C12

Histone Deacetylase Inhibitor Prevents Renal Fibrosis and Epithelial-mesenchymal Transition in Diabetes through Acetylation of Histone and Non-histone Protein

Hunjoo Ha · Hyunjin Noh* · Ji Yeon Seo* · Mi Ra Yu* · Young Ok Kim*
Yeun Kum Lee · Hi Bahl Lee*

Ewha Womans University, College of Pharmacy,
Hyonam Kidney Laboratory, Soon Chun Hyang University, Seoul, Korea*

Histone deacetylase (HDAC) inhibitors induce growth arrest and apoptosis in a variety of human cancer cells and were recently found to have anti-fibrotic potential on mammalian cells. We examined the effect of an HDAC inhibitor trichostatin A (TSA) on renal fibrosis and epithelial-mesenchymal transition (EMT) in streptozotocin-induced diabetic rats. TSA significantly inhibited fibronectin and collagen I overexpression and reversed alpha-SMA and E-cadherin expression in diabetic kidney. In a normal rat kidney tubular epithelial cell line NRK52E, chromatin immunoprecipitation assay confirmed that TSA-induced hyperacetylation of nucleosomal histone was associated with downregulation of fibronectin and upregulation of E-cadherin transcription. TSA also increased acetylation of heat shock protein 90 in NRK52E cells and this was associated with depletion of Raf-1 and inhibition of TGF-beta 1-induced phosphorylation of extracellular-regulated protein kinases 1/2. Our data demonstrate that HDAC inhibitor can prevent renal fibrosis and EMT in diabetes through hyperacetylation of both histone and non-histone protein.