

Molecular mechanisms of epidermal cornification during skin development

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The skin epidermis serves as a protective barrier that shelters the body from environmental insults and dehydration. Defects in skin barrier result in various forms of skin inflammatory diseases including psoriasis and atopic dermatitis, the most common diseases in the human population. Therefore, understanding molecular basis of skin barrier formation has important implications for establishing effective therapeutic strategies for such skin disorders.

One of the key aspects of terminal differentiation of epidermal keratinocytes is dynamic cellular remodeling, in which various filamentous proteins and lipids are cross-linked to form rigid bundles and cell organelles including nucleus and mitochondria are eliminated to induce cell death. Although each of these processes has been extensively studied, the molecular mechanism that coordinates these events to achieve the dramatic cellular remodeling is poorly understood. One candidate mechanism that enables such quick remodeling might be autophagy, a process that promotes cellular self-cannibalization. Autophagy is an intracellular bulk degradation system that delivers cytoplasmic organelles and proteins to the lysosome, where they are degraded to be quickly eliminated from the cell. Accumulating evidence indicates that autophagy has been implicated in wide range of the cellular remodeling that occurs during organogenesis, thereby enabling cells to rapidly differentiate or change their fate in order to acquire new functions. Therefore, we hypothesize that the induction of autophagy may play an important role in promoting epidermal terminal differentiation. In this study, we aim at obtaining an experimental proof for the involvement of autophagy in the regulation of epidermal terminal differentiation and barrier formation. Our study will uncover a novel role of autophagy in regulating epidermal barrier formation and provide new insights into development of novel therapeutic strategies for skin disorders.