2 型自然リンパ球とアレルギー

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Group 2 innate lymphoid cell and allergic inflammation

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Allergic disorders such as asthma and atopic dermatitis are chronic diseases involving chronic inflammation by hyper IgE production and M2 macrophage-mediated tissue remodeling. It is well known that IL-4 regulates IgE production from B cells and M2 macrophage differentiation. Therefore, IL-4 has a crucial role in chronic inflammation during allergic disorders.

Group 2 Innate lymphoid cells (ILC2s), a new type of innate lymphocyte that we originally reported as natural helper cells, are known to regulate type2 immune responses such as immunity against helminth infection and allergic responses. ILC2s rapidly produce large amounts of IL-5 and IL-13, which are hallmark cytokines of Th2 cells, prior to the acquired immune response, suggesting that ILC2s regulate the initiation of allergic disorders. On the other hand, although Th2 cells produce IL-4 as well as IL-5 and IL-13 after TCR stimulation, ILC2s fail to produce IL-4 even after stimulation with IL-33 or IL-25 which are known to induce IL-5 and IL-13 production by ILC2s. For this reason, ILC2s are not thought to contribute to chronic inflammation during allergic disorders. However, we found strong enrichment of K4 trimethylation on histone H3 at the *Il4* gene locus in naive ILC2s similar to that in differentiated Th2 cells. Further, we identified the physiological condition that induces IL-4 production in ILC2s, which is distinct from that in Th2 cells. Taken together, our data provides evidence that ILC2s may contribute to the pathogenesis of chronic allergic disorders through IL-4-mediated immune responses that are distinct from that of Th2 cells.