Objectives: The present study compares the relative performance of 4 IFN gene signatures in a cohort of 687 participants with self-reported SLE.

Methods: A centralised site, IRB-approved, SLE cohort was recruited using social media. Qualified participants with self-reported SLE were consented electronically and asked to provide medical record review consent, complete an online questionnaire regarding their disease as well as provide 3 fingerstick blood samples over approximately a 6 week period. Blood samples from 687 participants were tested using a multi-modular gene expression assay containing 11 IFN response genes (primarily from the IFN- α response pathway). Normalised gene expression values were calculated, and the resulting data analysed to determine concordance between IFN gene signatures.

Results: 10 of the 11 IFN response genes were highly correlated with one another ($\rho \geq 0.80$). The 4-gene signature of IFI27, IFI44, IFI44L, and RSAD2² identified 36.5% of the participants as IFN high. Three other literature reported IFN signatures^{3, 4, 5} provided similar classification results with participants being assigned to the same IFN sub-group over 90% of the time, and nearly identical patient distributions.

Abstract SAT0041 – Table 1

Signature	Genes	IFN High (%)	IFN Low (%)	% Agreement (95% CI) to Furie et al.
Furie et al. ²	IFI27, IFI44, IFI44L, RSAD2	36.5	63.5	N/A
Niewold et al. ³	EIF2AK2, IFIT1, MX1	36.3	63.7	94.8% (93.4–95.9)
Kirou et al. ⁴	EIK2AK2, IFIT1, IFI44	36.0	64.0	95.1% (93.7–96.2)
Westra et al. ⁵	IFI6, HERC5, IFIT1, MX1	36.0	64.0	94.8% (93.4–95.9)

Conclusions: The study demonstrated that commonly used IFN gene signatures provide similar IFN subtyping to the 90th percentile. The use of social media to engage patients directly along with self-collection of blood samples provides new opportunity for testing clinical study participants and potentially patients without requiring an office visit.

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Disclosure of Interest: M. Abedi Shareholder of: DxTerity, Employee of: DxTerity, F. Flores Employee of: DxTerity, P. Naranatt Employee of: DxTerity, J. Spangler Employee of: DxTerity, L. Pan Employee of: DxTerity, R. Terbrueggen Shareholder of: DxTerity, Employee of: DxTerity
DOI: 10.1136/annrheumdis-2018-eular.3758

SAT0042 EVIDENCE OF NETOSIS IN CIRCULATING NEUTROPHILS AND SKIN LESIONS WITH VASCULITIS AND PANNICULITIS IN BEHÇET'S DISEASE

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Background: Behcet's disease (BD) pathophysiology is poorly understood. It is characterised by recurrent episodes of acute inflammation consisting of neutrophil infiltration in affected organs and around blood vessels. Recently, NETosis, trapping and killing pathogens by activated neutrophils, has been described. These Neutrophil Extracellular Traps (NETs) were shown to promote inflammation in a number of autoimmune diseases such as Systemic Lupus Erythematosus, ANCA-Associated Vasculitis and Rheumatoid Arthritis. We hypothesise that in BD, neutrophils trigger inflammation and vasculitis via NETosis.

Objectives: The aim of this study is to demonstrate the implication of NETosis in the pathophysiology of this disease.

Methods: Blood specimens from BD patients and matched healthy volunteers were collected at the American University of Beirut Medical Centre. Circulating neutrophils were isolated and cultured in Roswell Park Memorial Institute (RPMI) 1640 medium. Cultured cells were treated with colchicine, dexamethasone or corresponding vehicle, and stimulated with serum from BD patients, controls or left unstimulated. The kinetic and amount of NET formation was assessed by cell counting using Hoechst 33 342 and Sytox green staining and fluorescent microscopy. Moreover, previously described NET-bound proteins (elastase, myeloperoxidase, citrullinated histone-3 and PR-3) were identified by immunolabeling and mRNA expression levels of PAD4, a key enzyme that promotes citrullination of arginine residues on chromatin, was evaluated in neutrophils from BD compared to controls. Finally, evidence of NETosis *in vivo* was assessed on paraffin embedded specimens from damaged organs of BD patients using immunolabeling and confocal microscopy.

Results: The percentage of unstimulated neutrophils undergoing NETosis *in vitro* was significantly higher in BD patients compared to controls. Treatment of unstimulated BD neutrophils with colchicine and dexamethasone resulted in significant decrease in NETs formation compared to controls. Interestingly, the percentage of NETs increased upon exposure of neutrophils to serum from BD patients. Moreover, PAD4 mRNA expression was 3 times higher in BD patients compared to controls. Immunolabeling assay demonstrated that NET-bound proteins were present in NETs scaffold of unstimulated neutrophils from BD patients *in vitro*. Additionally, NETs were detected in skin tissues of BD patients focally distributed in proximity to small vessels in vasculitis patients and to inflamed adipose tissue in panniculitis patients. These were associated with elastase and citrullinated histone-3 proteins.

Conclusions: We show here for the first time that circulating neutrophils from BD patients are prone to NETosis *in vitro*. NET formation was inhibited by the addition of colchicine and dexamethasone reflecting their therapeutic benefits in BD. The increase of NETosis upon serum stimulation suggests the presence of soluble factors and cytokines triggering NETs in BD. Combined, these results suggest a major role of NETs in the pathophysiology of BD.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.1440

SAT0043 IL-33/ST2-MEDIATED INFLAMMATION IN ENDOTHELIAL CELL IS DIRECTLY AGGRAVATED BY IL-6 DURING LUPUS NEPHRITIS

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Background: "Alarmins" are prototypic endogenous pro-inflammatory factors as they are released from necrotic cells and provoke local damage or systemic inflammation. Evidences are accumulating to support the inclusion of "Alarmins" as targets of autoreactivity as well as inducers in the pathogenesis of Systemic Lupus Erythematosus (SLE). Interleukin (IL)–33 is a novel member of the family of "Alarmins" because of its characteristics and functions in mediating host immune responses. On this background, we sought to determine the role of IL-33/ST2 axis in lupus pathogenesis. The role of IL-33/ST2 axis has not previously been described in lupus nephritis.

Objectives: This project will study the followings:¹ To determine whether IL-33 was present in renal glomerular endothelial cells;² To assess the functional and intracellular signal transduction mechanisms regulating the link between IL-33/ST2-mediated innate immunity and inflammation in human umbilical vein endothelial cells (HUVECs).

Results: This study, for the first time, showed that IL-33 was pathologically expressed in the kidney tissue of patients with lupus nephritis and not in that of subjects with relative normal renal tissues from atrophy. However, no significant difference was observed between patients with lupus nephritis and kidney cancer. Immunofluorescence (IF) for IL-33 in kidney was performed in lupus patients. IL-33 was clearly seen in glomeruli and also in peritubular areas. To determine whether the IL-33 staining in glomeruli area was in endothelium, multiple staining for IL-33, CD34 (a marker for endothelial cells) and 4',6-diamidino-2-phenylindole