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【タイトル】

皮膚常在細胞から産生されるIL-36alphaは炎症局所の活性化を引き起こしイミキモード誘発幹線様皮膚炎の発症に重要な役割を果たす

【発表論文】

IL-36α from Skin-Resident Cells Plays an Important Role in the Pathogenesis of Imiquimod-Induced Psoriasiform Dermatitis by Forming a Local Autoamplification Loop

【著者】

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【発表雑誌】

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【研究の要旨】

In this study, we found that *Il1f6*–/– mice developed milder psoriasiform dermatitis upon treatment with imiquimod, a ligand for TLR ligand 7 (TLR7) and TLR8, whereas *Il1f6*–/– mice showed similar susceptibility to dextran sodium sulfate–induced colitis to wild-type mice. These effects were observed in both cohoused and separately housed conditions, and antibiotic treatment did not cancel the resistance of *Il1f6*–/– mice to imiquimod-induced dermatitis. Bone marrow (BM) cell transfer revealed that IL-36α expression in skin-resident cells is important for the pathogenesis of dermatitis in these mice. Following stimulation with IL-36α, the expression of *Il1f6* and *Il1f9* (IL-36γ), but not *Il1f8* (IL-36β), was enhanced in murine BM-derived Langerhans cells (BMLCs) and murine primary keratinocytes but not in fibroblasts from mice. Upon stimulation with agonistic ligands of TLRs and C-type lectin receptors (CLRs), *Il1f6* expression was induced in BMLCs and BM-derived dendritic cells. Furthermore, IL-36α stimulation resulted in significantly increased

gene expression of psoriasis-associated Th17-related cytokines and chemokines such as IL-1α, IL-1β, IL-23, CXCL1, and CXCL2 in BMLCs and fibroblasts, and IL-1α, IL-1β, IL-17C, and CXCL2 in keratinocytes. Collectively, these results suggest that TLR/CLR signaling–induced IL-36α plays an important role for the development of psoriasiform dermatitis by enhancing Th17-related cytokine/chemokine production in skin-resident cells via a local autoamplification loop.