Circulating lymphoid tissue inducer-like cells in asthma

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The lung-associated lymphoid tissues are reorganized during the development of allergic asthma, as there is a Th2-biased inflammatory response to innocuous environmental antigens (allergens) in these patients instead of the default immune tolerance in healthy individuals. Lymphoid tissue-inducer cells (LTi-s) - the architects of the secondary lymphoid organs - are residing on the interface of B and T cell zones in adult lymph nodes. We investigated whether LTi-s may have a role in the pathogenesis of asthma. We isolated CD45+ CD3- CD4- CD20- CD14- CD56- IL-7Ralpha+ CD161+ c-Kit+ LTi-like cells from peripheral blood of healthy individuals and allergic asthmatic patients. Significantly lower circulating LTi-like cell counts was observed in asthma patients (363.1 ± 30.4 / mL) compared to healthy controls (773 ± 99.3 / mL), suggesting an increased demand for these cells in the lung-associated immune tissues, in asthma. Sorted LTi-like cells can be kept in cultures for up to 50 days in IL-7- and/or IL-15-enriched medium. Their proliferation can be inhibited by TGF-beta. LTi-like cells express CD40L and TLR-9; and approx. 40% of them express CCR6. LTi-like cells can regulate B cells, in vitro. In B-cell - LTi co-cultures the production of IL-13, IP-10, VEGF, IL-1alpha and especially IL-10 was increased, while IL-1beta, IL-6, IL-8 and RANTES were decreased. The pattern of immunoglobulin production by the B cells was substantially changed by LTi-s, as well. In addition, higher cell proliferation in LTi-B cell co-cultures was detected compared to B-cell or LTi alone cultures. In conclusion, LTi-like cells may play a role in the shaping of humoral immune responses and thus, in the pathogenesis of asthma.