Synopsis of Original Research Paper

The clarification of the mechanism of skin lesions in essential fatty acid deficiency states

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Essential fatty acids (EFA) and their downstream long-chain polyunsaturated fatty acid (PUFA) are localized to cell membranes as phospholipid esters and play critical roles in regulating membrane structure, dynamics, and permeability. It is reported that EFA deficiency state causes the disruption of the skin barrier. Therefore, changes of fatty acids during EFA deficiency might participate in pathologic changes in the skin. In EFA deficiency animals, 5,8,11-eicosatrienoic acid (Mead acid, C20:3n-9) is endogenously synthesized from oleic acid, and is detected in the plasma and tissues. Mead acid is thought to be used in biological membranes as a substitute for other PUFAs. In this study, we investigated the change of Mead acid in inflammation and the influence of the decrease of Mead acid on the skin barrier function during EFAD state.

To study change of fatty acid metabolism in the skin by inflammation, we investigated the change of Mead acid in human keratinocyte HaCaT cells of EFAD state. The mRNA of inflammatory cytokine, such as IL-1β and IL-6 were significantly increased by the stimulation of TNF-α. The mRNA of filaggrin and involucrin, which proteins correlate with barrier function, were decreased by TNF-α, suggesting that the barrier function was disrupted in HaCaT cells by inflammatory. The Mead acid composition in the cells with treatment of TNF-α was reduced 33% of the level in control cells, but other fatty acid compositions did not changed significantly. These results suggesteed that Mead acid synthesis was suppressed in EFAD keratinocytes by inflammation.

Next, we examined the influence of the inhibition of Mead acid synthesis on barrier function in human keratinocyte HaCaT cells. The level of Mead acid was significantly decreased by the addition of 50 μM Δ6 desaturase inhibitor sc26196. The mRNA level of filaggrin and involucrin was significantly decreased by the addition of sc26196. Moreover, we investigated the influence of Mead acid reduction on inflammatory response and ER stress. Although the IL-1β and IL-6 mRNA were unchanged by treatment of sc26196, the mRNA levels of ER stress marker genes, such as CHOP and GRP78 were significantly increased. These results suggested the possibility that inhibition of Mead acid synthesis induced the skin barrier dysfunction via up-regulation of ER stress.