【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.