sion of Gr-1 negative monocytes, also perivascular inflammatory cell infiltration in lungs. But they did not show any pathogenic autoantibodies. When introducing *Yaa* mutation, *Slam*^{129}.*Yaa* mice showed significant increase the serum levels of anti-RNP antibodies and anti-Sm antibodies. Although they showed significant increase of serum levels of IgM class anti-dsDNA antibodies, they did not show the elevation of IgG class anti-dsDNA antibodies. Also they developed nephritis but the pathological score was significantly lower than B6.FcγRIIB-/-.*Yaa* mice.
Conclusions: Autoimmune-prone SLAM haplotype plays a role for Gr-1 negative monocytosis and *Slam*^{129}.*Yaa* mice developed specific lupus phenotype with elevation of anti-RNP and anti-Sm autoantibodies.
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AB0141 LOW DOSE IL-2 CIRCUMVENTED MTOR SIGNALING IN T CELLS IN THE TREATMENT OF SLE

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Background: mTOR signaling is proved to be one of the most important pathway in the pathogenesis in SLE. However, in patients with SLE, whether mTOR pathway can be activated by low-dose IL-2 remained unclear.
Objectives: To clarify the effects of low-dose IL-2 therapy on mTOR signaling in the treatment of SLE.
Methods: Eight patients with active SLE were treated with 1 million IU IL-2. Phophrylation of S6 ribosomal protein (S6RP), AKT and pSTAT5 were measured before and after the first 2 week of low-dose rhIL-2 administration. C57BL/6 mice (male, 8–12 weeks old) were intraperitoneally immunized with SRB and followed by administration of different doses (low:10,000 IU and hight:300,000 IU) of rhIL-2 or PBS from day 3 to day 9. The ratio of Th1, Th2, Tfh, Th17, Tfh and Treg as well as the level of S6RP, AKT and pSTAT5 were assayed by flow cytometry
Results: Low-dose IL-2 was efficient and well tolerated in active SLE, and was associated with expansion of Treg cells ($p<0.001$) and reductions of Tfh and Th17 cells ($p\leq0.001$). No significant change of pS6RP and pAKT was observed. On the other hand, there was a signficiant induction of the activation of STAT5. In mouse studies, low-dose IL-2 inhibited the differentiation of Th17 cells and Tfh cells. Comparing with high dose IL-2 group, there was no significantly increased mTOR activity after low-dose IL-2 administration.
Conclusions: Low-dose IL-2 might circumvent mTOR pathway and play a regulatory role in the T cells in lupus
Disclosure of Interest: None declared
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AB0142 IGM ANTIBODIES AGAINST PHOSPHORYLCHOLINE PROMOTE POLARIZATION OF T REGULATORY CELLS FROM PATIENTS WITH ATHEROSCLEROTIC PLAQUES, SYSTEMIC LUPUS ERYTHEMATOSUS AND HEALTHY DONORS: A NOVEL IMMUNOLOGICAL CONCEPT

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Background: IgM antibodies against Phosphorylcholine (anti-PC) are negatively associated with atherosclerosis, cardiovascular disease (CVD) and systemic lupus erythematosus (SLE) where the risk of CVD and atherosclerosis is very high. We here study effects of IgM anti-PC on Th17 and T regulatory cells (Tregs).
Objectives: Immunomodulation in atherosclerosis and SLE could have a huge impact on disease prevention and treatment.
Methods: Mononuclear leukocytes were isolated from peripheral blood (PBMC) obtained from healthy blood donors, from six SLE patients with age- and sex-matched controls and from symptom-giving human atherosclerotic plaques. The proportion of Th17 ($CD4^+CCR6^+$) and Treg ($CD4^+CD25^+CD127^{dim/-}$) cells were determined by flow cytometry in $CD4^+$T cells after 6 days culture with Th17 or Treg-polarizing cytokines, with PMA and Ionomycin stimulation. IgM anti-PC were extracted from total IgM, with flow-through IgM as controls. Dendritic cells (DC) were differentiated from PBMC. Antibody peptide/protein characterization was done by a proteomics de novo sequencing approach.
Results: IgM anti-PC increased significantly the proportion of Tregs from healthy donors, SLE patients and from atherosclerotic plaque cells while control antibodies did not. T cells from SLE patients had a significantly lower proportion of Tregs and higher proportion of Th17 cells as compared to matched controls. IgM anti-PC but not control antibodies significantly reduced production of IL-17 and TNF-alpha in cell culture from SLE patients and from atherosclerotic plaque cells. IgM anti-PC interacted with CD40 and kept DCs in an immature stage potentially being tolerogenic. We identify differences on the IgM peptide expression level in anti-PC compared to control antibodies.
