reaction of astrocytes and patchy increase of lymphocytes were also observed. Furthermore, MHC class I and class II were also highly expressed in the vascular endothelium in FcγRIIB$^{-/-}$ *Yaa* mice.

Conclusions: Activation of myeloid lineage cells and reactive changes of glial cells and endothelial cells were observed in the central nervous system of lupus-prone FcγRIIB$^{-/-}$ *Yaa* mice. These results imply the role of innate immune mechanisms in the pathology of NPSLE.

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AB0126 AUTOPHAGY AND SYSTEMIC LUPUS ERYTHEMATOSUS: CLINICAL SIGNIFICANCE OF ATG14+, FOXP3+, AND CD25+ EXPRESSION ON T REGULATORY CELLS AND NK CELLS

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Background: Autophagy is a highly conserved protein degradation pathway, essential for removing protein aggregates and misfolded proteins in healthy cells. Autophagy and autophagy-molecules expression have been implicated in autoimmune diseases. Systemic Lupus Erythematosus (SLE) is a prototype of autoimmune disease whose main characteristic is the loss of immune tolerance. Recent evidences suggest that autophagy, and autophagy-related proteins participate in SLE immune regulation. However, little is known about the SLE clinical significance of autophagy-related proteins, T regulatory, and NK cells.

Objectives: To evaluate the expression of ATG14$^+$ (autophagy-related key regulator protein), FOXP3$^+$, CD25$^+$T regulators, CD56$^+$NK cells in active and inactive SLE patients.

Methods: The expression of ATG14$^+$, FOXP3$^+$, CD25$^+$, and CD56$^+$ were measured by flow cytometry, and expressed in percentages in T and NK cells of SLE patients (1997, ACR criteria), and healthy controls. Active SLE was considered by SLEDAI ($\geq$4). The organs affected and treatments were evaluated.

Results: A total of 40 SLE patients and 20 healthy controls were included. The mean expression of autophagy in 20 active SLE patients was 11.19% in comparison with inactive SLE patients, 7.13%, (p=0.04), and in healthy donors, 7.445% (p=0.0281). The FOXP3$^+$ expression in NK cells in active SLE was lower in comparison with inactive patients (0.98% vs 3.82% respectively). In healthy donors was 2.89%.

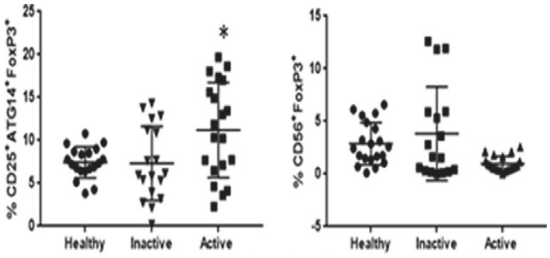

Figure 1: Expression in percentage of CD25$^+$ATG14$^+$FoxP3$^+$ (T reg) and CD56$^+$FoxP3$^+$ (NK cells) in SLE active and inactive patients and healthy controls. *p=0.04 Mann Whitney U test.

Conclusions: We found that in active patients autophagy is higher than in inactive patients. In inactive patients FOXP3 expression in NK cells is normal. These results can be due to the effect of the different treatments given according to clinical manifestations. Autophagy-related key regulator protein may be a new target of SLE treatment

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AB0127 ANTI-DS-DNA ANTIBODIES REGULATE ATHEROTHROMBOSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS THROUGH THE INDUCTION OF NETOSIS, INFLAMMATION AND ENDOTHELIAL ACTIVATION

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Background: The role of anti-dsDNA in the pathogenesis of the systemic lupus erythematosus (SLE) has been clearly established. However, the influence of these autoantibodies in the atherothrombotic status of SLE patients has not yet been evaluated

Objectives: 1. To analyse in vivo the involvement of anti-dsDNA antibodies in the development of CVD in SLE patients. 2. To evaluate in vitro the mechanisms underlying the effects of anti-dsDNA antibodies in these processes

Methods: The study was conducted in 50 SLE patients and 38 healthy donors. Endothelial function was assessed by measuring the post-occlusive hyperaemia using Laser-Doppler. Various markers of oxidative stress, inflammatory cytokines, prothrombotic mediators and NETosis, were quantified in purified leukocytes and plasma from SLE patients and controls. Activation of intracellular pathways was analyzed in monocytes using pathscan intracellular signaling array. In vitro, purified neutrophils, monocytes and lymphocytes from healthy donors and endothelial cells (ECs) were treated separately and in a trans-well co-culture system with anti-dsDNA antibodies isolated from the serum of SLE patients. Then, markers of inflammation, thrombosis, oxidative stress and NETosis were evaluated by flow cytometry (protein), RT-PCR (mRNA) and electron microscopy

Results: SLE patients showed impaired micro-vascular endothelial function (reduction of hyperaemia post occlusion area) and altered expression levels of pro-inflammatory proteins (IL6, IL8, MCP-1 and PCR), prothrombotic molecules (TF), oxidative stress markers (peroxides and mitochondrial membrane potential) and netosis-related molecules (NE, MPO and cell free-DNA). Monocytes from anti-dsDNA-positive SLE patients showed activation of various pathways related to inflammation, thrombosis and apoptosis (ErK, STAT-3, p38, JNK, GSK, Bad and Caspase-3). Association studies demonstrated that molecules related to inflammation and thrombosis, endothelial dysfunction, oxidative status and netosis were linked to the occurrence of thrombotic events, as well as to the presence of anti-dsDNA antibodies. In vitro treatment of purified leukocytes with anti-dsDNA antibodies promoted an increase in the production of NETosis, levels of peroxides and percentage of cells with altered mitochondrial membrane potential, as well as enlarged expression of a number of proinflammatory and prothrombotic molecules. In vitro treatment of HUVEC with anti-dsDNA antibodies promoted an increase in endothelial activation molecules (ICAM-1, VCAM-1 and E-selectin).

Conclusions: 1. Positivity for anti-dsDNA antibodies is linked to an increased pro-atherothrombotic status in SLE patients. 2. Anti-dsDNA antibodies, in vitro, promote NETosis on neutrophils, apoptosis on monocytes, modulate the expression of molecules related to inflammation and thrombosis, and induce endothelial activation. Together, that data suggest the involvement of such autoantibodies on atherothrombosis development in SLE

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AB0128 ALTERATIONS OF THE SPLICING MACHINERY COMPONENTS IN LEUKOCYTES FROM PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS INFLUENCES ITS DEVELOPMENT AND ATHEROTHROMBOTIC PROFILE AND DRIVES THE THERAPEUTIC RESPONSE

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Background: Recent studies emphasize the relevance of alternative splicing in the development of genetic and autoimmune diseases and suggest therapeutic possibilities based on the modulation of this process.

Objectives: To identify alterations in the leukocyte splicing machinery of patients with systemic lupus erythematosus (SLE) and to evaluate its influence on the development and activity of the disease, its atherothrombotic profile, and the response to specific therapies.

Methods: An array of selected components of the major-(n=12) and minor-spliceosome (n=4) and associated splicing factors (n=28) was developed, and their expression levels were evaluated using a Fluidigm methodology, in purified leukocytes from 36 SLE patients and 29 healthy donors (HD). In parallel, an extensive clinical/serological evaluation was performed. Carotid intimate media thickness (CIMT) was used as atherosclerosis marker. Endothelial activity was