

Sirtuin-6 inhibits epithelial to mesenchymal transition via inactivation TGF- β /smad signaling *in vitro* and *in vivo*

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Sirtuin6 (SIRT6), a member of NAD⁺-dependent deacetylases that plays a key role in aging, cancer, and metabolism, has been shown to have anti-fibrosis function in heart and liver, but whether SIRT6 plays a role in idiopathic pulmonary fibrosis (IPF) has been poorly explored. Epithelial to mesenchymal cell transition (EMT), a process by which fully differentiated epithelial cells convert to a mesenchymal phenotype, has been involved in the pathogenesis of IPF. In the present study, SIRT6 expression was upregulated in both TGF- β 1-induced EMT in A549 cells and bleomycin (BLM)-induced EMT in mice. Forced expression of SIRT6 by adenovirus transfection of A549 cells significantly abrogated TGF- β 1-induced EMT-like phenotype and EMT-associated cell behavior. In A549 cells, TGF- β 1-induced activation of TGF- β 1/smads3 signaling and increase of smad3-snail1 interaction was ameliorated by overexpression of SIRT6. Upregulation of EMT related transcription factors by TGF- β 1 treatment was also restored by overexpression of SIRT6. Further *in vivo* studies showed that lung targeted delivery of SIRT6 using adeno-associated virus transfection blunted BLM-induced pulmonary EMT and fibrosis as evidenced by a reduction of epithelium undergoing EMT and collagen deposition. Our findings unravel a novel role of SIRT6 as a key modulator in the phenotypic conversion of epithelial to mesenchymal cells and suggest it as an attractive potential therapeutic target for IPF.

Biography

Xue Zhou obtained her BS degree in Environmental Sciences from Wuhan University in 2003, and got her PhD degree in Environmental Health Sciences from New York University in 2010. She is currently Associate Professor at School of Public Health, Huazhong University of Science and Technology. She has more than 20 publications in reputed journals.

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