DERMATOPATHOLOGY

SIRT3-DEPENDENT MITOCHONDRIAL DYNAMIC REMODELING CONTRIBUTES TO OXIDATIVE STRESS-INDUCED MELANOCYTE DEGENERATION IN VITILIGO

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Introduction: Mitochondrial dysregulation has recently been implicated in oxidative stress-induced melanocytes destruction in vitiligo. However, the specific molecular mechanism involved in this process is merely investigated.

Objective: To investigate whether SIRT3 play an important role in vitiligo melanocyte degeneration by regulating mitochondrial dynamic.

Materials and Methods: We initially employed H2O2 treatment to induce oxidative stress in both normal human melanocyte cell line PIG1 and vitiligo melanocyte cell line PIG3V, and then testified the alterations of SIRT3 expression and activity in vitro. In addition, the expression and activity of SIRT3 in melanocyte of vitiligo lesional skin were examined in vivo. Subsequently, the cell apoptosis, functional status of mitochondria and mitochondria fusion and fission after SIRT3 knockdown in PIG1 and SIRT3 overexpression in PIG3V were analyzed. Moreover, we analyzed the upstream regulatory mechanism of SIRT3 expression and activity in vitiligo.

Results: We firstly found that both the expression and activity of SIRT3 were significantly impaired in PIG3V and melanocytes in vitiligo skin lesions, compared with normal controls. Mechanistically, SIRT3 deacetylated Optic atrophy 1 (OPA1) to regulate mitochondrial dynamic, coordinating mitochondrial dysfunction and excessive cytochrome c release by facilitating mitochondrial fission, which eventually resulted in melanocyte apoptosis under oxidative stress. In addition, it was potentiated carbonylation and dampened transcriptional activation of Peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC1α) that accounted for oxidative stress-induced SIRT3 dysregulation in vitiligo melanocyte.

Conclusions: Taken together, our results demonstrate that SIRT3-dependent mitochondrial dynamic remodeling contributes to oxidative-stress induced melanocyte degeneration in

vitiligo.