

〈教育セミナー〉

表皮機能の新展開

表皮カスパーゼの機能とその応用

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Role of Caspase-14 in DNA Degradation and Its Application to Cosmetic Products

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Abstract

Caspase-14 is expressed dominantly in the epidermis and its activation occurs at the onset of cornified cell formation. However, its physiological roles are still obscure. We have purified human caspase-14 from cornified cells and determined cleavage sites for the activation. Based on this information, we prepared constitutively active caspase-14 by reverse genetics. In addition, we developed cleavage-site directed antibody (D146 Ab), which recognized only the active caspase-14. Using these tools, we tried to analyze physiological functions of caspase-14. We constructed two kinds of active caspase-14 expression vectors, and introduced into keratinocyte. When active caspase-14 was expressed in a growing phase of cultured keratinocytes, it did not show any detectable changes. On the other hand, when keratinocytes were cultured until confluency and further differentiated by addition of calcium, active caspase-14 emerged in the transfected cells. Interestingly only those cells stained with D146 Ab were found to be TUNEL positive, indicating that DNA degradation occurred in active caspase-14 expressing keratinocytes only after the differentiation. We also found that serpin b3 suppressed caspase-14 activity. Serpin b3 is strongly up-regulated in rough skin as well as diseased skin with parakeratosis, whereas active caspase-14 was hardly detectable in such skins. We developed 1-Piperidine Propionic acid (1PP), which effectively suppressed expression of serpin b3. Application of 1 PP on human rough skin significantly improved skin condition. Collectively our results suggest that caspase-14 plays an important role in the nuclear digestion during the keratinocyte terminal differentiation and serpin b3 inhibits this reaction. Suppression of serpin b3 is beneficial for the improvement of skin condition.

Key words: keratinuzation, caspase-14, squamous cell carcinoma antigen 1 (SCCA1), denucleation, apoptosis.