[FRI0011] IL-10-PRODUCING REGULATORY B CELLS ARE DECREASED IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a characterized by extensive fibrosis and a plethora of autoantibodies, the latter being indicative of breakage of tolerance. Regulatory B cells (Bregs) producing interleukin (IL)-10 play a significant role in suppressing inflammatory immune responses and preventing autoimmunity
Objectives: To investigate the significance of IL-10-producing Bregs in SSc
Methods: The study groups consisted of 45 patients with SSc (12 with early SSc, 33 with established SSc [of whom 16 with SSc-associated lung fibrosis,SSc-LF]) and 10 healthy controls (HCs). As a disease controls for SSc-LF, 12 patients with rheumatoid arthritis-associated LF (RA-LF) were included. Peripheral blood monunuclear cells were isolated from patients and controls. Phenotypic analysis of immature/transitional Bregs (CD19+CD24highCD38high) and memory Bregs (Cd19+CD27+Cd24high) was carried out by flow cytometry using FACS Calibur. The function of bregs was evaluated by IL-10 expression after Bcell culture with toll-like receptor (TLR)9 stimulation, and flow cytometry analysis
Results: Memory Bregs were decreased in early SSc (1.85±0.38), established SSc (1.6±0.88), and SSc-LF (1.52±0.17) compared to HCs (6.3±0.49, $p<0.001$). There were more decreased in diffuse cutaneous SSc (dcSSc) than limited cutaneous SSc (lcSSc), but not significantly so. The lowest percentage of memory Bregs was in dcSSc-LF (1.36±0.16). Memory Bregs were also numerically decreased in RA-LF compared to HCs (1.58±0.26, $p<0.001$). Transitional Bregs were also numerically decreased in early SSc, and established SSc compared to HCs ($p<0.02$). Bregs IL-10 expression after Toll-like receptor (TLR)-9 stimulation (innate stimulus) was impaired in SSc, particularly in SSc-LF.
Conclusions: This is the first study to demonstrate that Bregs are reduced and functionally impaired in SSc, particularly SSc-LF. The impaired IL-10 production after innate stimulus may have clinical implications. The impairment of Bregs along with the reported increased expression of the stimulatory Bcell receptor CD19 in SSc support B cell autoaggression in SSc. These findings may offer a new therapeutic strategy for SSc, namely expanding Bregs ex-vivo and re-administering them to patients with SSc.
Disclosure of Interest: None declared
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Session: Adaptative immunity (T cells and B cells) in rheumatic diseases

[FRI0012] IL-10-PRODUCING REGULATORY B CELL DEFICIENCY IS A FEATURE OF PSORIATIC ARTHRITIS

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Background: In mice, IL-10-producing regulatory B cells (Bregs) suppress inflammatory immune responses and adoptive transfer of Bregs reduced imiquimod-induced psoriatic skin lesions in CD19(-/-) mice (1). Inflammatory Tcells and cytokines (Th1,Th17, TNFa) play a significant role in the pathogenesis of psoriasis and psoriatic arthritis (PsA).

Objectives: To assess the phenotypic and functional characteristics of Breg subsets, CD19(pos)CD27(pos)CD24(high) memory and CD19(pos)CD24(high)CD38(high) transitional Bregs in patients with PsA.
Methods: Peripheral blood mononuclear cells were isolated from 25 patients with PsA and 15 normal controls (NCs). The expression of surface CD19, CD24, CD27 and CD38 and cytoplasmic IL-10 by Bregs was examined by flow cytometry following bacterial CpG (ODN2006) stimulation using fluorochrome-conjugated monoclonal antibodies.
Results: Memory and transitional B regs were significantly decreased in PsA patients compared to NCs, respectively (2.2±0.42 *vs* 6.1±0.5, p=0.01 and 0.8±0.31 *vs* 1.5±0.21, p=0.03, respectively). The ratio of CD24(high) to CD24(low) B cells was also significantly decreased in PsA patients compared to NCs ($p<0.001$). IL-10 expressing Bregs after Toll-like receptor (TLR)-9 stimulation were primarily detected within memory than transitional B cell subsets in NCs; both subsets were significantly decreased in PsA compared to NCs ($p<0.05$). After ODN2006 stimulation for 24hrs, CD24(low) B cells from NCs are capable to produce IL10, in sharp contrast to CD24(low) from PsA which are unable to express IL10 ($p=0.037$).
Conclusions: This is the first study to demonstrate that Bregs are reduced and functionally impaired after innate stimulus in PsA. This suggests that Bregs may be implicated in the development of PsA.
References:
Yanaba K et al. J leuk Biol 2013;94:563
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