CD14 + monocytes was additionally confirmed by flow cytometry.

Results Macrophage activation was 4.8 (2.8;7.3) in SLE pts and 10,2(3.5;11,6) in control group, p>0,05. In SLE pts macrophage activation was independent of age, sex, body mass index, traditional risk factors (arterial hypertension, overweight, smoking, family history of cardiovascular diseases), SLADAI-2K. No association was found between macrophage activation and levels of ANA, C3, C4, and anti-dsDNA.

Conclusions No differences in macrophage activation were found in SLE pts and control group. Macrophage activation was independent of age, sex, traditional risk factors, and SLE-related parameters.

LP-096 PLASMABLAST-LIKE ANTIGEN-EXPERIENCED CXCR5-CD19LOW B CELLS ARE EXPANDED IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Double negative B cells represent a heterogeneous compartment and expansion has been linked to systemic lupus erythematosus (SLE) in previous studies.[1–3] Previously we found a novel CXCR5-CD19low subset in the DN compartment. Thus, we aimed to further characterize this population phenotypically and functionally.[4]

Methods For this study, we collected peripheral blood from a total of 79 patients with SLE and 80 healthy individuals as reference. We investigated baseline surface marker expression and Syk phosphorylation kinetics upon B cell receptor (BCR) stimulation of peripheral B cells and specifically the CXCR5-CD19low subset using flow cytometry. To check the subset for its capability of secreting antibodies, cell cultures were performed and soluble immunoglobulins were detected using a bead-based flow cytometry assay. Additionally, targeted RNA-seq was performed.

Results We found that the subset of CXCR5-CD19low B cells can be found among DN and CD27+ memory B cells and was increased in SLE. Frequencies correlated with PBs frequencies. Surface marker expression of CD38, CD95 and CD71 and IgA and IgG suggest an activated and antigen experienced phenotype. BCR stimulation show a reduced responsiveness similar to the kinetic of PBs. The capacity to secret IgA ex vivo suggests that CXCR5-CD19low B cells are antibody secreting cells which was further supported by the finding of elevated transcriptional expression of PRDM1, XBP-1 and IRF4, transcription factors known to regulate plasmablasts (PB) differentiation.

Conclusions Summing up, besides bimodal expression of CD27 the subset of CXCR5- CD19low B cells shared various characteristics with PBs such as phenotype and functionality like antibody secretion and reduced BCR responsiveness. CXCR5- CD19low seemed to be related to plasmacytosis as suggested by the correlation with PB frequencies. Our data suggest that CXCR5-CD19low B cells are precursors of PBs and targeting this subset in SLE may have therapeutic value.

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LP-097 DEGRANULATING PR3+ MYELOID CELLS CHARACTERIZE PROLIFERATIVE LUPUS NEPHRITIS

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Background Despite optimal treatment, lupus nephritis (LN) remains associated with irreversible kidney damage1. A better understanding of the mechanisms underlying LN pathogenesis is needed to develop better treatment targets. As part of the Accelerating Medicines Partnership (AMP), we discovered that urinary PR3, a neutrophil degranulation product, correlated with histological activity implicating neutrophil/monocyte degranulation in proliferative LN, the most aggressive type2. PR3 is a serine protease that can mediate kidney damage. Mature neutrophils with classical polylobate nuclei are rare in LN kidney biopsies. However, recent evidence displayed how immature, degranulating myeloid cells have been implicated in the pathogenesis of LN3, but their role in mediating kidney damage is not completely understood. We aimed to investigate PR3+ cells in LN kidney and their association with histopathological features, and define their immunophenotype.

Methods We performed multiplexed histology using serial immunohistochemistry (sIHC)4 on archival LN kidney biopsies to quantify the expression of PR3 and multiple cell lineage markers (20-plex). Image analysis including deconvolution, cell segmentation, glomerular annotation, and quantitative histology was performed using Indica HALO. The analysis was limited to renal cortex.

Results A total of 11 patients with LN who underwent a clinically indicated kidney biopsy were enrolled: 6 (55%) with pure proliferative LN (ISN/RPS class III or IV) and 5 (45%) with pure membranous LN. PR3+ cells were identified in all LN biopsies (range 343–7625 per sample). Most PR3+ cells did not show a polylobate nucleus. The majority of PR3+ cells were in the tubulointersitium (figure 1A). However, accounting for the smaller glomerular area, there was a higher density of PR3+ cells in the glomeruli (figure 1A-C). PR3+ cell abundance was higher in proliferative LN, especially in the glomeruli (figure 1A-C). Glomerular PR3+ cell density very strongly correlated with histological activity measured by the NIH Activity Index (Pearson's r=0.97, p=5*10–5; figure 1D). Preliminary serial IHC analysis showed that PR3+ cells coexpressed MPO and variably