Methods: The study involved 80 (59-f and 21-m) APS patients (pts) 24 pts had PAPS and 56 pts had APS following SLE. In the whole study group the mean age was: 39.3 ± 12.7 years (range 18-71), the duration of the disease was 8.8 ± 8.3 years (range 0-37).

The presence of aPL was detected in patients' serum using the commercially available tests: aPL-immunodot assay Anti-Phospholipid 10 Dot, for the qualitative detection of IgG or IgM antibodies. The statistical data analysis was performed using Statistica v13.0

Results: In the study group of 80 patients we have detected the presence of the following aPLs: a- cardiolipin IgM -37%, IgG -50.6%; a-phosphatidic acid IgM -19.7%, IgG -13.3%; a-phosphatidylcholine IgM and IgG -1.2%; a-phosphatidylethanolamine IgM -1.2% and IgG -0%; a-phosphatidylglycerol IgM - 5.0%, IgG -12.5%; a-phosphatidylinositol IgM-10.0%, IgG-12.5%; a-phosphatidylserine IgM-31.0%, IgG-50.6%; a-annexin V IgM -20%, IgG -10%; a- β -GP I IgM-44.5%, IgG-35.0%; a-prothrombin IgM -44.5%, IgG-30%.

Table 1

	PAPS n=24	SAPS n=56	P<0.05
aCL IgM aCL IgG	10 (41.6%)	20 (35.7%)	NS
a-phosphatidic acid IgM a-phosphatidic acid IgG	10 (41.6%) 8(33.3%) 3 (12.5%)	31 (55.3%) 8(14.3%) 8 (14.3%)	NS P=0.0515 NS
a-phosphatidylcholine IgM a-phosphatidylcholine IgG	0(0%) 0(0%) 0(2.2%)	1(1.8%) 1(1.8%) 0(0%)	NS NS NS
a-phosphatidylethanolamine IgM a-phosphatidylethanolamine IgG	0(0%) 0(0%)	0(0%) 0(0%)	NS NS
a-phosphatidylglycerol IgM a-phosphatidylglycerol IgG	2 (8.3%) 3 (12.5%)	2 (3.6%) 7 (12.5%)	NS NS
a-phosphatidylinositol IgM a-phosphatidylinositol IgG	5 (20.8%) 3 (12.5%)	3 (5.4%) 7 (12.5%)	P=0.0345 NS
a-phosphatidylserine IgM a-phosphatidylserine IgG	11 (45.8%) 12 (50.0%)	14 (25.0%) 29 (51.8%)	0,0655 NS
a-B2GPI IgM a-B2GPI IgG	17 (70.8%) 7(29.2%)	12 (28.6%) 21 (37.5%)	P=0,0004 NS
a-annexin V IgM a-annexin V IgG	6 (25.0%) 2 (8.3%)	10 (17.9%) 6(10.7%)	NS NS
a-prothrombin IgM a-prothrombin IgG	16 (66.7%) 8 (33.3%)	20 (35.7%) 16 (28.6%)	P=0.0108 NS

Table 2

Clinical symptoms	PAPS n=24	SAPS n=56
stroke	3 (12.5%) NS	5 (9.0%)
pulmonary embolism	6 (25.0%)	7 (12.5%)
thrombosis	14 (58.3%) NS	19 (34.0%)
obstetric complications	3/ (18.9%) NS	12/ (28.0%)
valve defects	4 (16.7%) NS	8 (14.3%)
livedo reticularis	2 (8.3%) NS	7 (12.5%)
nephropathy	5(20.8%) NS	19 (34.0%)
deep vein thrombosis	14 (58.3%) P=0,0422	19 (34.0%)
hypertension	12 (50.0%) NS	23 (41.0%)
convulsions/chorea	0(0%) NS	5 (8.9%)
migraine	1(0%) NS	4 (8.9%)
depression	1(4.2%)	2 (3.6%)

The following clinical symptoms of APS were also present: stroke -10%, arterial/venous thrombosis -34%, pulmonary embolism-16.3%, obstetric complications-25.4%, nephropathy - 30.0%, hypertension-43.8%, valve defects 15.0%, livedo reticularis 11.2%, convulsions/chorea-6.2%, thrombocytopenia- 23.7% of the study group.

During the study we detected statistically significant differences in the frequency of occurrence of aPLs between groups with PAPS and SAPS: a-phosphatidylinositol p=0,0345; a- β -GP I IgM p=0.004; a-prothrombin IgM p=0.0108 a-phosphatidic acid IgM p=0.045 (table 1)

There are no differences in the assessed clinical symptoms between pts with PAPS and SAPS, apart from significantly higher frequency of the deep vein thrombosis in pts with PAPS (p- 0.04).

Conclusion: The clinical pictures of PAPS and SAPS are similar. Only deep vein thrombosis occurs more frequently in pts with PAPS.

