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(角層研究の最前線)

角化過程におけるタンパク質の脱イミノ化

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Protein Deimination during Epidermal Cornification

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Abstract

Citrulline-containing proteins are present in the cornified layers of mammalian epidermis. Such citrulline residues are formed by the enzymatic deimination of arginine residues by peptidylarginine deiminase. Deiminated proteins in the cornified layers of man and rodents were analyzed by chemical modification of citrulline residues followed by probing with a monospecific antibody to chemically modified citrulline. Major deiminated proteins were found to be partially degraded/disulfide-cross-linked keratin K 1. At least two preferred acting sites of peptidylarginine deiminase were identified in mouse K 1, one in the V 1 and the other in the V 2 subdomains. These subdomains of K 1 are markedly enriched with glycine residues and contain only few charged amino acid residues. Affinity-purified polyclonal antibodies against a synthetic citrulline containing peptide corresponding to the deiminated sequence in the V 2 subdomain stained the cornified layers of normal human epidermis intensely. The antibodies also stained the psoriatic uninvolved epidermis, while negligible staining was observed in the involved epidermis showing hyperproliferation. Immunoblotting analyses with both anti-modified citrulline and anti-deiminated K 1 peptide antibodies also showed negligible deimination of K 1 in the involved epidermis. These data suggest that deimination of the V subdomains of K 1 may have important roles in the formation of functionally mature cornified layers.

Key words: cornification, protein deimination, peptidylarginine deiminase, keratins, psoriasis.