

PIGMENTATION

## FOLIC ACID PROTECTS MELANOCYTE AGAINST OXIDATIVE DAMAGE VIA INHIBITION OF KEAP1 AND ACTIVATION OF NRF2

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**Introduction:** Vitiligo is a disfiguring skin disorder characterized by the loss of functional melanocytes. Its pathogenesis is complicated and oxidative stress plays a critical role in the development of vitiligo. Thus, antioxidant therapy is a promising therapeutic strategy to prevent or even reverse the progression of depigmentation. As a common antioxidant, folic acid has been used in the treatment of various oxidative stress related diseases, however, whether it has therapeutic effect on vitiligo is unclear.

**Objective:** To investigate whether folic acid could protect human melanocyte against oxidative damage and to elucidate the underlying molecular mechanism involved.

**Materials and Methods:** PIG1 from the normal primary human melanocytes were cultured in Medium 254. 800µM H<sub>2</sub>O<sub>2</sub> was chosen to as the stimuli to induce cytotoxic effect on PIG1. CCK8 assay was used to estimate the cell survival rates. Flow cytometry was used to measure the intracellular ROS level and apoptosis rates. The nuclear translocation of Nrf2 was tested by immunofluorescence. Western blot and qRT-PCR were used to analyze the mRNA and protein expression levels of Keap1, Nrf2, HO-1, SOD2 and NQO1.

**Results:** In this study, we initially found that folic acid was able to ameliorate H<sub>2</sub>O<sub>2</sub>-induced oxidative damage in human melanocytes. In parallel, folic acid lessened the accumulation of intracellular ROS by potentiating the activity of antioxidant enzymes. Furthermore, we showed that folic acid protected melanocyte against oxidative stress by activating Nrf2 and its downstream genes HO-1, SOD2 and NQO1, and interfered with Nrf2 diminished the protection of folic acid against H<sub>2</sub>O<sub>2</sub>-induced apoptosis. At last, we showed that the down-regulation of Keap1 contributed to activation of Nrf2 induced by folic acid.

**Conclusions:** This study demonstrated that folic acid could protect melanocyte from oxidative damage and showed its therapeutic potential in the treatment of vitiligo.