Conclusions: IgM anti-PC increase Tregs and having low levels could contribute to both SLE and atherosclerosis (and CVD) and could thus represent a novel underlying mechanism in these conditions. This finding could also have therapeutic implications.
Disclosure of Interest: None declared
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AB0143 IMMUNOMODULATION FOLLOWED BY QUANTITATIVE TRANSCRIPTIONAL PROFILING TO CHARACTERIZE THE FUNCTIONAL ROLE OF THE SJÖGREN'S-ASSOCIATED NCRNA AC092580.4

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Background: Despite concerted efforts to characterize dysregulated transcriptional responses observed in Sjögren's syndrome and related autoimmune disorders (both in whole blood and target tissues), the functional roles of non-coding RNAs (ncRNAs), many of which have been identified as critical players in transcriptional regulation of disease, remain poorly defined.
Objectives: In the present study, we describe ongoing efforts to functionally characterize the upregulated ncRNA identified by RNA-seq and *in silico* approaches, *AC092580.4* (FC=2.54), which we hypothesize plays a role in T and NK cell responses.
Methods: To study the immunomodulation of the ncRNA *AC092580.4*, we carried out a time-course experiment (0–36 hrs) using either PMA/I (500x dil) or universal Type I Interferon. Relative gene expression changes were determined using the Livak method by qPCR using optimized primers for *GZMA* and *AC092580.4* normalized to *GAPD*. Healthy PBMCs were subjected to stimulation by PHA (1mg/mL; 3 days), PMA/I (500x dil; 3 days), or anti-CD3/CD28 ($50uL/1x10^6$cells; 1 day). An average 150-bp RNA-seq reads were generated for each sample; alignment was carried out using STAR (hg38) and comparisions of stimulated vs unstimulated cells were done using DEseq. Pearson's correlation (r) was calculated for all 3,748 differentially expressed (DE) transcripts to identify transcripts co-expressed with *AC092580.4*.
Results: Of the transcripts showing DE in our SS RNA-seq study, we identified 8 as having significantly correlated expression with *AC092580.4* in the SS^{Ro-} expression matrix ($r>0.70$ or <-0.65). To understand the possible effects of immunomodulation on relevant cells, we stimulated HSB-2 cells with PMA/I at various time points and assessed *AC092580.4* expression by. We observed downregulation of *AC092580.4* and the co-expressed transcript *GZMA* by PMA/I (trough: 12–16hrs; FC=0.09) followed by slow recovery at 36hrs (FC=0.59). To characterize these transcriptional changes further, we performed RNA-seq using healthy PBMCs exposed to various T cell stimulants. We observed marked upregulation of both *AC092580.4* and *GZMA* at 24/36hrs by all stimulants (FC=4.89–5.98). Other transcripts showed variable responses. *CAV2* is upregulated by PMA/I, but downregulated by CD3/CD28 and PHA. Stimulation by PHA leads to upregulation of *CD3D* (FC=1.56) and *SNRPD1* (FC=3.28) with little change in *RPL36A* (FC=1.09). Stimulation by CD3/CD28 similarly leads to upregulation of *CD3D* (FC=2.85) and *SNRPD1* (FC=10.04), but clear downregulation of *RPL36A (*FC=0.64*)*. We assessed *AC092580.4* expression in HSB-2 cells exposed to I IFN and observed initial upregulation (6hrs, FC=1.46) followed by gradual downregulation (36hrs, FC=0.18).
Conclusions: In the present study, we have initiated stimulation studies with to understand the immune relevance of *AC092580.4* and co-expressed targets. *AC092580.4* shows transcriptional induction by potent inducers of T cell responses (PMA/I, PHA, CD3/CD28) but is downregulated by type I IFN. Transcripts showing co-expressed with *AC092580.4* by whole-blood RNA-seq show divergent expression patterns according to the specific stimulus, suggesting a complex regulatory network governing dysregulated T and NK responses.
Disclosure of Interest: None declared
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AB0144 PREGNANCY OUTCOMES IN IMMUNE-MEDIATED RHEUMATIC DISEASES: A RETROSPECTIVE LONGITUDINAL STUDY IN A TERTIARY HOSPITAL

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Background: Autoimmune rheumatic diseases such as systemic lupus erythematosus (SLE), antiphospholipid antibody syndrome (APS) and Sjögren's syndrome (SS) are part of a clinical spectrum eligible to affect women in child-bearing ages, increasing pregnancy morbidity and affecting neonatal outcomes. Pregnancy complications include the teratogenic risk from immunosuppressive drugs, pregnancy-related disease flares, recurrent pregnancy loss, premature

delivery, intrauterine growth restriction (IUGR) and preeclampsia. Conceiving in periods of low disease activity helps to reduce these complications.
