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AB0034

LOOKING FOR A SLE SIGNATURE ON PERIPHERAL B CELL SUBSETS: DOES A PREPONDERANT CD38+PLASMA-BLAST-SUBPOPULATION LACK CD73 AS A SIGN OF A DISTURBED ADENOSINE AXIS?

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Background: Systemic Lupus Erythematosus (SLE) is an autoimmune disorder characterised by polyclonal Bcell activation, production of dsDNA-autoantibodies and cytokines. Subsets of Bcells play a central role in SLE-pathogenesis. The inflammatory milieu is characterised by the accumulation of adenosine, which confers immunosuppressive effects.

Objectives: In SLE, the role of CD73, an enzyme involved in the extracellular generation of adenosine from ATP, is not well characterised. This study aimed to characterise expression of CD73 Bcell subsets of SLE-patients as compared to healthy controls (HC).

Methods: Bcell subsets were characterised from peripheral blood of 23 SLE patients attending the outpatient clinic at the Rheumatology Unit of University Hospital Düsseldorf and of 15 HC by FACS. All patients fulfilled the revised SLE-criteria of ACR and were randomly collected in clinical remission state (SLEDAI 1.1±1.9).

Results: By comparison of Bcell subsets between SLE and HC, CD38 was dominantly expressed by SLE-patients (SLE 74.2%±12.9% vs. HC 64.2%±12.2%; p(MWU)=0.018). Furthermore, SLE-patients showed an increase in CD19 +IgD CD27+CD38 high plasmablasts (SLE 2.1%±3.4% vs HC 0.4%±0.4%, p(MWU)<0.001). Furthermore, SLE-plasmablasts showed decreased CD73 expression as compared to HC(SLE 2.1%±1.9% vs HC 3.5%±2.2%; p(MWU)=0.034). SLE-Bcells revealed a trend towards an augmented CD38highCD138+plasmacell fraction (SLE 0.40%±0.5% vs HC 0.08%±0.07%; p=0.07), without any difference in CD73 expression. On the other hand, exhausted-memory B cell fraction (CD19 +IgD CD27-CD21-CD138-), showed an increased CD73 expression in SLE (SLE 13.7%±9.2% vs HC 6.2%±5.4%; p=0.004).

Conclusions: Our study confirms CD38 +plasmablasts as being increased in peripheral blood from SLE patients as compared to HC. Furthermore, the data reveal a deficiency for CD73 on SLE plasmablasts, which suggests a decreased anti-inflammatory capacity of SLE plasmablasts as compared to HC, supporting the notion of a disturbed adenosine axis in SLE. On the other hand, the enlarged CD73 +exhausted memory pool in SLE could point to an accelerated flow of CD73 +B cells into an exhausted B cell fraction. These findings support the hypothesis of dysregulation of the adenosine axis in SLE even in inactive SLE patients.

REFERENCES:

- [1] Szabo K, Papp G, Szanto A, Tarr T, Zeher M. A comprehensive investigation on the distribution of circulating follicular T helper cells and B cell subsets in primary Sjogren's syndrome and systemic lupus erythematosus. *Clinical and experimental immunology* 2016;183(1):76–89.
- [2] Jacobi AM, Reiter K, Mackay M, Aranow C, Hiepe F, Radbruch A, et al. Activated memory B cell subsets correlate with disease activity in systemic lupus erythematosus: delineation by expression of CD27, IgD, and CD95. *Arthritis and Rheumatism* 2008;58(6):1762–73.
- [3] Deaglio S, Dwyer KM, Gao W, Friedman D, Ushuva A, Erat A, et al. Adenosine generation catalyzed by CD39 and CD73 expressed on regulatory T cells mediates immune suppression. *The Journal of Experimental Medicine* 2007;204(6):1257–65.
- [4] Hasko G, Linden J, Cronstein B, Pacher P. Adenosine receptors: therapeutic aspects for inflammatory and immune diseases. *Nature Reviews Drug Discovery* 2008;7(9):759–70.

