REGULATORY B CELLS IN HEALTHY VOLUNTEERS AND IN RHEUMATOID ARTHRITIS PATIENTS

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Background: In the past few years a novel subset of B cells was discovered that downregulate the immune response. The pleiotrophic cytokine, IL-10 seemed to be responsible for this function. B cells with the immunosupressive capacity were named regulatory B cells (Breg). Breg cells suppress CD4+ T cell proliferation as well as inflammatory cytokine synthesis (INFγ and TNF) by T cells, inhibit antigen presentation and pro-inflammatory cytokine production of dendritic cells and macrophages, furthermore, enhances regulatory T cell proliferation. Rheumatoid arthritis (RA) is a systemic autoimmune disease that can cause joint inflammation and tissue destruction. Both B and T cells play an important role in the development of the disease. In the absence of Breg cells disease symptoms exacerbates in collagen-induced arthritis, the animal model of rheumatoid arthritis.

Therefore, this study was undertaken to investigate differences between IL-10 producing capacity of B cells from RA patients and healthy controls without and with stimulation. Our aim was to identify the optimal stimuli (BCR, CpG, CD40L) to induce Breg cells' IL-10 production. We also aimed to examine, which other inflammatory cytokines (IL-6, TNF) are produced by B cells beside IL-10.

Materials and methods: Samples were collected from healthy donors and RA patients in heparinized blood collection tube. Intracellular IL-6, IL-10 and TNF were measured in purified B cells and in PBMC. Cytokines were detected in B cells prior or after stimulation by intracellular fluorescent staining using specific antibodies.

Results: In our experimental conditions, CpG and CD40L dual stimulation for 48h was found to be optimal for IL-10 induction in B cells. The main source of IL-10 was a subset of the memory B cell population (CD19+ CD27+) in the unstimulated samples, but also some naive B cells produced IL-10 after stimulation. Besides IL-10, other inflammatory cytokines (IL-6, TNF) were also detected. We have shown that less B cells from RA patients produced IL-10 compared with the healthy controls after stimulation.

Conclusion: We detected differences in the suppressive cytokine, IL-10 producing Breg cells of RA patients and healthy controls. The lower capability of activation-induced IL-10 production by Breg cells in RA patients may promote disease exacerbation.

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