Objectives: This project aims to describe the occurrence of pregnancy complications among women with immune-mediated rheumatic diseases and to study the associated clinical factors.
Methods: A retrospective longitudinal study was performed including consecutive pregnant women with immune-mediated rheumatic diseases seen in a multidisciplinary group for autoimmune diseases during pregnancy, in a tertiary hospital, between January 2010 and December 2015. Clinical and demographic data, as well as and pregnancy outcomes, were collected through consultation of clinical files. The factors associated with pregnancy manifestations (premature delivery, flares during pregnancy, recurrent pregnancy loss and foetal growth restriction) were studied using Mann-Whitney, qui-square and fisher tests (SPSS 24.0). Significance level was set as <0.05.
Results: We included 151 gestations from a total of 140 women with a mean age of 32,5±4,4 years; 4 gestations were twin pregnancies. Within these 151 gestations, 54 (35,8%) women had SLE, 17 (11,3%) had Sjögren's syndrome, 17 (11,3%) had rheumatoid arthritis, 41 had APS (27,2%), 11 (7,3%) had Behçet's disease, 4 (2,6%) had systemic sclerosis, 8 (5,3%) had mixed connective tissue disease and 16 (10,6%) had other immune-mediated diseases. 35 (23,2%) had anti-SSA/La antibodies, 18 (11,9%) had anti-SSB antibodies, 6 (4,0%) had anti-URNP antibodies and 43 (28,5%) had anti-nuclear antibodies. Seven (4,6%) of the women developed gestational diabetes and 4 (2,6%) developed gestational hypertension. Furthermore, 54 (35,8%) women had had previous miscarriages. Prematurity occurred more frequently among neonates with IUGR (53.8% vs 46.1%; p=0.04), and was associated with gestational diabetes (21.4% vs 2.9%; p=0.018). It also occurred more frequently in multiple pregnancies (75% vs 16.4%; p=0.001), mothers taking glucocorticoids (28.6% vs 9.2%; p=0.003) and active rheumatic disease at conception (23% vs 6.8% p=0.03). No statistically significant differences were observed in the occurrence of different pregnancy complications among different diseases or in presence of different antibodies.
Conclusions: Our study proved a link between immune-mediated rheumatic diseases and specific pregnancy outcomes such as prematurity and IUGR. Outcomes were worse when taking glucocorticoids, when gestational diabetes were developed and when conception occurred in a period of active disease.
Disclosure of Interest: None declared
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AB0145 TLR4 SIGNALING PATHWAY MEDIATES THE SENESCENCE OF BONE MARROW- MESENCHYMAL STEM CELLS FROM SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Previous studies of our research group revealed the senescence of bone marrow-mesenchymal stem cells from systemic lupus erythematosus patients,which participated in the development of SLE. "Inflammatory microenvironment" played a very important role in cellular senescence. In the preliminary experiments, we discovered the level of HMGB1 in serum and Peripheral blood mononuclear cells from SLE patients was higher than those of The healthy control group.
Objectives: The aim of this study was to investigate whether HMGB-1 can lead to senescence BM-MSCs from SLE patients and its possible mechanism.
Methods: Tewelve female SLE patients and healthy subjects were enrolled in the study. All patients were females, and their age distribution was similar to that of the cases. All BM-MSCs were Isolated by density gradient centrifugation. Western Blotting and immunofluorescence were used to distinguish the difference of expression and localization of TLR4 signaling pathway between normal group and SLE group. Different concentrations (0.01,0.1,1,10ug/ml) of HMGB-1 (the endogenous ligand of TLR4) stimulated normal BM-MSCs, then detecting expression of TLR4 signal by WB, observing the activity of β-gal of cells, the changes of cytoskeletal structure by F-actin staining and the distribution of cell cycle by flow cytometry. We used small interfering RNA (siRNA) to interfere the expression of TLR4.
Results: BM-MSCs from SLE patients showed prominent features of senescence, characterized by impaired capacities of proliferation, increased SA-β-gal activity, and disordered cytoskeleton distribution, and abnormal activation of TLR4 signaling transduction, high level of phosphorylated p65. IκBα. After stimulation of HMGB1 in normal MSCs,TLR4 signaling was activated. And, the cell volume and the number of SA-β-gal positive in SLE BM-MSCs was increased. The organization of cytoskeleton was neatly disordered. The rate of cell proliferation was decreased. The inhibitors of HMGB-1 and small interfering RNA (siRNA) of TLR4 can significantly reverse the senescence.
