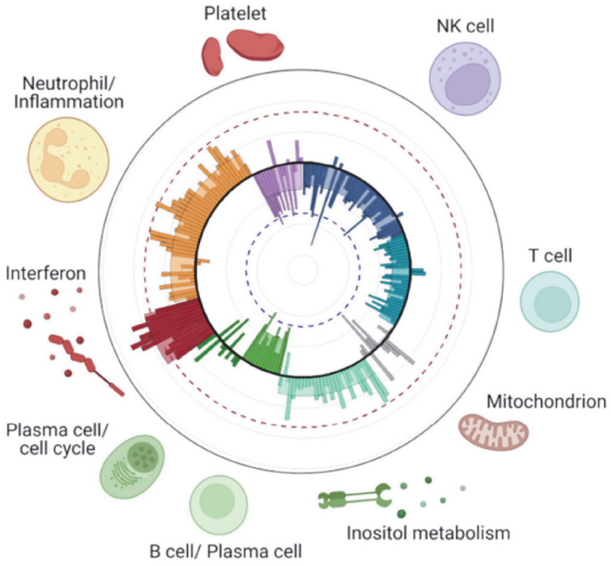

Abstract PO.1.5 Figure 1

Results My PROSLE allows to molecularly summarize patients in 206 gene-modules, clustered into 9 main lupus signatures (Example in figure 1, the combination of which revealed highly differentiated pathological mechanisms. We show that dysregulation of certain gene-modules is strongly associated with specific clinical manifestations, the occurrence of relapses or the potential presence of long-term remission and drug response. Therefore, My PROSLE could be used to accurately predict these clinical outcomes.

Conclusions My PROSLE (https://myprosle.genyo.es) allows molecular characterization of individual Lupus patients and it extracts key molecular information to support more precise therapeutic decisions.

PO.1.6 INVESTIGATING MONOCYTE TRANSCRIPTOMICS AND TARGETED PROTEOMICS SIGNATURES IN SLE WITH ATHEROSCLEROSIS UNCOVERS HETEROGENEITY IN INFLAMMATORY PROFILES

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Purpose Accelerated atherosclerosis and the build-up of fatty lipids in the arteries leading to an inflammatory cascade and cardiovascular disease (CVD) are a leading cause of mortality in women with systemic lupus erythematosus (SLE). Despite this, lipid-lowering drugs have shown mixed efficacy in SLE and a female-focused mechanistic understanding of atherosclerosis in the context of SLE is lacking.

Methods A well-characterised cohort of CVD-free women with SLE were non-invasively scanned for the presence of subclinical atherosclerotic plaques and monocyte bulk-RNAsequencing (n=18) and targeted proteomics (n=29) were performed. To explore molecular gene and protein signatures of atherosclerosis in SLE, it is important to acknowledge how they interact within the interactome whereby clusters of connected genes and proteins can offer insight into shared function or disease association. Disease module identification using a modularity optimization method (MONET) was applied to multiple networks (ConsensusPathDB and STRINGdb) and modules were ranked by number of seed genes (n seeds=372) or proteins (n seeds=10) differentially expressed between SLE patients with and without subclinical atherosclerotic plaques that were represented in the module. Pathway enrichment analysis was applied to key modules to elucidate potential mechanisms underpinning subclinical atherosclerosis pathology in SLE.

Results Highly enriched modules were defined by inflammatory mechanisms. The highest ranked module (n seed genes=3, proteins=2 across both networks) implicated genes and proteins involved in the complement pathway as associated with atherosclerosis in SLE, supporting prior knowledge that complement is dysregulated in SLE pathology and emerging evidence suggesting a role for complement in atherosclerotic plaque development. Other key modules suggested dysregulation of genes and proteins associated with mitochondrial function and inflammatory interferon signalling. Interferon-regulated genes, known to be elevated in SLE, were downregulated in SLE patients with subclinical plaque. Notably, unsupervised hierarchical clustering applied to interferon-gene signature-derived scores stratified patients into three distinct subgroups based on interferon response ($p<0.0001$) that could not be explained by differences in routine disease measures or known clinical predictors. Interferon response did not predict the presence of plaques and 55% of plaque patients showed a low interferon-response, potentially indicative of an anti-inflammatory profile.

Conclusions SLE and atherosclerosis are both characterised by chronic inflammation. Complement and interferon production are critical regulators of the inflammatory response and contribute to immune dysfunction in SLE. Nevertheless, we have established a complex signature of genes and proteins associated with inflammatory functions as both up and downregulated in SLE patients with subclinical atherosclerosis, suggesting a potential dysregulation or dampening of inflammatory processes. This presents an exciting opportunity for improved patient stratification to identify SLE patients at greatest risk for CVD.

PO.1.7 URINARY METABOLOMIC PROFILE OF SYSTEMIC LUPUS ERYTHEMATOSUS AND LUPUS NEPHRITIS BASED ON LIQUID AND GAS CHROMATOGRAPHY/MASS SPECTROMETRY (LC-QTOF-MS AND GC-QTOF-MS)

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Purpose Systemic lupus erythematosus (SLE or lupus) is a chronic autoimmune disease, and kidney involvement with SLE, lupus nephritis (LN), is a frequent and severe complication of SLE that increases patient morbidity and mortalityis. The current gold standard for classifying LN progression is a renal biopsy, an invasive procedure with potential risks. Undergoing a series of biopsies for monitoring disease progression and treatments is unlikely suitable for patients with LN. Thus,

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