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Inhibition of Histone Deacetylase Activity Suppresses Inflammation Induced by TNF-α in Human Renal Epithelial Cells and Unilateral Urethral Obstruction in Rats

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Inflammation may be a key feature in many pathological conditions. The histone deacetylase (HDAC), which modulates the accessibility of transcriptionally active promotor regions, may play role in the regulation of inflammatory gene expression. We investigated the effect of trichostatin A (TSA), a specific HDAC inhibitor, on the inflammation in normal rat kidney epithelial cells (NRK-52E). Whether renal obstruction alters histone acetylation was also examined. The protein expression of HDAC 2 and 5 was increased by tumor necrosis factor (TNF)-α treatment, which was attenuated by TSA in cultured NRK-52E. The expression of p-ERK, phosoho-AKT, phosphor-stat 3, nuclear factor-κB (NF-κb), α-smooth muscle actin, fibronectin and tumor growth factor (TGF)-β, was also attenuated by TSA. siRNA of HDAC 2 and 5 also diminished the expression of p-ERK, p-P38 and NF-κb proteins. In another series of experiment using unilateral urinary tract obstruction (UUO) rat model, the protein expression of HDAC 2 was increased, while that of HDAC 5 was not affected. In addition, the expression of TGF-β, p-ERK, p-AKT, and p-stat 3 proteins was increased. It is suggested that a pharmacological HDAC inhibition may induce anti-inflammatory activity and anti-fibrotic effect by inactivation of HDAC and inflammatory markers.

Key Words: HDAC, TSA, 염증
HDAC, TSA, Inflammation