Background Pulmonary arterial hypertension (PAH) is one of the most important complications that seriously threatens the prognosis of patients with systemic lupus erythematosus (SLE). We aim to investigate candidate biomarkers and targeted therapy for the early diagnosis and timely treatment of SLE-PAH patients.

Methods 1) In order to screen susceptible genes of SLE-PAH, a number of 150 peripheral blood from SLE-PAH patients were subject to whole-exome sequencing (WES), and genome-wide association study (GWAS) was performed by comparing with 934 healthy controls.

2) The transcriptional expression levels of the above screened genes on peripheral blood of SLE-PAH patients were examined by RT-qPCR for further validation.

3) Intervention experiments on pulmonary artery endothelial cells (PAEC) were performed to figure out the potential pathogenesis of the selected gene in vitro. RNA-seq and gene ontology were applied to identify downstream pathways.

4) Established by pristane injection and hypoxia induction, SLE-PAH mice model was established. Pulmonary arterial pressure (PAP) was measured by right heart catheterization with/without tail-intravenous injection of therapeutic vectors.

Results 1) The tumor necrosis factor receptor-associated factor 5 (TRAF5) was identified as a susceptible gene of SLE-PAH based on WES and GWAS.

2) The significant reductions of TRAF5 on transcriptional level in peripheral blood of SLE-PAH patients were identified, indicating clinical diagnosis values.

3) Knockdown of TRAF5 significantly increased early apoptosis of PAEC and triggered the pathogenesis of PAH through distinct pathways.

4) SLE-PAH mouse model was successfully established since they showed phenotypes of lupus and the mean PAPs were over 40mmHg. Tail-intravenous injection of TRAF5-overexpression vector attenuated PAH phenotypes.

Conclusions Lack of TRAF5 triggers the pathogenesis of PAH in SLE patients through inducing abnormal apoptosis of PAEC. TRAF5 is a susceptible gene of SLE-PAH and it could be a candidate biomarker for diagnosis and therapy for SLE-PAH patients.

Concurrent session 10: immune cells

LO-037 ALTERED PERIPHERAL NON-CLASSIC MONOCYTE AND NKT COUNTS AND CD8+ TCR DIVERSITY OF SYSTEMIC LUPUS ERYTHEMATOSUS IDENTIFIED VIA INTEGRATED HIGH-DIMENSIONAL FLOW CYTOMETRY, CYTOF, METABOLIC PROFILING AND TCR CLONALITY ANALYSES

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Background The phenotypic, signaling and metabolic diversities of leucocytes of systemic lupus erythematosus (SLE) impede comprehensive identification of immunopathologically-relevant alterations in leucocytes associated with active SLE. We aimed to identify these alteration signatures in leucocytes from patients with active SLE by an integrated platform comprising high-dimensional flow cytometry, cytometry by time of flight (CyTOF) and RNA sequencing (RNA-seq).

Methods Peripheral blood mononuclear cells (PBMCs) of SLE patients and healthy subjects were subjected to high-dimensional flow cytometry and CyTOF for studying alterations of myeloid cells and lymphocytes. Bulk RNA-seq was conducted for 8 sorted cell populations. Data were subjected to integrative analyses with Cytozoom that identified cellular signatures of active SLE. Differences in T-cell and B-cell receptor