Synopsis of Original Research Paper

Role of the IL-17 family cytokines in the development of contact hypersensitivity

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Interleukin-25 (also called IL-17E), which is a member of the IL-17 family of cytokines, is preferentially produced by epithelial cells and immune cells such as macrophages, mast cells, basophils, eosinophils and T cells. IL-25 treatment in mice induces Th2-cytokine production, resulting in the development of eosinophilia in the lungs and guts and increased serum IgG1 and IgE. Moreover, IL-25 can induce Th2 cell differentiation and activation, suggesting to the involvement of Th2-type immune responses such as nematode infection and allergic disorders. Indeed, it was shown that IL-25 is crucial for host defense against *Trichuris muris* and *Nippostrongylus brasiliensis* using IL-25-deficient mice, and for the development of allergic airway inflammation using mice treated with anti-IL-25 neutralizing Ab. On the other hand, IL-25 can inhibit Th17 cell differentiation dependently of IL-13, contributing to the suppression of Th17-mediated autoimmune diseases. Therefore, these observations suggest that IL-25 is considered to be a potent enhancer of the Th2-type immunity, but a suppressor of the Th1 and Th17-type immunity.

Contact hypersensitivity (CHS) is classically considered to be a IFN-γ-producing Th1 and Tc1 cell-mediated cutaneous allergic disease. On the other hand, the role of Th2 cells/cytokines in the pathogenesis of CHS is also investigated using gene-deficient mice. IL-4-deficient mice show the reduced CHS induced by TNCB and DNFB, but normally developed CHS induced by oxazolone. Contrast to IL-4-deficient mice, DNFB-induced CHS was normally developed in IL-13-deficient mice. Mice deficient in STAT6, which is an essential transcription factor for Th2 cell development and IL-4 and IL-13 signals, show the significant attenuation of CHS induced by oxazolone, TNCB, FITC or paraphenylemediamine, suggesting that IL-4 and/or IL-13 is important for the induction of CHS. We and other investigators demonstrated that Th17 cells/cytokines are also involved in the development of CHS induced by DNFB and TNCB. Therefore, it is considered that both Th2 and Th17 cells/cytokines are required for the optimal development of CHS, and IL-25 may be involved in the induction of CHS by enhancing Th2-type, but suppressing Th17-type, immune responses. However, the precise role of IL-25 in the pathogenesis of CHS is poorly understood. Thus, in the present study, we investigated the contribution of IL-25 to the development of CHS using IL-25-deficient mice.