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Class II 히스톤 탈아세틸화제 활성도 차단의 신장섬유화증 예방효과에 대한 연구

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Blocking Class Histone Deacetylase Activity Inhibits Renal Fibrosis

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Introduction: Fibrosis is the final, common pathological outcome of many chronic kidney diseases. Although histone deacetylases (HDACs) have been reported to be involved in renal fibrosis, it is still unclear which class of HDAC is involved in the pathophysiology of renal fibrosis.

Objective: To investigate which class of HDAC is involved in pathogenic renal fibrosis and evaluate anti-fibrotic effect of the defined HDAC inhibitors.

Methods: The enzyme activity of class I and class II was examined on TGF-beta 1-induced epithelial-to-mesenchymal transition (EMT) of the human renal proximal tubular epithelial cell line HK-2. By using the pan-HDAC inhibitor (SB939), class I-specific HDAC inhibitor (MS275), and class II-specific HDAC inhibitor (MC1568), we defined the roles of class I and class II enzymes in EMT. To confirm the role of HDACs in vivo, we used the unilateral ureteric obstruction (UUO) model of renal fibrosis.

Results: We found that class II enzyme activity was markedly induced on TGF-beta 1-induced EMT but class I enzyme was not induced. Treatment of pan-inhibitor SB939 strongly inhibited TGF-beta 1-induced upregulation of collagen type I and alpha-SMA. Class II-specific inhibitor MC1568 had the similar effects of SB939, but class I-specific inhibitor MS275 did not have the effects. UUO model with SB939 treatment was markedly inhibited accumulation of alpha-SMA and deposition of collagen type I.

Conclusion: Our results demonstrate that class II HDACs contribute to renal fibrosis and suggest that class II-selective inhibitors have a therapeutic potential for the treatment of renal fibrosis.

Key Words: 신장섬유화증, 히스톤 탈아세틸화제
Renal fibrosis, Histone deacetylases, TGF-beta 1