coagulation system, and fibrinolysis. Patients with SLE face an approximately 50% thrombosis risk after diagnosis, However, the underlying mechanisms are intricate, and anticoagulation recommendations are lacking.

Methods The review was conducted in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statements. PubMed and Embase were searched without time restrictions to identify studies evaluating mechanisms of thrombosis based on the six mentioned pro-coagulable categories in SLE.

Results Thirty-one studies were included. Figure 1 illustrates the literature search process. Thirty studies employed *in vitro* investigations utilizing a case-control design, and one animal study was identified. Autoantibodies (mainly aPL) were the subject of investigation in 80% of studies. The studies highlighted pro-coagulable interactions between autoantibodies and all other investigated pro-coagulable categories. Ten studies identified cross reactivity between aPL and other SLE autoantibodies. There was a paucity of studies exploring the impact of anti-inflammatory or anti-thrombotic treatments within the investigated mechanisms.

Conclusions The thrombosis risk mechanisms mediated by aPL in SLE are well-documented. These mechanisms may also be shared with other autoantibodies in SLE, potentially explaining the increased thrombosis risk observed in aPL-negative SLE patients. Interactions between the pro-coagulable categories were frequently reported in the literature and appear pivotal in SLE thrombosis risk. Further research is warranted to elucidate the effects of different treatments on thrombosis mechanisms in SLE.

P118 INCREASED ATHEROTHROMBOTIC RISK IN SLE PATIENTS: THE ROLE OF OXIDATIVE STRESS IN FIBRINOGEN STRUCTURAL AND FUNCTIONAL MODIFICATIONS

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Objective Patients with systemic lupus erythematosus (SLE) show accelerated atherosclerosis and are at higher risk of developing myocardial infarction, stroke and peripheral vasculopathy, carrying an overall 2- to 10-fold higher risk of cardiovascular events as compared to the general population. The pathogenetic mechanisms underlying this increased risk are still unclear, but several studies suggest a central role of oxidation in promoting vascular damage in SLE. Consequently, this study aimed to investigate the potential role of oxidation-mediated structural and functional alterations of fibrinogen in the pathogenesis of atherothrombosis in SLE.

Methods A cross-sectional study was conducted enrolling 144 adult SLE patients and 90 matched controls, and the production of reactive oxygen species (ROS) by leucocytes and overall redox status were assessed. Furthermore, the structural and functional characteristics of fibrinogen (including thrombin-catalysed fibrin polymerisation and the susceptibility of fibrin to plasmin-induced lysis) and their correlation with redox parameters were investigated.

Results Compared to controls, SLE patients showed increased ROS production by lymphocytes, monocytes, and neutrophils, mainly due to neutrophil NADPH oxidase (42432 ± 18998 vs. 13234 ± 4223 RLU/s, $p=0.001$), in parallel with increased plasma lipid peroxidation, reduced antioxidant defences and increased fibrinogen oxidation (294 (256–329) vs 163 (121–184) RFU, $p < 0.0001$). SLE patients also presented marked alterations in fibrinogen and clot structure, mainly characterised by reduced porosity and by a dense fibrin network with reduced average filaments size. A significant difference was found in alterations of the functional characteristics of fibrinogen, especially in thrombin-catalysed fibrin polymerisation and in fibrin susceptibility to plasmin-induced lysis. Additionally, these functional and structural alterations significantly correlated with redox parameters, which in turn correlated with SLE disease activity.

Conclusions These data suggest that ROS induce structural and functional changes to fibrinogen in SLE. This could represent a novel pathogenetic mechanism underlying atherothrombosis in SLE.

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P119 T-BET+ B CELLS CAN SERVE AS PROGNOSTIC AND THERAPEUTIC TOOLS FOR HUMAN SYSTEMIC LUPUS ERYTHEMATOSUS

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Objective This study aims to clarify whether T-bet$^+$ B cells, as well as the sub-populations of age-associated B cells/ABCs (CD19$^+$CD21$^-$CD11c$^+$T-bet$^+$) and double-negative B cells/DN (CD19$^+$IgD$^-$CD27$^-$CXCR5$^-$T-bet$^+$), serve as prognostic and/or therapeutic tools for systemic lupus erythematosus (SLE) in humans.

Methods Flow cytometry was used to enumerate and immunophenotype T-bet+ B cells and ABCs/DN subsets, found in the peripheral blood of 10 healthy donors and 22 active SLE patients, in order to identify correlations between the cell populations and the clinical profiles of the subjects. Moreover, in order to evaluate the effects of traditional and modern pharmaceutical agents on T-bet+ B cells' percentage, 24h-long primary cell cultures combined with *in vitro* pharmacological treatments (of 1h) were performed. Various concentrations of hydroxychloroquine, anifrolumab and fasudil (a ROCK kinase inhibitor) have been tested. Last, data derived from previous published single-cell RNA sequencing (scRNA-seq) studies, regarding 6 healthy donors and 11 active SLE patients, were used for a meta-analysis focusing on T-bet+ B cells, so as to

allow characterization of the genes and pathways associated with the biology of this specific transcription factor.

