〈シンポジウム〉
（抗老化化粧品のストラテジー―シミ対策化粧品のストラテジー）

内因性抗酸化物質誘導によるメラニン合成の抑制

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Suppression of Melanogenesis by Induction of Endogenous Intracellular Antioxidant in Human Melanocytes

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Abstract

Ultraviolet (UV)-induced melanogenesis is caused by several types of melanogen, which are released in skin following UV radiation. Among them, nitric oxide (NO) has recently been shown to function as a potent mediator. Metallothionein (MT), which functions in metal homeostasis and metal detoxification, also acts as an intracellular antioxidant that has been reported to scavenge NO. We investigated the existence and induction of MT in melanocytes, and its inhibitory effect on NO-induced melanogenesis. MT expression was detected in melanocytes, however, at a lower level than in keratinocytes and fibroblasts, and its induction was possible with the addition of zinc chloride and dexamethasone. Further, an NO-stimulated increase of tyrosinase activity in melanocytes was remarkably suppressed when MT was induced prior to NO stimulation, and the same suppressive effect of melanogenesis was observed when α-melanocyte stimulating hormone and endothelin-1 were used as stimulators, during which the degree of suppression corresponded to the level of induced MT protein. Next, to study the mechanism of melanogenesis inhibition by MT, its effects on tyrosinase expression and the direct inhibition of tyrosinase were also examined. Changes in tyrosinase protein expression were not observed in melanocytes, even when MT was induced, while the suppressive effect of MT induction toward increased tyrosinase activity was neutralized by the addition of anti-MT antibody to the melanosome fraction. Further, purified human MT showed an ability to inhibit tyrosinase activity in melanocytes. Our results demonstrated that MT induction may be effective to suppress melanogenesis stimulated by NO as well as other melanogens, and this suppressive effect might be due to a direct inhibition of tyrosinase activity by the induced MT.

Key words: metallothionein, intracellular antioxidant, tyrosinase, melanogenesis.