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Inhibition of KLHL3 ameliorates renal fibrosis in UUO mice.

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Objectives : It has been known that Kelch-like 3 (KLHL3) regulate some electrolyte in kidney tubules. In human, the mutation of KLHL3 induce hypertension, characterized by pseudoaldosteronism (decreasing aldosterone). We evaluated whether the KLHL3 could be fair target of RAAS inhibition, resulting in inhibition of renal fibrosis in unilateral ureteral obstructed (UUO) mice.

Methods : 10-week-old male B6 mice background KLHL3 KO mice and wild type mice were divided into 4 groups; wild, KLHL3 KO, wild with UUO, and KLHL3 KO with UUO. Mice were sacrificed at 7 days after surgery and kidney tissue were collected. Real time RT-PCR, western blot and immunohistochemistry for molecular study and H&E stain and PAS stain for histologic examination were performed.

Results : KLHL3 KO with UUO mice showed improvement of renal cell survival, renal function, and pathologic damage compared to wild type UUO mice. Wild type with UUO kidney showed decrease of renal expression of KLHL3 and WNK4, and increase of renin and angiotensin I receptor, compared to sham mice. However, KLHL3 KO with UUO reduced the renal expression of renin, angiotensin I receptor, alpha-SMA, collagen IV, and TGF-ß in UUO kidney, compared to wild type with UUO mice.

Conclusions : Inhibition of KLHL3 KO ameliorate renal fibrosis in UUO kidney via inhibition or renin angiotensin system.

Keywords : KLHL3, renal fibrosis, unilateral ureteral obstruction