Conclusions: HMGB-1 binded to TLR4, and by activating MyD88/IRAK/TRAF pathway, promoted NF-κB signal transduction, thereby affected the expression of cell cycle-related proteins, and then resulted in senescence of MSCs from SLE patients.
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AB0146 INVOLVEMENT OF PERIPHERAL CD8 T CELL SUBSETS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Although the mainstream of pathogenesis of systemic lupus erythematosus (SLE) is thought to be interactions between antigen-presenting cells like dendritic cells, helper T cells, B cells and cytokines, previous reports suggested CD8 T cells also involve in the pathogenesis of SLE[1,2]. However the associations between subsets of CD8 T cells and clinical manifestations remains unclear.
Objectives: We conducted standard immunophenotyping analysis with peripheral blood from SLE patients and focused on CD8 T cell subsets to elucidate the association with clinical phenotype and serological markers.
Methods: Peripheral blood was obtained from inactive SLE patients and healthy subjects as controls and also from active SLE before and 3 months after treatment. CD8 T cell subsets were measured by flow cytometry with fresh whole blood samples.
Results: Thirty-four active SLE patients and 38 inactive patients and 22 healthy controls (HCs) whose age and sex were matched with those in SLE patients were enrolled. Mean SLE disease activity index (SLEDAI) was 14.2 and 1.8 in active and inactive patients, respectively. Among CD8 T cell subsets, the proportion of HLA-DR+ cells was significantly higher in SLE patients than HCs and positively correlated with SLEDAI (p=0.016, rho =0.283), and was also higher in patients with nephritis than patients without nephritis (p=0.074), though it did not reach statistical significance. The proportion of naive CD8 T cells positively correlated with the titer of anti-dsDNA antibody (p=0.011, rho =0.30) and C1q immune complex levels (p=0.043, rho =0.25), and negatively correlated with serum complement levels (p=0.019, rho = -0.34). The proportion of central memory CD8 T cells (Tcm) negatively correlated with SLEDAI ($p<0.001$, rho = -0.43), the titer of dsDNA antibody ($p<0.001$, rho = -0.51) and C1q immune complex levels ($p<0.001$, rho = -0.44), and positively correlated with serum complement levels ($p<0.001$, rho =0.49), and was lower in the patients with nephritis (p=0.041), skin rash ($p<0.001$), and fever (p=0.002) than the patients without them. The proportion of effector memory CD8 T cells (Tem) was lower in SLE and negatively correlated with the titer of anti-dsDNA antibody (p=0.028, rho = -0.26). Sixteen active patients were treated with prednisolone (PSL) 50mg (mean) with concomitant immunosuppressant; eight were treated with cyclophosphamide. Mean SLEDAI decreased from 15.9 to 3.9 at 3 months after the treatments. The proportion of naïve CD8 T cells significantly decreased (p=0.003), and the proportions of HLA-DR+ cells and Tem increased at 3 months (p=0.011 and p=0.007, respectively). The proportion of Tem increased and negatively correlated with SLEDAI only with those who were treated with cyclophosphamide.
Conclusions: Pathological state of SLE positively correlated with the proportion of naïve CD8 T cells and negatively correlated with the proportion of Tem and these subsets were affected by treatment with PSL and immunosuppressant particularly cyclophosphamide. These results indicate that CD8 T cells are involved in pathophysiology and could potentially become a biomarker or a treatment target in SLE patients.
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AB0147 THE EFFECT OF TREATMENT WITH HYDROXYCHLOROQUINE ON SOLUBLE TISSUE FACTOR LEVELS IN PATIENTS WITH ANTIPHOSPHOLIPID ANTIBODIES AND ANTIPHOSPHOLIPID SYNDROME WITH AND WITHOUT UNDERLYING SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Antiphospholipid syndrome (APS) is characterized by venous, microvascular and/or arterial and/or obstetric morbidity (obstetric APS) in patients who are persistently positive for antiphospholipid antibodies (aPL)[1]. The mainstay of treatment is based on anticoagulation therapy; however, increasing interest is currently received by the antimalarial hydroxychloroquine (HCQ). The use of HCQ has been associated with a reduced risk of thrombosis but HCQ's antithrombotic mechanism of action is unclear particularly in patients with aPL and APS.
Objectives: The aim of our study was to assess soluble tissue factor (TF) levels in HCQ naïve-patients with persistent aPL or APS at baseline and 12 weeks after commencing HCQ. We hypothesise that HCQ lowers levels of soluble TF.