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REFERENCE

1. Scharer, Christopher D., *et al*. 'Epigenetic programming underpins B cell dysfunction in human SLE.' *Nature immunology* 2019; 20.**8**; 1071–1082.

P104 CORRELATION BETWEEN INTERSTITIAL CD8+ T CELL INFILTRATION AND FIBROTIC PROCESSES IN A MOUSE MODEL OF LUPUS NEPHRITIS

[1,2]Pauline Montigny, [1]Aurélie Degroof, [3]Davide Brusa, [1,4]Frédéric Houssiau, [1,4]Bernard Lauwerys. *[1]Pôle de Pathologies Rhumatismales Systémiques et Inflammatoires, UCLouvain, Louvain; [2]Service de Rhumatologie, CHU UCL Namur, Yvoir; [3]Plateforme de Cytométrie de Flux, Institut de Recherche Expérimentale et Clinique, UCLouvain, Louvain; [4]Service de Rhumatologie, Cliniques Universitaires Saint Luc, Bruxelles, Belgium*

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Background Tubulo-intersitial damage during lupus nephritis (LN) is associated with poor renal prognosis in the long run. Here, we describe the progression of tubulo-interstitial fibrosis and immune cells infiltration with emphasis on CD8+ T cells, in parallel with renal outcomes in a mouse lupus model.

Methods We collected blood, urine and kidneys from 39 B6/Sle1.Sle2.Sle3 lupus-prone mice, before disease onset and at different stages of disease progression. RNA was extracted from kidneys and hybridized on Mouse Gene 2.0 ST exon arrays. Histopathological scores (NIH Activity and Chronicity Indexes) and digital quantification of fibrosis, IgGK deposits, CD8+ and CD3+ T cells were performed on total kidney. Renal CD8+ T cell phenotypes were determined by flow cytometry. Plasma urea and albuminuria were measured by immunoenzymatic assays.

Results IgGκ deposits, CD8+ T cell infiltration and interstitial fibrosis increase with the progression of renal disease, evaluated by histopathological scores and plasma urea. Further, digital quantifications allowed us to identify a significant correlation (r=0,45, p=0,011) between local CD8+ T cell population and fibrosis, while total CD3+ cells population and IgGκ deposits did not display such association. Moreover, characterization of CD8+T cell subpopulations showed that fibrosis is more specifically linked to effector functions of CD8+ T cells. Transcriptomic analyses supported this association, with a high correlation coefficient between mean expression of effector functions transcripts and the presence of a fibrotic signature (r=0,92, p<0,0001).

Conclusions Our results support the association between CD8 + T cell tubulo-interstitial infiltration and renal outcomes in a mouse lupus model. Further, a strong correlation is identified between effector functions of CD8+ T cells and fibrotic processes, opening new avenues of research in the pathogenesis of LN.

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P105 EXPRESSION DIVERSITY OF INTERFERON-STIMULATED GENES IN PERIPHERAL BLOOD CELLS FROM PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Kanwal Siddiqi, Søren Jacobsen. *Copenhagen Lupus and Vasculitis Clinic, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark*

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Background A central facet of the immunopathogenesis of systemic lupus erythematosus (SLE) is the activation of interferon (IFN) signalling. In SLE patients, several types of IFNs are upregulated as well as the genes that are stimulated by IFNs. Sustained expression of interferon-stimulated genes (ISGs) may have adverse effects including altered T cell function, tissue inflammation and organ damage. The distinct association of the IFN gene signature to SLE disease activity is still uncertain.

Methods Peripheral blood samples from 34 SLE patients and 15 healthy controls were collected in PAXgene tubes. RNA from peripheral blood cells (PBCs) was extracted using the PAXgene Blood RNA Kit. The mRNA transcripts of 105 ISGs were measured using the multiplexed Nanostring nCounter Gene Expression platform. Bioinformatics and statistical analysis were performed using nSolver and SPSS.

Results We found that SLE patients had significantly higher expression levels of a wide range of ISGs, as compared to healthy controls. The 5 most upregulated ISGs in PBCs were IFI27, IFI44L, USP18, RSAD2 and ISG15. Using principal component analysis we identified two subsets of ISGs of which one included the mentioned top-five expressed ISGs; this gene cluster consisted of ISGs with predominantly antiviral functions and STAT1/STAT2, and did not associate with clinical disease activity or history of nephritis in SLE patients. Instead these genes associated with anti-SSA/SSB antibodies and PBC expression of PDCD1 and LAG3, which are markers of CD8 T cell exhaustion. The second group of ISGs associated with clinical disease activity, STAT3 and NFKB expression.

Conclusions Our results indicate the presence of ISG subsets that are differentially associated to clinical, serological and immunological features of SLE. Thus, the IFN gene signature in SLE may consist of a highly complex network of ISGs that can be clustered, and each in their way contribute to the pathogenesis of SLE. Also, this challenges the construction IFN gene signatures and scores with respect to what purpose they are intended for.

P106 PENTAMERIC, BUT NOT MONOMERIC C-REACTIVE PROTEIN, LIMITS THE SNRNP-IMMUNE COMPLEX TRIGGERED TYPE I INTERFERON RESPONSE: IMPLICATIONS FOR LUPUS PATHOGENESIS

[1]Cecilia Svanberg, [1]Helena Enocsson, [1]Klara Martinsson, [2]Lawrence Potempa, [2]Ibraheem Rajab, [1]Jonas Wetterö, [1]Marie Larsson, [1]Christopher Sjöwall. *[1]Linköping University, Linköping, Sweden; [2]Roosevelt University, Chicago, USA*

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Background Systemic Lupus Erythematosus (SLE) is an autoimmune systemic disease affecting multiple organs and which is characterized by autoantibodies directed against nuclear constituents. Common autoantibody targets include double-stranded (ds) DNA and small nuclear ribonucleoproteins (snRNPs; i.e. U1-snRNP). Uptake of immune complexes (ICs) by plasmacytoid dendritic cells (pDCs) can activate endosomal toll-like receptors (TLRs) such as TLR-7 and TLR-9 if nucleic acids are present in the ICs. Such activation is dependent on IC internalization by Fcγ receptor type IIa (FcγRIIa), and results in production of type I interferons (IFNs), a hallmark of SLE and a target for therapeutic interventions. The acute phase protein C-reactive protein (CRP)