Results T-bet+ B cells, as well as ABCs and DN, displayed a statistical significant expansion in the patients, compared to the healthy donors. Interestingly, percentages of T-bet+ B cells and DN B cells positively correlated with the SLEDAI scores of the patients. Cell culture experiments conducted, revealed that all three drugs tested are capable of depleting T-bet+ B cells (while leaving unaffected the total numbers of lymphocytes, T cells and B cells, respectively). According to bioinformatics analyses, moreover, T-bet in B cells seems to affiliate with transcription factors that play a role in germinal centers' development (such as BCL6 and IRF8) in lupus patients, while in healthy individuals it affiliates with JUN. Additionally, an analysis regarding intracellular communications amongst B cell populations revealed that the transcription factor of interest is closely associated with inflammatory secretome during lupus.

Conclusions T-bet+ B cells associate with SLEDAI, thus can serve as a prognostic biomarker of lupus severity. Furthermore, these cells promote disease pathogenesis and can be targeted for therapeutic interventions.

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P120 UNVEILING CD4+ METABOLIC DYSREGULATION IN SYSTEMIC LUPUS ERYTHEMATOSUS: IMPLICATIONS FOR TARGETING MITOCHONDRIAL DYSFUNCTION

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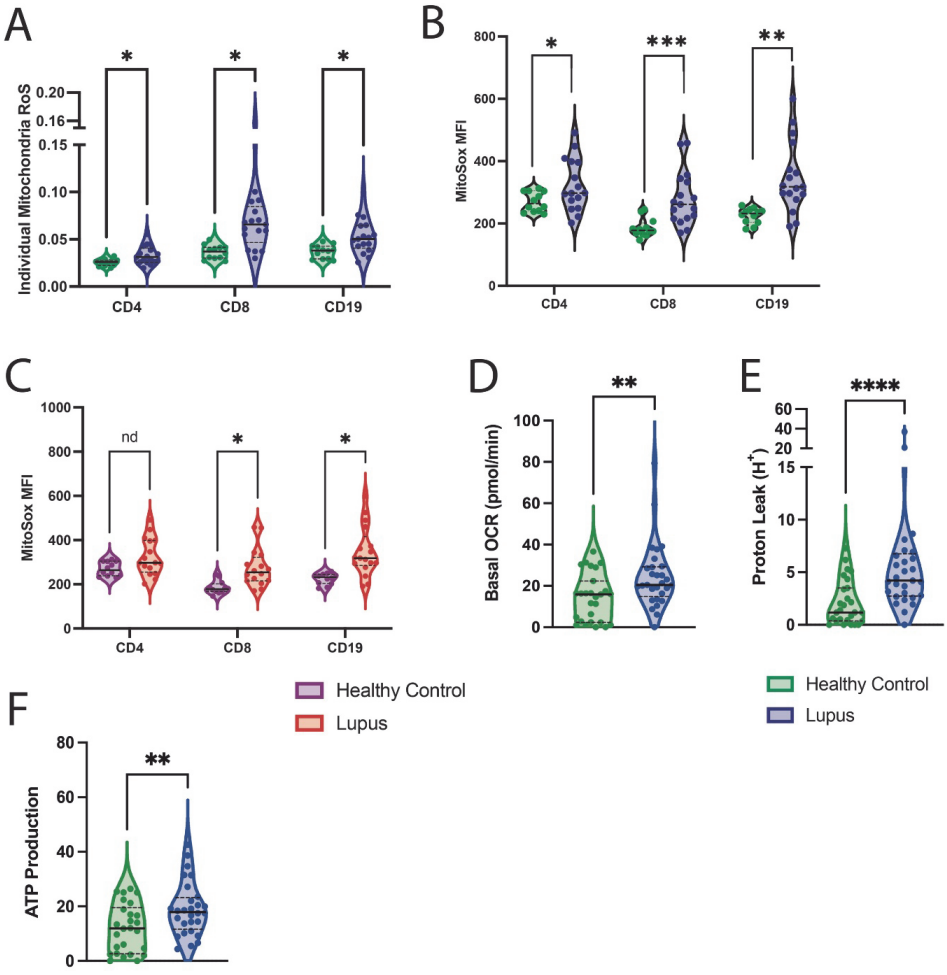
Objective Systemic lupus erythematosus (SLE) is characterized by persistent stimulation of the adaptive immune response and oxidative stress from Reactive Oxygen Species (ROS) generation. Mitochondria, central to energy metabolism through Oxidative Phosphorylation (OXPHOS), are implicated in the pathogenesis of SLE. This study aimed to assess abnormal mitochondrial function and associated ROS production in the adaptive immune response of SLE patients.

Methods Initially peripheral blood mononuclear cells (PBMCs) were isolated from SLE patients (n=37) and age/sex-matched healthy controls (HC, n=20). Flow cytometry (FC) was employed to quantify mitochondrial mass and mitochondria-



Abstract P120 Figure 1