

(第3号様式)

学 位 論 文 要 旨

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論 文 名 ヘパリン類似物質の抗炎症作用の解析

学位論文要旨

Epidermal keratinocytes initiate skin inflammation by activating immune cells. The skin barrier is disrupted in atopic dermatitis (AD) and epidermal keratinocytes can be exposed to environmental stimuli, such as house dust mite (HDM) allergens. We showed previously that HDM allergens activate the NLRP3 inflammasome of keratinocytes, thereby releasing pro-inflammatory cytokines. Because heparinoid is an effective moisturizer for atopic dry skin, we considered that it acts not only as a moisturizer but also as a suppressant of the triggers of skin inflammation (for example HDM). We tested this hypothesis in cultured normal human keratinocytes pre-treated with heparinoid and then stimulated with HDM allergens. HDM allergen-induced interleukin (IL)-1 β release from keratinocytes was inhibited significantly by heparinoid pretreatment without affecting cell viability. However, heparinoid did not affect caspase-1 release, suggesting that heparinoid did not affect HDM allergen-induced inflammasome activation. Heparinoid treatment not only decreased intracellular levels of pro-IL-1 β , but also suppressed IL-1 β messenger RNA (mRNA) expression in

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keratinocytes. Among the intracellular signaling pathways, the activation of extracellular signal-regulated kinase and p38 pathways, which are required for IL-1 β expression in keratinocytes, was inhibited by heparinoid treatment. The inhibitory effect of heparinoid on IL-1 β mRNA expression was also confirmed with living skin equivalents. Our results demonstrated that heparinoid suppresses the initiation of keratinocyte-mediated skin inflammation.

キーワード (3 ~ 5)	Heparinoid IL-1 β ERK p38 atopic dermatitis
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