Some classic and novel aPLs occur more frequently in pts with PAPS than in SAPS, and maybe could become a biomarker of PAPS

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AB0178 TRANSCRIPTION PROFILING OF PERIPHERAL B CELLS IN ANTIBODY-POSITIVE PRIMARY SJÖGREN'S SYNDROME REVEALS INTERFERON SIGNATURE AND UPREGULATED EXPRESSION OF GENES WHICH MAY BE PREDICTIVE OF TRANSFORMATION TO LYMPHOMA AND CORRELATED TO CHRONIC PULMONARY NON-TUBERCULOUS MYCOBACTERIAL (NTM) INFECTION

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Background: Primary Sjögren's syndrome (pSS) is the second most common systemic autoimmune disease (after RA), with a prevalence of about 0.5% in the general population and it occurs primarily in women at a ratio of women to men of 9:1. Key features of the disease include infiltration of salivary and lacrimal glands by lymphocytes, production of inflammatory cytokines, and the production of auto-antibodies. Nevertheless, systemic manifestations can arise in a proportion of pSS with pulmonary manifestation and higher incidence of NTM infection. Also, B-cell non-Hodgkin lymphoma (NHL) development represents a severe complication, afflicting approximately 5% of patients. The risk of NHL occurrence in the setting of pSS, has been previously estimated to be 7-19 fold higher than the general population. B activation is one of the proposed hypotheses, that accord with the known biological findings, including hypergammaglobulinemia, presence of auto-antibodies including SSA/Ro60/TROVE2, SSA/Ro52/TRIM21 and SSB/La48.

Objectives: B cells play a key role in the pathogenesis of pSS. The aim of this study was to analyze the transcriptome of B cells from patients with pSS and healthy controls to decipher the B cell-specific contribution to pSS.

Methods: RNA of negatively selected B cells from 5 ANA, SSA (both Ro60 and Ro 52), SSB and rheumatoid factor positive untreated female patients with pSS and 5 healthy controls was subjected to whole transcriptome sequencing. A false discovery rate corrected significance threshold of a < 0.1 was applied to define differential gene expression.

Results: RNA-sequencing identified 56 and 23 up and down differentially expressed genes, respectively, and hierarchical clustering showed a clear separation between the two groups. Ingenuity Pathway Analysis revealed that these genes may play a role in interferon signaling (IFIT3, IFIT1, OAS1, MX1, STAT2, IFI35, IFITM1, ISG15, IFI27, IFI44L, IFI44, and PARP9), chronic mycobacterial infection (IFI35,IFI44,IFI44L,IFIT1,IFIT3,IFITM1,MX1,OAS1,OAS2,OAS3, STAT2) and transformation to myeloproliferative disorders, especially B cell lymphomas (CD160, CD38, ENAM, FUT4, GADD45B, IFI35, IFI44, IFI44L, IFIT3, IFITM1, ISG15, JCHAIN, MX1, OAS1, OAS2, OASL, RGS16, RNF213, RSAD2, SARS2, SATB1, SMAD7, and STAT2).

Conclusion: Upregulated expression of type I and type II interferon (IFN)-induced genes was observed, establishing an IFN signature in pSS B cells. There are also genes that may play a role in other concomitant conditions like mycobacterial/NTM infection and higher risk for developing myeloproliferative conditions. This adds insight into the autoimmune process and suggests potential targets for future functional and prognostic studies.

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AB0179 THE TRANSCRIPTION FACTORS IKZF1 AND IKZF3 CONTROL B CELL ACTIVATION AND DIFFERENTIATION IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The transcription factors *IKZF1* (Ikaro) and *IKZF3* (Aiolos), essential for the maturation, differentiation and survival of B cells, have been linked to Systemic Lupus Erythematosus (SLE). The cereblon modulator Ibrutinib, which induces degradation of *IKZF1* and *IKZF3*, is undergoing clinical trials in SLE. However, the role of *IKZF1* and *IKZF3* in aberrant plasmablast development and pathogenesis of SLE has not been fully elucidated.

Objectives: To assess the mechanism of *IKZF1* and *IKZF3* control of gene expression underlying activation and differentiation of B cells in SLE patients.

Methods: CD19⁺ B cells were isolated from the peripheral blood of patients with SLE recruited at Barts Health NHS Trust (n=25). B cells were cultured for 5 days and stimulated with IL-2, IL-10, IL-15, CD40L and TLR-7 ligand Resiquimod to induce plasmablast differentiation together with ibrutinib (10 nM) or control at either day 0 or 18h prior to harvest at day 4. At day 5, cells were harvested for fluorescence-activated cell sorting (FACS) and measurement of IgG and IgM in supernatants by ELISA. RNA extraction and RNA-sequencing were performed on FACS-sorted CD27⁺IgD⁺ naïve B cells and CD20^{low}CD27⁺CD38⁺ plasmablasts and matched baseline B cells.

