UVB stimulates TGase I expression via NF-κB activation which is attenuated by astaxanthin through inactivation of MSK1 in human keratinocytes

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Introduction

Exposure of ultraviolet radiation to the skin causes inflammation and subsequent hyperkeratosis in the epidermis. The hyperkeratotic skin is characterized by roughened and thinned skin surface which is predominantly based on the formation of hardened and thickened cornified cell envelopes. Transglutaminase (TGase) I and III have been documented to play essential roles in epidermal keratinization. Recent study with TGase-III knockout mice demonstrated that these animals display no obvious defect in skin keratinization (1) suggesting that TGase-III is of unique functional importance especially in hair keratinization, while TGase-I is mainly responsible for epidermal keratinization. Although it seems likely that UVB-induced thinned and roughened skin results from thickened cornified cell envelopes which are associated with a possible accentuated expression of TGase-I, little is known about mechanisms involved in UVB-induced altered epidermal keratinization. In this study, we examined effects of UVB irradiation on protein expression of TGase-I and elucidated their stress signaling mechanisms involved in cultured human keratinocytes.

Results

We then examined the gene and protein expression of TGase-I in cultured human keratinocytes after a single UVB exposure. UVB exposure significantly increased the expression of TGase-I at both mRNA and protein levels, respectively (Fig. 1). It is known that UVB exposure to human keratinocytes activates epidermal keratinocytes via signaling pathways including p38 MAPK, JNK, ERK, and PKC-δ (2). We examined the effects of the signaling pathway on the upregulated expression of TGase-I after UVB exposure (3). TNF-α, a pro-inflammatory cytokine, was used as the stimulus for the upregulated expression of TGase-I after UVB exposure (3). We determined that the expression of TGase-I was significantly increased in UVB-exposed keratinocytes (Fig. 2 and 3). UVB exposure significantly increased the gene and protein expression of TGase-I in a dose-dependent manner (Fig. 4). UVB exposure increased the expression of TGase-I in a time-dependent manner (Fig. 5). UVB exposure increased the expression of TGase-I in a time-dependent manner (Fig. 6). UVB exposure increased the expression of TGase-I in a time-dependent manner (Fig. 7).

Conclusion

As depicted in Fig. 9, UVB-stimulated TGase-I expression is mainly mediated via NF-κB pathway during which post-irradiation treatment with AX inhibits MSK1 phosphorylation, resulting in attenuated phosphorylation of NF-κB p65, which in turn leads to down-regulation of UVB-enhanced expression of TGase-I in a ROS depletion-independent manner.

References