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Knockdown of Peroxiredoxin V (Prdx V) exacerbates unilateral ureteral obstruction-induced renal fibrosis

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Objectives: Renal fibrosis is closely associated with chronic inflammation. Peroxiredoxin V (Prdx V), an atypical 2-Cys member of the Prdxs family, functions as anti-inflammatory effector as well as a thiol-dependent peroxidase in its catalytic cysteine-dependent manner. Recently, we demonstrated that overexpression of Prdx V attenuated TGF-β induced fibrosis in NRK49F cell lines. However, the relevance and the underlying mechanism of Prdx V to renal pathobiology remains poorly understood.

Methods: To investigate the role of Prdx V in renal fibrosis, we used a transgenic mouse model with PrdxV siRNA expression controlled by U6 promoter (C57BL/6J-Tg(U6-PrdxVsi)1Thlee/Krb; Prdx Vsi mice). Both Prdx V^{wt} and Prdx V^{si} mice were subjected to unilateral ureteral obstruction (UUO) by ligation of the left ureter for 7 days (Control vs UUO group, n = 8 per each group).

Results: We found increased renal fibrosis in UUO-induced Prdx V^{si} mice compared with UUO-induced Prdx V^{wt} mice. Knockdown of Prdx V exacerbated epithelial-to-mesenchymal transition (EMT) as well as the increase of oxidative stress by UUO. In canonical TGF-β signals, the increase of Smad4 that plays a critical role in nucleocytoplasmic shuttling of Smad2/3 is remarkable in UUO-induced Prdx V^{si} mouse kidney. In non-canonical TGF-β signals, site specific-epidermal growth factor receptor (EGFR)-mediated Stat3 activation is accentuated in UUO-induced Prdx V^{si} mouse kidney.

Conclusions: Prdx V is an anti-fibrotic effector that sustains renal physiology. Negative regulation of TGF-β signaling by Prdx V could be a therapeutic target to protect renal fibrosis.