Nature Reviews Nephrology **11**, 445 (2015); published online 16 June 2015; doi:10.1038/nrneph.2015.97

RENAL FIBROSIS

Activation of JAK3/STAT6 contributes to the development of renal fibrosis

Bone marrow-derived fibroblast precursors (fibrocytes) contribute to the pathogenesis of renal fibrosis, but the mechanisms that underlie their activation and recruitment to the kidney are not fully understood. Now, data from Jingyin Yan and colleagues implicate JAK3/STAT6 signalling in fibrocyte activation.

The researchers detected activated STAT6 in bone marrow-derived monocytes after culturing them in the presence of the profibrotic cytokines IL–4 and IL–13. These cytokines also enhanced the expression of extracellular matrix (ECM) proteins and α-SMA, which were attenuated upon application of the JAK3-specific inhibitor, CP690,550, as well as in bone marrow-derived monocytes isolated from STAT6$^{-/-}$ mice.

The researchers replicated their findings *in vivo* using a mouse model of renal fibrosis induced by unilateral ureteral obstruction (UUO). UUO mice treated with CP690,550 exhibited diminished expression of α-SMA, fibronectin and collagen I, and reduced cellular apoptosis in their obstructed kidneys compared to UUO mice treated with vehicle. Moreover, these mice showed fewer myeloid fibroblasts on kidney tissue sections as compared to vehicle-treated mice.

Mice transplanted with STAT6$^{-/-}$ bone marrow cells accumulated fewer bone marrow-derived fibroblasts in their kidneys and developed less renal fibrosis after 10 days of UUO compared to mice transplanted with STAT6$^{+/+}$ bone marrow cells. These findings suggest an important role for JAK3/STAT6 signalling in the activation of bone marrow-derived fibroblasts, expression of ECM proteins, and the development of renal fibrosis.

Jessica K. Edwards

Original article Yan, J. *et al.* JAK3/STAT6 stimulates bone marrow-derived fibroblast activation in renal fibrosis. *J. Am. Soc. Nephrol.* doi:10.1681/ASN.2014070717