025 Immunological changes in atopic dermatitis patients treated with different dosing intervals of dupilumab
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Dupilumab, a fully human IgG4 monoclonal antibody targeting the interleukin-4 receptor alpha (IL4Ra), substantially improves disease severity in patients with atopic dermatitis (AD). While several studies have shown that dose reduction of dupilumab is possible in patients with controlled AD, the associated biological effects are currently unknown. Therefore, we studied the dupilumab levels in serum and the amount of bound dupilumab (anti-IgG4) in serum and blood mononuclear cells (PBMCs). In addition, we examined SSc B cells with elevated IgE levels (RIIB+). SSc B cell subsets indicated that the role of IL-31 in B cell biology. Using flow cytometry, the frequency of IL-31 transgenic (EIl31+) mice indicated that next to the induction of pruritus and skin lesions, mice also presented enlarged lymph nodes with increased B cell frequency. Therefore, we aimed at characterizing the role of IL-31 signaling in B cell biology using flow cytometry, the frequency of total B cells and specific B cell subsets was assessed in peripheral lymph node and bone marrow of IL-31 transgenic (EIl31+) mice and wild-type controls. Moreover, IL-31RA expression was analyzed on human B cell subsets from peripheral blood of healthy and atopic dermatitis patients. We observed a significantly increased frequency of CD19+ B cells in bone marrow and peripheral lymph nodes in IL-31 transgenic mice. Detailed analyses of B cell subsets indicated that EIl31 transgenic mice showed a higher frequency of plasmablasts in peripheral lymph nodes. In human, memory B cells represented the major population expressing IL-31RA within the B cell compartment. Furthermore, atopic dermatitis patients with elevated IgE levels (>1000 kU/l) showed a higher IL-31RA expression on memory B cells compared to healthy donors. This is of particular interest since DOCK8 acts as a negative regulator of IL-31. DOCK8 deficiency-related hyper-IgE syndrome presents with elevated serum IgE levels and severe atopic dermatitis with increased IL-31 expression. Taken together, these findings point to a novel role of IL-31 in B cell biology and an atopic IgE-producing phenotype.

026 Targeting pathogenic MICA-NKG2D interactions by statins: A novel adjunct treatment strategy for alopecia areata management
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Alopecia areata (AA) is a lifelong cutaneous autoimmune disease. Thus, SSc B cells may exhibit compensatory elevation in the expression levels of FcRIIB. However, the role of FcRIIB on SSc naive and DN memory B cells was not fully understood. The severity of fibrosis in the skin and lungs was significantly greater in BLM-treated FcRIIB+ mice than in BLM-treated wild-type (WT) mice. In the skin of BLM-treated mice, the numbers of CD27+ T cells, CD450/macrophages, IL-17 production by splenic and skin CD450 T cells and MICA expression by splenic and skin DCs were significantly decreased. Therefore, FcRIIB plays an inhibitory role in skin and lung fibrosis. On the other hand, the expression levels of FcRIIB on SSc naive and DN memory B cells were significantly increased compared to healthy controls. Increased FcRIIB expression levels on double negative memory B cells were associated with presence of interstitial lung disease. Thus, SSc B cells may exhibit compensatory elevation in the expression levels of FcRIIB in order to suppress the abnormal activation of B cells.

027 Memory B cells of atopic individuals preferentially express IL-31RA: a putative role in IL-31 in B cell biology
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The novel cytokine IL-31 and its receptor have been shown to play a central role in bridging the immune system with neurons, epithelial surfaces and connective tissues. Although increasing evidence has demonstrated their role in inflammation, their involvement in the development of distinct leukocyte subsets is not fully understood. Detailed analyses of IL-31 transgenic (EIl31+) mice indicated that next to the induction of pruritus and skin lesions, mice also presented enlarged lymph nodes with increased B cell frequency. Therefore, we aimed at characterizing the role of IL-31 signaling in B cell biology using flow cytometry, the frequency of total B cells and specific B cell subsets was assessed in peripheral lymph node and bone marrow of IL-31 transgenic (EIl31+) mice and wild-type controls. Moreover, IL-31RA expression was analyzed on human B cell subsets from peripheral blood of healthy and atopic dermatitis patients. We observed a significantly increased frequency of CD19+ B cells in bone marrow and peripheral lymph nodes in IL-31 transgenic mice. Detailed analyses of B cell subsets indicated that EIl31 transgenic mice showed a higher frequency of plasmablasts in peripheral lymph nodes. In human, memory B cells represented the major population expressing IL-31RA within the B cell compartment. Furthermore, atopic dermatitis patients with elevated IgE levels (>1000 kU/l) showed a higher IL-31RA expression on memory B cells compared to healthy donors. This is of particular interest since DOCK8 acts as a negative regulator of IL-31. DOCK8 deficiency-related hyper-IgE syndrome presents with elevated serum IgE levels and severe atopic dermatitis with increased IL-31 expression. Taken together, these findings point to a novel role of IL-31 in B cell biology and an atopic IgE-producing phenotype.

028 A role for FcRIIB in systemic sclerosis
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Systemic sclerosis (SSc) is a systemic autoimmune disease characterized by excessive fibrosis of the skin and internal organ. FcRIIB, a low-affinity receptor for the Fc fragment of IgG, is expressed on the surface of several leukocyte subsets and functions in negative feedback pathways to down-regulate B cell antigen receptor signaling. To elucidate the role of FcRIIB in the development of fibrosis, a murine bleomycin (BLM)-induced scleroderma model was examined in mice lacking FcRIIB (FcRIIB−/− mice). FcRIIB expression on B cells of patients with SSc and healthy controls was also examined. The severity of fibrosis in the skin and lungs was significantly greater in BLM-treated FcRIIB−/− mice than in BLM-treated wild-type (WT) mice. In the skin of BLM-treated mice, the numbers of CD27+ T cells, CD450/macrophages, IL-17 production by splenic and skin CD450 T cells and MICA expression by splenic and skin DCs were significantly decreased. Therefore, FcRIIB plays an inhibitory role in skin and lung fibrosis. On the other hand, the expression levels of FcRIIB on SSc naive and DN memory B cells were significantly increased compared to healthy controls. Increased FcRIIB expression levels on double negative memory B cells were associated with presence of interstitial lung disease. Thus, SSc B cells may exhibit compensatory elevation in the expression levels of FcRIIB in order to suppress the abnormal activation of B cells.