SIRT6

Sirtuin-6 (SIRT6) is a stress responsive protein deacetylase and mono-ADP ribosyltransferase enzyme encoded by the SIRT6 gene.

SIRT6 functions in multiple molecular pathways related to aging, including DNA repair, telomere maintenance, glycolysis and inflammation.

SISIRT6 inhibits PCBP2 expression through deacetylating H3K9ac and SIRT6 acts as a tumor suppressor in human glioma [1].

Chen et al. showed that Sirtuin 6 (Sirt6), one of the Sirtuin family members which are widely studied in aging, DNA repair, metabolism, inflammation and cancer, was expressed in normal nasal mucosa using immunohistochemical staining and Western blot assay. Sirt6 expression levels were decreased in CRSwNP tissue. Sirt6 expression levels were modulated by small interfering RNA transfection in human nasal epithelial cells (HNE). We found that depletion of Sirt6 suppressed the number of human nasal epithelial cell cilia, and dramatically induced HMGB1 translocation from nucleus to cytoplasm in the HNE cells. Glycyrrhizic acid (GA) and glycyrrhetinic acid (GTA) are specific chemical compounds that may be isolated from the licorice plant. GTA has been shown to have anti-inflammatory and anti-allergic activity: it binds selectively to HMGB1 protein released extra-cellularly and inhibits its cytokine activities through a scavenger mechanism on the protein accumulation. In an in vitro study we used the 18-β-stereoisomer of GTA to enhance Sirt6 expression levels, inhibiting through this mechanism the translocation of HMGB1 protein from nucleus and reversing its extracellular accumulation stimulated by lipopolysaccharides. These findings reveal a previously unknown role for nasal mucosa steady-state conditions in the control of Sirt6 activity, and provide evidence for a relationship between HMGB1 and Sirt6 in CRSwNP, and promising benefits of glycyrrhetinic acid for CRSwNP patients [2].

In order to investigate the role which sirtuin-6 (SIRT6) plays in lumbar spinal epidural fibrosis (EF) and scar formation in vitro and in vivo, SIRT6 and transforming growth factor β (TGF-β) protein levels in the lumbar disc of patients were detected using western blotting in patients who had undergone a laminectomy. The results demonstrated that SIRT6 expression was significantly reduced in the lumbar discs of patients in whom an epidural scar had formed, but the expression pattern of TGF-β2 was much higher. Subsequently, a pcDNA-SIRT6 expression vector was constructed and transfected into the primary fibroblasts isolated from the epidural scars. Flow cytometric and MTT analyses indicated that overexpression of SIRT6 suppressed the proliferation of the fibroblasts, and TGF-β2 and interleukin-1α expression, as well as collagen type I (Col I) production. The results of bioinformatics and molecular biological analyses demonstarted that TGF-β2 was a target of microRNA-21 (miR-21) and SIRT6 overexpression suppressed the levels of TGF-β2 through promoting the expression of miR-21. Finally, by injecting the pcDNA-SIRT6 vector, it was possible to observe that SIRT6 suppressed EF and epidural scar formation in vivo. In conclusion, we noted that SIRT6 suppressed EF and epidural scar formation in vitro and in vivo. It was also noted that SIRT6 overexpression suppressed TGF-β2 levels by promoting the expression of miR-21 [3].

Feng et al. found that overexpression of SIRT6 using an adenovirus inhibited glioma cell growth and induced marked cell injury in two glioma cell lines (U87-MG and T98G). Fluorescent terminal

deoxyribonucleotidyl transferase (TdT)-mediated biotin-16-dUTP nick-end labelling (TUNEL) assay showed that SIRT6 overexpression induced obvious apoptosis in the T98G glioma cells. Immunoblotting and immunofluorescent staining demonstrated that SIRT6 overexpression promoted the mitochondrial-to-nuclear translocation of apoptosis-inducing factor (AIF), a potent apoptosis inducer. Moreover, we found that SIRT6 overexpression largely reduced oxidative stress and suppressed the activation of the JAK2/STAT3 signaling pathway in glioma cells. Finally, we showed that SIRT6 mRNA and protein levels in human glioblastoma multiforme tissues were significantly lower than the levels in peritumor tissues. In summary, our data suggest that SIRT6 suppresses glioma cell growth via induction of apoptosis, inhibition of oxidative stress and inhibition of the activation of the JAK2/STAT3 signaling pathway. These results indicate that SIRT6 may be a promising therapeutic target for glioma treatment [4].

1)
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