Synopsis of Original Research Paper

Research for the mechanism of cellular response to ceramides that show skin protection

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It is well known that ceramide forms corneocyte lipid-bound envelop in skin to protect from external stimuli. In order to clarify the other physiological role of ceramide, neurotrophic factor biosynthesis and secretion from Swiss 3T3 fibroblasts were examined. C-2 ceramide and C-6 ceramide potently augmented the secretion of neurotrophic factors from 3T3 cells, determined by the differentiation of PC-12 cells when they were cultured under the conditioned medium of 3T3 cells with the ceramides. Sphingomyelinase and phosphatidylcholine-specific phospholipase C, which produce endogenous ceramides, also elicited the secretion of neurotrophic factors from 3T3 cells. Stimulation of cannabinoid receptors is known to produce ceramide through an activation of sphingomyelinase. 3T3 cells express CB1 and CB2 receptors, and the stimulation of the receptors in the cells by 2-arachidonylglycerol resulted in the secretion of neurotrophic factors. Sphingomyelinase and phosphatidylcholine-specific phospholipase C stimulated the NGF and IL-6 mRNA expressions, which were inhibited by GF109203X, a protein kinase C inhibitor. In addition, C2-ceramide activated the phosphorylation of MAPK/ERK, p38 MAPK and JNK. These results suggest that ceramide may have neurogenerative and/or neuroprotective activity in peripheral tissues including skin by a mediation of the secretion of neurotrophic factors. Therefore, the drugs, which activate ceramide biosynthesis, inhibit cramide degradation, or activate ceramide-mediated cellular signaling pathway, may be useful for neurotrophic factor secretion. The neurotrophic factor secretion would contribute to the protection of skin from external stimuli by forming the functional systems of the tissues.