Synopsis of Original Research Paper

Immunoelectron microscopic analysis of stratum corneum corneodesmosomal degradation process

Akemi Ishida-Yamamoto

Department of Dermatology, Asahikawa Medical College

The epidermal stratum corneum provides a critical permeability barrier between the body and the environment. Our skin establishes a basket-weave like appearance in the cornified layers. The cells there are attached only at the cell periphery by corneodesmosomes which are modified desmosomes. These corneodesmosomes spare wide spaces at the central (non-peripheral) area for the lipid layers to form a continuous permeability barrier. To establish this structure while maintaining steady state thickness of the stratum corneum, degradation process of corneodesmosomes must be under strict control. Uncontrolled activation of proteases involved in this process could lead to severe skin phenotypes such as those seen in Netherton syndrome, a severe autosomal recessive disease caused by gene mutations in *SPINK5* which encodes a protease inhibitor LEKTI. Our understanding of the mechanisms which control the degradation of corneodesmosomes is limited. For example, it is unknown why corneodesmosomes persist only at the cell periphery in fully developed corneocytes. To explore this, we analyzed the precise distribution of two major components of the extracellular part of corneodesmosomes, corneodesmosin (CDSN), and desmoglein 1 (DSG1) in normal adult human epidermis. Distributions of corneodesmosomal components were analyzed using montage pictures of post-embedding immunoelectron microscopy performed on the back skin samples. The upper and lower cell surface of corneocytes from the first to the fifth layers were divided into the central half and the peripheral half, and colloidal gold particles associated with corneodesmosomes were counted and distribution densities per membrane length were calculated. Marked decrease in label densities was noted on the central areas of the upper cell surface from the second deepest layer for CDSN and DSG1. Central labeling was virtually lost by the fifth layer, whereas peripheral labeling densities were relatively high up to the fifth layer. The present study clearly demonstrated that the degradation of two major corneodesmosomal components, CDNS, and DSG1 is initiated from the central areas of corneocytes soon after the cells move into the cornified layer. This suggests that the molecular basis for the selective degradation resides in the deepest layer of the stratum corneum.