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Insulin-like growth factor binding protein 3 specific DNA aptamer attenuated renal tubular fibrosis

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Objectives: Insulin-like growth factor binding protein 3 (IGFBP3) is a predominant IGFBP family member of six IGFBPs. Emerging evidence has indicated that IGFBP3 has cell- and tissue-specific effects, and it is an important mediator of fibrosis in various cell types and the organs. However, to date, the effect of IGFBP3 on renal fibrosis has not been fully evaluated. This study is to investigate whether IGFBP3 is involved in renal cellular fibrosis and IGFBP3 inhibition by aptamer treatment is effective for attenuating renal tubular fibrosis.

Methods: IGFBP3 and fibrosis-related protein expression were evaluated in unilateral ureteral obstruction (UUO) mouse. In vitro, the proximal tubular cells (NRK-52E) were treated with TGF-β1 (10 ng/ml). IGFBP3 inhibition was performed by IGFBP3 small interfering RNA (siRNA, 100 pmol/ml) and IGFBP3 aptamer (200 pmol/ml) for 48 hours, respectively. Changes of fibrosis related protein expression were examined by real-time PCR and Western blot.

Results: IGFBP-3 and fibrosis-related protein expressions were up-regulated in the kidney of UUO rats. In TGF- β1-stimulated NRK-52E cells, IGFBP3 protein expression was increased in dose- and time-dependent manners. TGF-β1 treatment induced IGFBP3 and fibrosis-related protein expression, including fibronectin and type I collage in renal proximal tubule cell. IGFBP3 small interfering RNA treatment significantly abrogated the increase in fibrosis-related protein expression induced by TGF-β1. Furthermore, the IGFBP3-binding DNA aptamer also significantly attenuated fibrosis-related protein expression upregulated by TGF-β1 treatment.

Conclusions: This study suggests that IGFBP3 is significantly associated with pathogenesis of renal tubulointerstitial fibrosis. Furthermore, IGFBP3 aptamer treatment can be a potential therapeutic option for renal tubulointerstitial fibrosis in chronic kidney disease patients.