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皮膚に及ぼす食の免疫学的影響の理解と応用

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Diet-Mediated Immune Regulation in the Skin

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Abstract

Immune system is regulated by not only genetic background but also environmental factors including diets. Accumulating evidence indicates that ω 3 fatty acids exert anti-inflammatory properties and recent advances in the metabolome analysis revealed that fatty acid metabolism plays a key role in the regulation of skin allergic inflammation. We found that fatty acid metabolism varies among tissues. For example, 17,18-epoxyeicosatetraenoic acid (17,18-EpETE) and 12-hydroxyeicosapentaenoic acid (12-HEPE) were generated from eicosapentaenoic acid in the gut and skin, respectively when mice were maintained on a diet containing linseed oil which is high in ω 3 α -linolenic acid. In addition, both 17,18-EpETE and 12-HEPE ameliorated contact hypersensitivity by inhibiting neutrophil infiltration through different mechanisms. 17,18-EpETE acted directly on neutrophils to block pseudopod formation in a GPR40-dependent manner, while 12-HEPE acted on keratinocytes to suppress chemokine production for neutrophil recruitment in an RXR α -dependent manner. We further found that maternal intake of linseed oil ameliorated skin allergic inflammation in their pups, which was mediated by breast milk containing 14-hydroxydocosapentaenoic acid (14-HDPA). In pups, 14-HDPA induced the expression of TNF super family, TRAIL, on plasmacytoid dendritic cells and consequently inhibited inflammatory cytokine production from T cells. As another example, when mice were maintained on a diet containing coconut oil which has little amounts of essential fatty acids, mead acid was uniquely produced from oleic acid, which in turn ameliorated contact hypersensitivity through the inhibition of neutrophil pseudopod formation, leukotriene B₄ production and increment of vascular permeability. These results demonstrate that the fatty acid composition and metabolism are a critical determinant of beneficial effects of dietary lipids on the control of skin allergic inflammation.

Key words: dietary lipids, essential fatty acids, metabolism, dermatitis, allergy.