

# Elucidation of the novel regulation mechanism in autophagy that contributes to the prevention of skin aging

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We have shown that skin tissue aging is caused by normalized chronic skin stress, such as exposure of the skin to ultraviolet light in sunlight and repair (wound healing) of the skin from abrasions and lacerations. Ultraviolet rays (UV) from sunlight exposure can cause cell apoptosis in the skin epidermis, resulting in the disruption of the barrier. Previously, we have demonstrated that BNIP3 stimulates autophagy in epidermal keratinocytes and has a protective effect in these cells upon UVB irradiation. In this study, we found that the accumulation of reactive oxygen species (ROS) by UVB irradiation was sufficient to trigger the activation of JNK and ERK mitogen-activated protein kinase (MAPK) in human primary epidermal keratinocytes. In turn, activated JNK and ERK MAPK mediated the upregulation of BNIP3 expression. Treatment with an antioxidant reagent or a specific inhibitor of MAPK, U0126, and a JNK inhibitor significantly attenuated the expression of BNIP3 triggered by UVB, followed by the induction of cell death by apoptosis. Furthermore, UVB-induced apoptosis was significantly stimulated by chloroquine or bafilomycin A1, an inhibitor of autophagy. Moreover, BNIP3 was required for the degradation of dysfunctional mitochondria upon UVB irradiation. These data clearly indicated that BNIP3-induced autophagy, which occurs via UVB-generated ROS-mediated JNK and ERK MAPK activation, has a crucial role in the protection of the skin epidermis against UVB irradiation.