Synopsis of Original Research Paper

# Regulation of skin inflammation with IL-33 decoy receptor

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Interleukin (IL)-33 is a member of the IL-1 cytokine family. Epithelial cells and vascular endothelial cells produce IL-33 in the nucleus and release it by stress, injury, or necrosis. IL-33 induces the production of Th2-associated cytokines via its receptor, ST2L on type 2 innate lymphoid cells, Th2 cells, and mast cells. Therefore, IL-33/ST2L signaling may contribute to development of allergic diseases such as asthma and atopic dermatitis. The ST2 gene produces a soluble secreted form, soluble ST2, in addition to a transmembrane form, ST2L, by alternative splicing. Soluble ST2 consists of only extracellular domain of ST2L. In previous study, we found that soluble ST2 acted as an IL-33 decoy receptor. Soluble ST2 specifically binds to free IL-33 and inhibits a binding activity of IL-33 for its receptor on target cells. To explore the function of soluble ST2 in vivo, we established that a transgenic mouse that constitutively express murine soluble ST2 cDNA under CAG promoter (ST2-Tg mouse). Here, we show that soluble ST2 is a critical repressor for skin inflammation in a murine model of house dust mite (HDM)-induced atopic dermatitis. Skin inflammation of ST2-Tg mice exhibited a lower development compared to that of wild-type mice. Levels of IL-13, total IgE, and HDM-specific IgE in sera were reduced in ST2-Tg mice. Furthermore, we examined HDM-specific response of lymph node cells in vitro. Analysis of cytokines in culture supernatants revealed the reduction of IL-4, IL-5, and IL-13 productions in ST2-Tg mice. We also applied ST2-Tg mice to hapten-induced contact hypersensitivity (CHS) model with fluorescein isothiocyanate (FITC). Migration of skin dendritic cells and ear swelling developed normally in ST2-Tg mice. These results suggest that soluble ST2 contributes to suppressions of skin inflammation and Th2-type immune response in atopic dermatitis. Therefore, soluble ST2 is a potential therapeutic agent for allergic diseases such as atopic dermatitis.