Synopsis of Original Research Paper

Epidermal peptides regulate barrier formation of the skin

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The defense system of the skin consists of three layers: the barrier, innate immunity, and acquired immunity. The barrier is the homeostatic defense in the outermost parts of the organism. In the body surface, the epithelial–immune microenvironment (EIME) governs the induction and direction of biological defense. Epidermal keratinocytes organize barrier system of the skin. However, the precise role for keratinocytes and the molecular mechanisms that control barrier formation and induction of innate and acquired immunity against a variety of external factors remain unknown. To explore new mechanisms in the regulation of defense system of the skin, we performed transcriptome analysis of the skin of four different animal models of atopic dermatitis. We identified only one common orphan gene, *C10orf99* (human)/*2610528A11Rik* (mouse orthologue), of which expression is highly induced in the epidermis. We found that C10orf99 peptide, a product of the orphan gene, regulates late differentiation of keratinocytes. In addition, gene expression levels of inflammatory mediators are higher in normal human epidermal keratinocytes transfected with *2610528A11Rik*-expressing plasmids than those transfected with empty plasmids. Furthermore, the results of pilot studies suggest that disulfide bonds in the N-terminus rather than conserved regions in the C-terminus in a C10orf99 peptide are essential for its molecular function in the induction of C10orf99-response genes. Our results propose that when the homeostasis of skin defense is breached by external factors, cellular stress induces the expression of C10orf99 peptide, which may be involved in the induction of the defense system of the skin and inflammation at the affected site. Thus, C10orf99 peptide is a potential therapeutic target, as its production is a common event in inflammatory skin diseases regardless of the type of inflammation.