

# NOVEL ROLE OF IL-20 CYTOKINE SUBFAMILY IN THE PATHOGENESIS OF CHRONIC KIDNEY DISEASE

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## Introduction:

Regardless of the etiology, kidney fibrosis is the final outcome of progressive kidney diseases. Our recent study showed that levels of interleukin (IL)-20 subfamily members, including IL-19 and IL-24 significantly increased in newborn rat kidneys underwent unilateral ureteral obstruction (UUO). However, their precise role in the pathomechanism of renal fibrosis has not been investigated.

**Method:** To study the role of IL-20 cytokine subfamily we applied a mouse model of UUO induced kidney fibrosis on wild type and IL-20 receptor beta gene knockout (IL-20R $\beta$  KO) mice. Masson's trichrome and Picro-Sirius Red staining were used to investigate the renal accumulation of extracellular matrix proteins. Real-time RT-PCR and western blot method were performed to measure the renal expression of fibrosis associated molecules. We also investigated the *in vitro* effect of IL-24 treatment on transforming growth factor beta (TGF- $\beta$ ) and platelet derived growth factor B (PDGF-B) expression of human proximal tubular epithelial (HK-2) cells by real-time RT-PCR and flow cytometry.

**Results:** We found elevated level of IL-19, IL-24 and IL-20R $\beta$  in the fibrotic kidneys. IL-20R $\beta$  KO mice showed reduced extracellular matrix deposition and decreased  $\alpha$ -smooth muscle actin expression compared to wild-type mice following UUO. Treatment of renal epithelial cells with IL-24 increased their TGF- $\beta$  and PDGF-B production.

**Conclusion:** Our study provides direct evidence of the pathogenic role of IL-20 cytokine subfamily in the development of renal fibrosis, possibly through the IL-24 mediated production of pro-fibrotic factors. Therefore, inhibition of IL-24 may have therapeutic effect in treatment of chronic kidney diseases.

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