Pruritogenesis in a rat model of atopic dermatitis; Toll-like receptor-mediated activation of mast cells

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Chronic pruritus of atopic dermatitis (AD) causes the patients to scratch the affected skin and thereby deteriorates the disease. Thus, relieving pruritus has been accepted as an optimal management of AD. In a series of our studies examining the pathophysiological mechanisms underlying AD using a rat model, we have found that enhanced responses of DRG neurons to serotonin released from mast cells contribute to persistent pruritus of AD. Mast cells express a variety of Toll-like receptors (TLR) allowing the immune cells to recognize pathogen-associated molecules. Some of TLR ligands are endogenous molecules which are released from damaged or inflamed tissues. In the present study, we examined whether TLR signaling on the mast cells plays a role in chronic pruritus of atopic dermatitis. Bone marrow mast cells (BMMC) were obtained from adult male rats and used for RT-PCR, quantitative real-time RT PCR and serotonin ELISA. Of total 12 TLRs (TLR1 to TLR12) checked in the present study, 10 TLRs (TLR1 to TLR10) were expressed by BMMC of which mRNA expression of pro-inflammatory cytokines (IL-1β, TNF-α, IL-4, IL-5, IL-6 and IL-13) were significantly increased when stimulated by TLR ligands, such as LTA, LPS, polyI:C (pIC), and extract of necrotic neuronal cells. In addition, TLR-mediated activation of BMMC led to increase of serotonin content in the culture medium. Our results indicate that Toll-like receptor mediated activation of mast cell drives chronic pruritus by secreting serotonin and pro-inflammatory cytokines