日本香粧品学会誌　Vol. 31, No. 4, pp. 318–324 (2007)

〈シンポジウム II〉『環境と皮膚』

体内環境と皮膚　女性ホルモンと皮膚

エストロゲンの皮膚老化防止作用

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Prevention of Skin Aging by Estrogen

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Abstract

Background: Skin aging is accelerated in postmenopausal women. Topical or systemic treatment with estrogen may prevent skin aging, which is not sufficiently evidenced by *in vitro* investigative data. We aimed to obtain *in vitro* evidence in adult skin keratinocytes that estrogen prevents skin atrophy, delayed wound healing, and impaired resistance against apoptosis, associated with skin aging. **Results 1:** Stimulatory effects of estrogen on the growth of keratinocytes. 17β-Estradiol (E2) stimulates the growth of keratinocytes by inducing cyclin D2 expression *via* CREB phosphorylation by protein kinase A, dependently on cAMP. These effects of E2 may be mediated via cell surface GPR30. **Results 2:** Inhibitory effects of E2 on oxidative stress-induced apoptosis. E2 enhances Bcl-2 expression and counteracts H_2O_2-induced apoptosis by phosphorylating CREB *via* membrane GPR30-mediated cAMP/protein kinase A pathway in keratinocytes. **Results 3:** Stimulatory effects of estrogen on the production of growth factors to enhance wound healing. E2 enhances GM-CSF production via activation of AP-1 and also enhances HB-EGF production *via* activation of AP-1 and Sp1. These effects of E2 may be dependent on unknown membrane G-protein-coupled receptors, and on the receptor-mediated signaling pathway, phosphatidylinositol-specific phospholipase C/protein kinase Cα/mitogen-activated protein kinase kinase/extracellular signal-regulated kinase. **Conclusion:** E2 may prevent or reverse age-associated epidermal thinning and delayed wound re-epithelialization by inducing cyclin D2, GM-CSF, and HB-EGF. E2 may normalize the impaired resistance against oxidative stress in aged skin *via* Bcl-2 induction.

Key words: estrogen, cyclin D2, GM-CSF, HB-EGF, Bcl-2.