Results: Ibrutinib from day 0 (n=9) significantly reduced the number of CD20^{low}CD27⁺CD38⁺ plasmablasts (number of sorted CD20^{low}CD27⁺CD38⁺ plasmablasts mean±SD 48727±86122 in untreated, 3248±8335 in ibrutinib, p=0.03). Accordingly, ibrutinib significantly inhibited the production of IgM and IgG from SLE B cells (p=0.017 and 0.050, respectively). Ibrutinib given at day 4 did not affect the numbers of plasmablasts or the production of IgM and IgG (n=16). However, ibrutinib induced a significant modulation of several genes both in naïve B cells and plasmablasts, as assessed by RNA-seq on sorted cells (400 and 461 differentially modulated genes in naïve B cells and plasmablasts, p adjusted <0.05). Pathway analysis showed that ibrutinib treatment resulted in downregulation of JAK-STAT signalling downstream of IL12 (FDR=7.92E-04), IL12 signalling (FDR0.0014), and p53 signalling regulation of cell death (FDR=0.0043) and showed a trend to upregulation of RUNX1 signalling and Rho GTPase cycle.

Conclusion: Our work confirms the importance of *IKZF1* and *IKZF3* in modulating gene expression required for B cell differentiation in SLE, as shown by the ability of ibrutinib to inhibit the differentiation of SLE B cells into plasmablasts. Inhibition of *IKZF1* and *IKZF3* modulated the expression of several transcriptional programmes in naïve B cells and plasmablasts. While larger scale analysis will be needed to confirm the functional consequences of *IKZF1* and *IKZF3* modulation in naïve B cells and plasmablasts, our results confirm their relevance in SLE as important regulators of B cell activation and differentiation.

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AB0180 VALIDATION OF COMPLEX IMMUNOPHENOTYPING STRATIFICATION OF PATIENTS WITH LUPUS AND SJÖGREN'S SYNDROME WITH THERAPEUTIC POTENTIAL

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Background: There is a current paucity in effective treatments for patients with primary Sjögren's syndrome (pSS) and systemic lupus erythematosus (SLE). Their overlapping symptoms mean that they are often treated with similar biologic therapeutics, despite being distinct diagnoses. Our pilot research sought to stratify patients by novel, complex immune signatures, to potentially facilitate a more personalised approach to prescribing medication, irrespective of clinical diagnosis. From a cohort of 40 patient patients with SLE, pSS or combined SS/SLE, and 33 healthy controls; five distinct clusters were originally identified.

Objectives: Here we aimed to validate the original patient endotypes from our pilot data with a new patient cohort, and refine the identified clusters to be of more realistic clinical benefit.

Methods: A new cohort of patients with SLE (n=32), pSS (n=31) and SS/SLE (n=15) donated peripheral blood samples while attending appointments at UCLH clinics. None had received B-cell depletion therapy in the preceding 48 months. Complex phenotyping of peripheral T and B-cell subsets was performed by flow cytometry. Unsupervised clustering, statistical comparison to healthies and Receiver Operator Characteristic (ROC) analysis, as per our previous work, were used to stratify patients using immune signatures into distinct endotypes considering only those markers where sensitivity and specificity were above 80% (AUC>0.80). Characteristics of new clusters were compared with previous findings to refine the number of markers and unique groups.

Results: Five distinct endotypes across the three disease groups were identified after unsupervised clustering of CD19+ B-cell, CD4+ and CD8+ T-cell subsets. Two of these clusters serve to validate groupings from our original data- one with a distinct B cell fingerprint (Bm1, IBm5 and Total CD19+) with AUC=0.87, AUC=0.81 and AUC=0.83 respectively, and another with a T cell fingerprint (Total CD4+, Total CD8+, CD8+ naïve, CD8+ effector memory T cell subsets) with AUC>0.80 for all of them. Clinical diagnoses and symptoms treatment did not differ significantly between clusters.

Conclusion: Our results demonstrate a novel method to re-classify patients using clustered immune phenotype abnormalities. Two distinct groups demonstrated either B or T-cell immunophenotypes, likely reflective of their underlying immunopathogenesis. Stratification by patient endotype has the potential to facilitate a better-informed selection of biologic therapeutics for individual patients; and highlights pathways for further mechanistic research.

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AB0181 ASSOCIATION BETWEEN SINGLE NUCLEOTIDE POLYMORPHISMS (SNPS) OF THE BAFF GENE AND FATIGUE IN PRIMARY SJÖGREN'S SYNDROME

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Background: Primary Sjögren's Syndrome (SS) is characterized by B lymphocyte hyperactivity with B cell activating factor (BAFF) acting as an important regulator. Single Nucleotide Polymorphisms (SNPs) of the *BAFF* gene have been implicated in the pathogenesis of several autoimmune diseases including lupus and SS both of which are characterized by heightened fatigue levels, often compromising quality of life.

Objectives: To explore potential associations between several *BAFF* gene SNPs and fatigue status experienced by primary SS patients.

Methods: Fatigue status was assessed by Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F) scale in 178 primary SS patients. Five SNPs (rs9514827, rs1041569, rs9514828, rs1224141, rs12583006) of the *BAFF* gene were tested in DNA extracted from peripheral blood of all patients enrolled in the study using the RFLP-PCR method. A cut-off value of <30 was used, which indicates severe fatigue. Analysis of *BAFF* SNPs in association with fatigue levels was performed by the online platform SNPStats.

Results: The frequency of T/T genotype of both rs9514828 and rs1224141 was reduced in primary SS patients with severe fatigue compared to those without