

## Sulforaphane Attenuates Fibrosis of Dystrophic Muscle in Mdx Mice via Nrf2-Mediated Inhibition of TGF- $\beta$ /Smad Signaling

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**Abstract :** Backgrounds: A few lines of evidence show that Sulforaphane (SFN) has anti-fibrosis effect in liver tissue via Nrf2-mediated inhibition of TGF- $\beta$ /Smad signaling. However, its effects on muscular dystrophic fibrosis remain unknown. This work was undertaken to evaluate the effects of SFN on fibrosis in dystrophic muscle. Methods: 3-month-old male mdx mice were treated with SFN by gavage (2 mg/kg body weight per day) for 3 months. Gastrocnemius, tibial anterior and triceps brachii muscles were collected for related analysis. Fibrosis in skeletal muscles was analyzed by Sirius red staining. Histology and morphology of skeletal muscles were investigated by H&E staining. Moreover, the expressions of Nrf2, NQO1, HO-1, and TGF- $\beta$ /Smad signaling pathway were detected by western blot, qRT-PCR, immunohistochemistry and immunofluorescence assays. Results: Our results demonstrated that SFN treatment significantly decreased and improved morphological features in mdx muscles. Moreover, SFN increased the expression of muscle phase II enzymes NQO1 and HO-1 and significantly decreased the expression of TGF- $\beta$ 1/p-smad2, p-smad3,  $\alpha$ -SMA, fibronectin, collagen I, PAI-1, and TIMP-1 in Nrf2 dependent manner. Additionally, SFN significantly decreased the expression of CD45 and TNF- $\alpha$ . Conclusions: Collectively, these results show that SFN can ameliorate muscle fibrosis in mdx mice by Nrf2-induced inhibition of TGF- $\beta$ /Smad signaling pathway, which indicate Nrf2 may be useful for the treatment of muscular dystrophy.

**Keywords :** sulforaphane, Nrf2, TGF- $\beta$ /smad signaling, duchenne muscular dystrophy, fibrosis

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