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HL156의 AMPK 활성화가 신장 섬유화를 억제시키는 효과에 관한 연구

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HL156, a Novel and Potent Adenosine-monophosphate-activated Protein Kinase (AMPK) Activator, Protects Against Renal Fibrosis in Unilateral Ureteral Obstruction (UUO) Model

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Renal fibrosis is defined as an excessive deposition of extracellular matrix (ECM) and leads to the end-stage renal failure. Inhibitory action of adenosine-monophosphate-activated protein kinase (AMPK) on the smad-3 signaling has been suggested. HL156 is a novel and potent AMPK activator. The present study was implemented to investigate the protective effects of HL156 on renal fibrosis in *in-vivo* and *in-vitro* models. Renal fibrosis were prepared by unilateral ureteral obstruction (UUO) from Wistar rats. Rats were divided into four groups: (i) sham-operated group; (ii) sham plus HL156 (20 mg/kg) group; (iii) UUO group and (iv) UUO plus HL156 (20 mg/kg). Rats received HL156 (20 mg/kg) by oral gavage or distilled water for 10 days. HL156 treated-UUO rats exhibited amelioration of renal fibrosis compared with UUO control rats. Immunohistochemistry showed decreased expression of alpha smooth muscle actin (αSMA), type IV collagen, and fibronectin in the HL-treated UUO group. In the kidney tissue of the HL-treated UUO group, the mRNA and protein expression levels of TGF-β1, p-smad3, αSMA, fibronectin and type IV collagen were down-regulated and E-cadherin expression was up-regulated. From TGF-β1 treatment to NRK-52E cells, parallel changes were observed from HL156 co-treated cells. HL156 co-treatment inhibited TGF-β1-induced smad3 signaling pathway and markers of epithelial-to-mesenchymal transition (EMT). Our findings suggest that HL156 protects against renal fibrosis in vivo and in vitro models.

Key Words: AMPK, HL156, 신장 섬유화
AMPK, HL156, Renal fibrosis