B6 male mice, and kidneys were extracted on Day 3, Day 7, and Day 14, and the degree of fibrosis and renal interstitial fibroblast markers aSMA and PDGFβ antibody immunofluorescence staining were performed. In previous research, through proteomics analysis after TGFβ (2ng/ml, 24hr) treatment in primary tubular peithelial cells and kidney proteomics analysis in 5/6 nephrectomy CRF rat model, an indicator called Transgellin (TAGLN) was found as a significant indicator in the process of renal fibrosis. We divided patients into CKD 1&2, 3, and 4&5 groups, and performed TAGLN staining. In NIH3T3, embryonic mouse fibroblast cell line, after treatment with rTGFβ (2ng/mL, 4ng/ml), the expression levels of fibronetcin, αSMA, PDGFRβ, and Transgelin were checked.

Results: On the 3rd and 7th day of UUO surgery, the expression of αSMA and PDGFβ double positive increased not only in the interstitium but also in the tubular epithelial cells. In the IHC staining results of kidney tissue samples from CKD 3 and 4&5 CKD patients, TAGLN expression also tended to increase in interstitium around glomerulus and tubular epithelial cells. After rTGFβ treatment in NIH3T3 cells, the expression levels of aSMA, PDGFβ, and Transgelin increased in a dose dependent manner with rTGFβ.

Conclusions: The fibrogenic activity of renal fibroblasts and the expression of TAGLN occurs mainly in interstitum and tubular epithelial cells. In future studies, it will be necessary to find out the role of TAGLN in the process of renal fibroblast fibrosis and the interaction with tubular epithelial cells.

aSMA, PDGFβ double positive renal fibroblasts in UUO