Conclusions: The data suggest that activation of B cells from SLE patients require CD40/CD40L interaction to increase PD-L1 expression, which is, however, reduced compared to HD. Diminished PD-L1 expression upon B cell stimulation is consistent with impaired inhibition of T cells in SLE (figure 1).

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AB0151

CHARACTERIZATION OF THE PLASMATIC GLYCOPROTEIN AND LIPOPROTEIN PROFILES OF SYSTEMIC LUPUS ERYTHEMATOSUS BY NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

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Background: Systemic Lupus Erythematosus (SLE) is an autoimmune disease associated with systemic inflammatory processes. Chronic inflammation alters the number and type of non-cellular elements, including lipoproteins and glycoproteins.

Objectives: Here we investigate the plasmatic lipoprotein and glycoprotein profiles associated with SLE.

Methods: Plasma samples were obtained from 50 healthy control individuals and 50 SLE patients. All patients fulfilled the ACR criteria for classification of SLE. ¹H-NMR was used to determine the lipoprotein and glycoprotein profiles from cases and controls. For the lipoprotein profiles, VLDL, LDL, IDL and HDL concentration, lipid composition and particle properties were quantified. The glycoprotein profile was decomposed in four reproducible peak regions LMW, Glyc-B, Glyc-A, Glyc-Lipid and baseline, and quantified for concentration, position and aggregation state. Association analysis to disease was performed using logistic regression fitting for age, gender and body mass index. Classifiers were built using recursive-partition algorithm and classification accuracy was evaluated using receiver operating curves.

Results: We found a significant perturbation of the lipoprotein profile in SLE patients compared to controls. A statistically significant ($P<0.05$) reduction of cholesterol-LDL and HDL lipoproteins as well as an increase in triglyceride VLDL was found in SLE. Particle number for LDLs, were found to be reduced compared to controls ($P<0.05$), and mostly due to lower quantities of large LDL particles ($P<0.005$). The glycoprotein profile was also significantly altered for several NMR measures. The most significant changes were related to the reduction of the width and area of the Glyc-Lipid peak in SLE patients ($P<0.005$ and $P<0.05$,

respectively). Using the plasma molecular patterns to predict the presence of SLE, we found a significant classifier for the lipoprotein pattern (ROC AUC(95% CI)=0.85(0.78–0.93)), and an optimal classifier for the glycoprotein pattern (ROC AUC(95%CI)=0.90(0.84–0.97))

Conclusions: SLE is characterized by perturbations of the plasmatic lipoprotein and glycoprotein profiles. The increase of triglyceride VLDL in patients compared to controls, could explain the increased risk for cardiovascular disease observed in SLE. Our results also show that SLE patients have a significantly different glycoprotein profile compared to controls. In both cases, plasmatic ¹H-NMR profiling could be a valuable source of informative biomarkers for SLE.

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AB0152

MICROARRAYS GENE EXPRESSION PROFILING OF MONOCYTES FROM SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: NOVEL GENES AND PATHWAYS INVOLVED IN THE DISEASE

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Objectives: 1. To identify altered genes and pathways in monocytes from Systemic Lupus Erythematosus (SLE) patients involved in the pathogenesis of the disease. 2. To evaluate the contribution of anti-dsDNA antibodies to the regulation of these processes.

Methods: Eighty three subjects, including 53 SLE patients and 30 healthy donors (HDs), were recruited. Total RNA was extracted from monocytes isolated of 6 subjects, analyzed as exploratory cohort- and microarray studies were performed in an Agilent G4112F platform (Whole Human Genome Microarray 44k). By using the Ingenuity Pathway Analysis Software (IPA) the altered gene, pathways, and network profiles were identified and functionally categorised. The top differentially expressed genes were validated by RT-PCR in monocytes purified from all the subjects enrolled. The inflammatory profile was evaluated in serum by multiplex assay. The activation of intracellular proteins was analysed by PathScan intracellular signalling protein array. Correlation and association studies were performed with clinical and analytical variables. The effect of anti-dsDNA antibodies in the altered gene expression signature was evaluated by *in vitro* studies on monocytes from HD

Results: Microarray gene expression profiling identified 553 significantly altered genes in monocytes from SLE patients in relation to HDs ($p<0.05$ and fold change >2). IPA analysis showed that the altered genes were mainly related to inflammatory and immunological disease (32.4%), as well as cardiovascular (22.5%), neurological (21.9%), musculoskeletal (10%), renal (6.5%), dermatological (4.5%) and reproductive system disorders (2.2%). The top altered canonical pathway identified was the interferon signalling, and the main altered genes, validated by RT-PCR, were PGC1- α (master regulator of mitochondrial biogenesis and oxidative stress), IFI27, IFI44, IFI44L, IFIT1, IFI6 and RSAD2 (interferon signalling), EDNRB (endothelin receptor involved in the vascular system homeostasis), SERPINB10 (serpine related to haematopoiesis and apoptosis), CDKN1B and CCND2 (proliferation regulators), and IL22RA1 and CMKLR1 (inflammatory mediators). The altered gene signature was associated with the presence of anti-dsDNA antibodies, and clinical features of SLE (early atherosclerosis and nephropathy), and correlated with the disease activity and the levels of inflammatory serum markers (CRP, ESR, C3, C4, IL8, MCP1, IFN γ , IP10, PDGFBB). The activation of numerous intracellular signalling proteins was also noticed. *In vitro* studies demonstrated the modulation of several genes by effect of anti-dsDNA.

Conclusions: Gene expression profile allowed the identification of relevant genes and pathways altered in monocytes of SLE patients, which were associated with the pathogenesis of the disease and modulated, at least partially, by anti-dsDNA. The identification of relevant genes whose products regulate specific pathological processes might contribute to the development of targeted therapies in SLE

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