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Class I HDAC participates in renal interstitial fibrosis in uric acid nephropathy by regulating TGF-β/Smad signaling pathway

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Objectives: At present, studies have confirmed the potential therapeutic significance of epigenetic modification of histones in the pathogenesis of renal fibrosis. Histone deacetylase (HDAC) inhibitors are proven to be effective anti-fibrotic drugs. This study aims to investigate the effect of MS-275, a selective class I HDAC inhibitor, in renal interstitial fibrosis of hyperuricemia nephropathy.

Methods: To establish an in vitro model of hyperuricemia nephropathy, human renal tubular epithelial cells were cultured, and uric acid was added. MS-275 was used for further cell culture, after which HDAC1, E-cadherin, α-smooth muscle actin (α-SMA) were detected. The protein and mRNA expressions of HDAC1, E-cadherin, α-smooth muscle actin and fibronectin were detected. The expression of TbetaRI and Smad3 phosphorylation in each group were detected.

Results: The results showed that the expression of HDAC1 was significantly reduced in the MS-275 group. After hyperuric acid induction, in the hyperuric acid group, the expression of fibronectin and α-SMA was increased, and the expression of E-cadherin, was decreased, suggesting epithelial mesenchymal transdifferentiation. However, treatment with MS-275 inhibited these fibrotic reactions. Results showed that TbetaRI and p-smad-3 expression were increased after hyperuric acid induction. The results of further exploration of the regulatory pathway showed that after induction of hyperuric acid, the expression of TbetaRI and the expression of phosphorylated Smad-3 increased. However, MS-275 inhibited this change.

Conclusions: This study demonstrated that selective class I HDAC inhibitor can improve the mesenchymal transdifferentiation of renal tubular epithelial cells induced by high uric acid. We showed that MS-275 is involved in the regulation of the fibrosis mechanism through the TGF-β/Smad signaling pathway, suggesting that blocking class I HDAC may be an effective way for the treatment of renal interstitial fibrosis. This study will enrich the pathogenesis of hyperuricemia nephropathy and provide experimental basis for exploring new clinical diagnostic markers and treatment methods.