

## Experimental UUO model에서 DPPVI inhibition (LC15-0444)의 신기능 보호 효과

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### Renal Protective Effects of DPPIV Inhibition (LC15-0444) on Experimental UUO Model

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**Background:** Dipeptidyl peptidase IV (DPPIV) is an exopeptidase which modulates the function of various substrates, among which insulin-releasing incretins are the most well known. It is also known to modulate substrates involved in metabolism, glucose regulation, inflammation, cell migration, and cell differentiation. In the kidney, DPP4 is highly expressed on the surface in the proximal tubular cells and is highly active. However, the roles of DPP4 and its inhibitors are not fully understood in the renal setting. Therefore, we investigated the role of DPP4 inhibitor in experimental renal fibrosis model.

**Methods:** 8-week-old C57/BL6 mice were divided into 3 groups: I) sham II) vehicle+UUO, III) DPP4 inhibitor (LC15-0444)+UUO group. After inducing UUO C57Bl/6J mice were placed on a normal chow diet with DPP4 inhibitor (LC15-0444, 150mg/kg/day) as a food admix for 2 weeks.

**Result:** Interestingly, DPPIV activity was significantly increased in the obstructed kidney, which was ameliorated by DPPIV inhibition. Administration of LC15-0444 resulted in a significant decrease of microalbuminuria and proteinuria. However, there were no significantly changes of DPP4 activities in the heart and plasma. Gene expressions of MCP-1, PAI-1, Type IV collagen and TGF beta 1 in kidney were significantly decreased in DPP4 inhibitor (LC15-0444) group. In addition, Urinary excretion of 8-isoprostane was markedly increased in UUO, and DPPIV inhibition significantly decreased urinary excretion of 8-isoprostane. In cultured proximal tubule cells, DPPIV expression was upregulated by angiotensin II stimulation, and suppressed by DPPIV inhibition. Altogether, these results suggest that activation of DPP4 in kidney has a role in the progression of renal disease and DPPIV inhibition may provide renoprotective effects independent of its hypoglycemic effects.

**Conclusion:** In our study showed that DPP4 inhibitors have anti-inflammatory and anti-fibrotic processes in the kidney.

**Key Words:** DPP4, UUO 모델, 근위세뇨관 세포  
DPP4, UUO model, Proximal tubular cell