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Peroxiredoxin 5 Protects TGF-β Induced Renal Fibrosis by Modulating Stat3 Activation

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Background: Peroxiredoxin 5 (Prdx5), an atypical 2-Cys Prdxs family, is thiol-dependent peroxidase that reduces oxidative stress by catalyzing intra-molecular disulfide bond. Prdx5 has been known to have not only anti-oxidant effects but also regulatory function of inflammation. Renal fibrosis is a common final pathway of progressive kidney disease, which is primed by production and secretion of proinflammatory cytokines in injured kidney resident cells. We investigated the physiological role and regulatory mechanism of Prdx5 in the pathogenesis of renal fibrosis.
Methods: As in vivo and in vitro model of renal fibrosis, Sprague-Dawley rat were subjected to unilateral ureteral obstruction (UUO) for 1 or 7 days. NRK49F, fibroblast-like rat proximal tubule cells were treated with transforming growth factor β (TGF-β) for 0, 1, 3, or 5 days. To assess whether Prdx5 play a role in TGF-β induced renal fibrosis by modulation of its' peroxidase activity, wild type Prdx5 (WT) and double mutant Prdx5 (DM), converted two active site cysteine to serine at Cys 48 and Cys 152 residue, were transiently expressed in NRK49F cells.
Results: The protein expression of Prdx5 was reduced in UUO kidneys. Upregulation of fibrotic markers, such as fibronectin, vimentin, and α-SMA, were declined at 5 days in time point of higher Prdx5 expression in TGF-β treated NRK49F cells. The overexpression of wild type Prdx5 by transient transfection in NRK49F cells attenuated the TGF-β induced upregulation of fibronectin, vimentin, and α-SMA. On the other hand, the transient transfection of double mutant Prdx5 did not prevent the activation of fibrotic markers. Overexpression of Prdx5 decreased the TGF-β induced upregulation of Stat3 phosphorylation, while phosphorylation of Smad 2/3 was not changed.
Conclusion: Prdx5 protects TGF-β induced renal fibrosis in NRK49F cells by modulating Stat3 activation in a peroxidase activity dependent manner.

Key Words: Prdx5, TGF-β, Stat3