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**Sirtuin-1 protects hair follicle stem cells from TNF $\alpha$ -mediated inflammatory stress via activating the MAPK-ERK-Mfn2 pathway**

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**Abstract**

**Objective:**

Stem cell transplantation is a promising tool to treat burn injuries. However, the inflammatory microenvironment in damaged skin limits the efficiency of stem cell-based therapy via poorly understood mechanisms. The aim of our study is to explore the contribution and mechanism of Sirtuin-1 (Sirt1) in TNF $\alpha$ -mediated inflammatory stress in hair follicle stem cells (HFSCs).

**Methods:**

Cellular viability was determined using the MTT assay, TUNEL staining, western blot analysis and LDH release assay. Adenovirus-loaded Sirt1 was transduced into HFSCs to overexpress Sirt1 in the presence of TNF $\alpha$ . Mitochondrial function was determined using JC-1 staining, mitochondrial ROS staining, immunofluorescence staining and western blotting.

**Results:**

Sirt1 was downregulated in response to the TNF $\alpha$  treatment. Additionally, TNF $\alpha$  stress reduced the viability, mobility and proliferation of HFSCs, and these effects were reversed by the overexpression of Sirt1. At the molecular level, Sirt1 overexpression attenuated TNF $\alpha$ -mediated mitochondrial damage, as evidenced by increased mitochondrial energy metabolism, decreased mitochondrial ROS generation, stabilized mitochondrial potential and blockage of the mitochondrial apoptotic pathway. Furthermore, Sirt1 modulated mitochondrial homeostasis by activating the MAPK-ERK-Mfn2 axis; inhibition of this pathway abrogated the protective effects of Sirt1 on HFSC survival, migration and proliferation.

**Significance**

Based on our results, the inflammatory stress-mediated HFSC injury may be associated with a decrease in Sirt1 expression and subsequent mitochondrial dysfunction. Accordingly,

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