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AB0035

A PHYSIOLOGICAL NETWORK OF IGG AUTOANTIBODIES TARGETING G PROTEIN COUPLED RECEPTORS

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Background: Since the time when Paul Ehrlich conceived the term “horror auto-toxicus”, autoantibodies have been associated with the development of autoimmune diseases. However, several works have recently shown the presence of autoantibodies in sera from healthy subjects (n=489), who do not develop autoimmune diseases.

Objectives: Here, we report a network of immunoglobulin G (IgG) autoantibodies targeting G protein-coupled receptors (GPCRs), growth factors and growth factor-related molecules in sera from healthy subjects.

Methods: Autoantibody levels in sera were assessed using ELISA. Autoantibody network was analysed by exploratory factor analysis (EFA), dandelion plot method, hierarchical clustering, and multi-study factor analysis (MFA). We also reverse engineered autoantibody functions through *in silico* evaluation of autoantibody target interactions using STRING and gene ontology (GO). To test the autoantibodies functionality we assessed the *in vitro* production of IL-8 by PBMCs and neutrophil migration in response to IgG from healthy subjects as well as ETAR-immunised and control mice. Leukocyte cellularity to secondary immune organs was analysed comparing ETAR-immunised with control mice.

Results: Gender, age and the presence of pathological conditions (systemic sclerosis n=84, Alzheimer's disease n=91 and ovarian cancer n=207) changed correlations between the autoantibodies and their hierarchical clustering distribution. Notably, subjects at age below and above 65 years or with pathological conditions exhibited particular autoantibody hierarchical clustering signatures. In addition, females at age above 65 years, representing the group of subjects with higher risk to develop SSC, displayed the closest link to SSC in terms of autoantibody hierarchical clustering. Finally, autoantibody directed against the endothelin receptor type A (ETAR) showed an essential role in the autoantibody network by orchestrating neutrophil trafficking *in vitro* and in ETAR-immunised mice.

Conclusions: Our data provide a framework for the existence of a physiological network of autoantibodies and reveal a new paradigmatic view on these physiological molecules.

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AB0036

ROLE OF PROGRAMMED DEATH-1 PATHWAY ON CD8+ T CELLS CYTOTOXICITY IN PRIMARY BILIARY CHOLANGITIS

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Background: Primary Biliary Cholangitis (PBC) is a chronic progressive autoimmune disease. It has been proven that there was abnormal activation of CD8 +T cells. Previous studies have shown that abnormal expression programmed death-1 (PD-1) and its ligand (PD-L1) in PBC. However, no study was found to confirm the abnormality of PD-1/PD-L1 pathway in CTL in PBC.

Objectives: To investigate the role of PD-1 and its ligand PD-L1 on CD8+ T cells cytotoxicity in the immunological mechanism of PBC.

Methods: The expression of PD-1 in peripheral CD8+ T cells of 69 patients diagnosed with PBC as well as 58 health controls (HC) was detected by flow cytometry. Plasma cytokines related to PD-1/PD-L1 pathway were detected by ELISA. The co-localization of PD-1 and CD-8, PD-L1 and CK19 in portal region in liver biopsy was analysed by immunofluorescence assay. Meanwhile, the relative gene expression of PD-1 regulatory pathway in CD8+ T lymphocytes were measured by RT-PCR. And co-culture of PD-1+ CD8+ CTL and HiBEC was done *in vitro* to detect the cytotoxicity, proliferation and cytokine expression of CD8+ CTL and the apoptosis of HiBEC.

Results: The proportion of peripheral PD-1+ CD8+ T cell decreased in PBC (12.0%±8.8%) than HC (19.9%±12.5%) (p<0.001). The plasma concentration of IL-10, IFN-γ and TGF-β in the PBC group were higher than that in HC (8.29±9.00 pg/ml v.s. 4.43±5.08 pg/ml, p=0.0066; 51.94±52.94 vs 26.71±26.26 pg/ml, p=0.0015; 1302.0±1972.8 pg/ml vs 205.8±298.9 pg/ml, p=0.0018, resp.). Compared with HC (n=19), *Tbet* gene expression in CD8+ T lymphocytes was increase