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Knockout of PTP4A1 ameliorate renal fibrosis induced by unilateral ureteral obstruction in mice.

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Objectives : Inhibitors targeting protein tyrosine kinases (PTP) have been explored as potential anti-fibrotic agents. PTP4A1, a member of a sub-class of prenylated PTPs, is recognized for its role in promoting the growth and migration of tumor cells. However, its role in the context of renal function remains poorly understood. This study aimed to assess whether PTP4A1 could serve as a target for mitigating renal fibrosis.
Methods : en-week-old male PTP4A1 knockout (KO) mice and wild-type mice were categorized into four groups: wild-type, PTP4A1 KO, wild-type with unilateral ureteral obstruction (UUO), and PTP4A1 KO with UUO. Mice were sacrificed seven days post-surgery, and kidney tissues were collected. Molecular studies and histologic examinations were conducted.
Results : PTP4A1 KO mice with UUO exhibited a reduction in renal tubule-interstitial damage and fibrosis compared to wild-type UUO mice. PTP4A1 KO with UUO resulted in decreased renal expression of α-SMA and TGF-β in UUO-afflicted kidneys, compared to wild-type UUO mice. Wild-type UUO kidneys demonstrated reduced expression of E-cadherin compared to sham mice. However, PTP4A1 KO UUO kidneys displayed an increase in E-cadherin expression compared to wild-type UUO mice. In vitro, silencing of PTP4A1 in TGF-β-treated HK2 cells led to an increase in E-cadherin expression and a decrease in the phosphorylation of AKT and GSK3ß.
Conclusions : PTP4A1 KO attenuated renal fibrosis in UUO-afflicted kidneys, suggesting that PTP4A1 could be a promising target for therapeutic intervention in renal fibrosis.