AB0194

BTLA EXPRESSION IS REDUCED ON SLE B CELL SUBSETSAnnika Wiedemann¹, Ana-Luisa Stefanski^{1,2}, Andreia Lino¹, Thomas Dörner¹.¹Charité Universitätsmedizin Berlin, Dept. of Medicine, Rheumatology and Clinical Immunology, Berlin, Germany; ²University Hospital of Bern, Department of Rheumatology, Immunology and Allergology, Bern, Switzerland

Background: B- and T-lymphocyte attenuator (BTLA/CD272) is a co-receptor constitutively expressed on B cells [1, 2]. Upon B cell activation via the B cell receptor (BCR), BTLA co-localizes with Src homology region 2 domain-containing phosphatase-1 (SHP-1) and thus negatively regulates BCR signaling [2]. A recent study found that CD4+ T cells from SLE patients fail to upregulate BTLA upon activation [3], however, data on BTLA expression and function for B cells in autoimmunity is missing.

Objectives: To assess BTLA expression on conventional naïve (CD20⁺CD27⁻), conventional memory (CD20⁺CD27⁺) B cells and on CD27⁺CD38⁺ expressing plasma cells (PC) in peripheral blood mononuclear cells (PBMCs) of patients with systemic lupus erythematosus (SLE) and healthy donors (HD).

Methods: PBMCs were isolated from EDTA blood taken from 7 female SLE patients (age 38, mean disease activity 5 (SLEDAI)) and 6 female HD (mean age 28) by Ficoll density gradient centrifugation according to the manufacturer's protocol. Cells have been stained and expression of BTLA was assessed by flow cytometry.

Results: Analysis of BTLA surface expression on B cell subsets in SLE patients and HD revealed decreased expression of BTLA on naïve SLE B cells (*p=0.0173, Mann-Whitney U Test (MWU), BTLA median fluorescence intensity (MFI) 9006±1450) compared to naïve HD B cells (11957±941). A similar tendency was found for memory SLE B cells (p=0.0823 MWU) compared to HD memory but not SLE PC and HD PC. Remarkably, an inverse correlation was found for BTLA expression on naïve SLE B cells and SLE PC with Siglec-1 expression on monocytes (*p=0.0333 Spearman's rank correlation (SRC) naïve B cells, *p=0.0167 PC), a marker for interferon signature, and the same trend was seen for SLE memory B cells (p=0.0583 SRC). Inverse correlation of BTLA expression was also found with disease activity (SLEDAI) with these B cell populations but did not reach significance (p=0.0583 naïve B cells, p=0.1361 memory B cells, p=0.0833 PC).

Conclusion: Herein, we document that B cell subsets of SLE patients express lower levels of the negative regulator BTLA than HD. Additionally, an inverse correlation between BTLA expression on B cell subsets and Siglec-1 on monocytes were found suggesting its involvement in disease and consideration BTLA as therapeutic target in SLE. We hypothesize that reduced BTLA expression is a feature of post-activated B cells. Further studies need to delineate functional properties of BTLA expression and activation in autoimmune B cells.

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THE IMPACT OF KETOGENIC DIET AND HIGH-FAT-HIGH-GLUCOSE DIET IN PRISTANE INDUCED LUPUS-LIKE NEPHRITIS MURINE MODEL

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Background: Systemic lupus erythematosus is a chronic systemic inflammatory disease which commonly involves kidneys[1]. Aside from the use of conventional immunosuppressants, dietary components and metabolites may likely affect our immune system.

Objectives: An interest in the anti-inflammatory property of ketogenic diet (KD) has recently come to attention.

It not only alters the balance between Th17 and Treg cells[2], its metabolite, beta-hydroxybutyrate was known to block NLRP3 inflammasome-mediated inflammation[3-6]. High-fat-high-glucose diet (HFGD), on the other hand, was known for a proinflammatory property. Aim to understand the immune modulatory effect of KD and HFGD in cases with systemic lupus erythematosus, a chronic systemic inflammatory disease with glomerulonephritis, pristane induce lupus like nephritis murine model was used.

Methods: Pristane induced lupus nephritis mice were divided into groups fed with regular chow (CD), KD and HFGD along with healthy controls. The diets were kept for 6 months with regular body weight and urine protein monitoring. Serum samples were collected for metabolic evaluation and immune survey bimonthly. The mice were sacrificed 6 months after diet change. Kidneys, lymph nodes, spleen, blood and guts were collected for evaluation.

Results: KD and HFGD were both well tolerated by experimental mice. Two months after diet change, higher level of beta-hydroxybutyrate and triglyceride but lower sugar level was noted in mice fed on KD when compared to those fed on CD and HFGD (all p<0.05). Mice fed on KD and HFGD have a much lower RBC and platelet count than those fed on CD in the experimental mice group (both p<0.05). Although global lymphocyte counts were much lower in those pristine treated mice, Th17 lymphocytes were significantly higher in the blood as well as kidneys among those fed on HFGD (all p<0.05). This is compatible with their high serum concentration of anti-dsDNA, anti-nRNP and anti-Sm and the rapid progressing proteinuria. Renal, hepatic and intestinal histopathology was still under analysis at present.

Conclusion: In conclusion, food plays a critical role in immune modification. Despite the reported anti-inflammatory effect of KD, it does not mitigate lupus nephritis progression. HFGD formula, however, accelerated the autoimmune phenotype for cases with lupus like glomerulonephritis.

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