Role of group 2 innate lymphoid cells in IL-4-mediated immune responses

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Elevation of IgE in serum is known to be a typical symptom of helminth infection and allergic disorders such as asthma and atopic dermatitis. It is well known that antigen-specific Th2 cells induce IgE class switching in B cells through IL-4, leading to the production of antigen-specific IgE. A complete loss of IgE in the absence of IL-4 indicates that IL-4 is an essential factor in IgE-mediated immune responses and diseases.

Group 2 innate lymphoid cells (ILC2s), a new type of innate lymphocyte that we originally reported as natural helper cells, are known to regulate type 2 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. Although Th2 cells produce IL-4 as well as IL-5 and IL-13 after TCR stimulation by antigen, 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 IL-4-mediated immune responses. However, we observed elevation of ‘polyclonal’ IgE during type 2 immune responses. Further, we identified the physiological condition that induces IL-4 production in ILC2s in the absence of antigen, which is distinct from that in Th2 cells. Taken together, our data provide evidence that ILC2s regulate polyclonal IgE production in B cells through IL-4 production, leading to IL-4-mediated immune responses that are distinct from that of Th2 cells.