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Impact of IL-11 as a renal fibrosis marker in chronic kidney disease using mouse model

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Objectives: Fibrosis is a common pathophysiology of chronic kidney disease (CKD) progression, but the role of IL-11, which is highly expressed in the fibroblast remains elusive. Herein, we aimed to evaluate the role of IL-11 in the fibrosis pathway and apoptosis.

Methods: We examined the impact of IL-11 in the UUO model using B6 mouse aging 7 to 8 weeks. An *in-vitro* experiment was performed using primed human tubular epithelial cells (hTECs) to figure out the role of recombinant IL-11 induced fibrosis. In addition, we examined the change in the expression of phosphorylated STAT3 (pSTAT3) and IL-18 after treated recombinant TGFβ (rTGFβ) and rTGFβ with an anti-IL-11 antibody (Ab) via fluorescence-activated cell sorting (FACS). Finally, we evaluated an impact on apoptosis using TGFβ and TGFβ with an anti-IL-11 Ab.

Results: Expression of IL-11 in bulk-tissue RNA-sequencing was significantly higher in the kidney lysates from the UUO model than those from sham. The levels of IL-11 expression in kidney sections from the UUO model were remarkably correlated with the intensity of COL1 in the look-up section. Two days after treating rIL-11 with doses of 100 or 500 ng/mL, the expression of COL1 mRNA was dose-dependently increased in the UUO model. rTGFβ treatment significantly increased the expression of COL1, STAT3, and CXCL1 mRNA, while anti-IL-11 Ab restored the mRNA expressions of the molecules. Also, rTGFβ treatment increased the expression of pSTAT3 and IL-18. Anti-IL-11Ab significantly abrogated these expressions by 60% and 33% in pSTAT3 and IL-18, respectively. Finally, the Annexin V assay revealed relevant increases in apoptotic cells treated with rTGFβ, and anti-IL-11Ab significantly attenuated the increase.

Conclusions: IL-11 has a role in the induction of fibrosis. The inhibition of IL-11 significantly attenuates the fibrotic changes, indicating that IL-11 pathway could be a treatment target for CKD progression.