박스터 연구비

혈관 내피 기능 조절에 의한 내피세포-중간엽세포로의 이환 억제를 통한 신장 섬유화 억제 기전 연구

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Inhibition of Soluble Epoxide Hydrolase Attenuates Kidney Fibrosis by Modulation of Endothelial Mesenchymal Transition

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Background: Soluble epoxide hydrolase (sEH) in endothelial cells determines the plasma concentrations of epoxyeicosatrienoic acids (EETs), which may act as vasoactive agents to control vascular tone. Regardless of disease origin, fibrosis is a final common pathway in chronic kidney disease that leads to disease progression and ultimately organ failure. Here we show that kidney fibrosis was reduced by regulation of sEH activity.

Methods: Unilateral ureteral obstruction (UUO) was used as a model of kidney fibrosis in C57BL/6 mice and controlled sEH activity by continuous release of the sEH inhibitor 12-(3-adamantan-1-ylureido)-dodecanoic acid (AUDA) (8 mg/kg/day) via implantable subcutaneous osmotic pump for 1 or 2 wks. Endothelial mesenchymal transition (EndMT) was induced by adding recombinant TGF-β2 (rTGF-β2) in human umbilical vein endothelial cells (HUVECs).

Results: By treatment of rTGF-β2, HUVEC showed morphologic change like fibroblast and expressed high expression of mesenchymal marker fibroblast specific protein-1 (FSP-1). AUDA treatment restored the morphologic change and the expression of FSP-1 in HUVEC. Histological examination revealed that fibrosis UUO model was protected by AUDA treatment. The protective effect of the sEH inhibitor was achieved by suppression of EndMT. AUDA increased the expression of endothelial markers vWF, VE-cadherin, and CD31, in contrast, decreased TGF-β and FSP-1.

Conclusion: The results of this study suggest that treatment with sEH inhibitors can reduce kidney fibrosis by regulation of EndMT.

Key Words: 내피기능, 신장 섬유화, 내피세포-중간엽세포로의 이환
Endothelial function, Kidney fibrosis, endMT