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.Fc$\gamma$RIIB-/-.*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.
**References:**
[1] Sato-Hayashizaki A, Ohtsuji M, Lin Q, Hou R, Ohtsuji N, Nishikawa K, Tsurui H, Sudo K, Ono M, Izui S, Shirai T, Takai T, Nishimura H, Hirose S. Presumptive role of 129 strain-derived Sle16 locus in rheumatoid arthritis in a new mouse model with Fc$\gamma$ receptor type IIb-deficient C57BL/6 genetic background. Arthritis Rheum. 63(10):2930–8, 2011.
[2] Kawano S, Lin Q, Amano H, Kaneko T, Nishikawa K, Tsurui H, Tada N, Nishimura H, Takai T, Shirai T, Takasaki Y, Hirose S. Phenotype conversion from rheumatoid arthritis to systemic lupus erythematosus by introduction of Yaa mutation into Fc$\gamma$RIIB-de ficient C57BL/6 mice. Eur J Immunol. 43:1–9, 2013.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2017-eular.4175

## AB0141 LOW DOSE IL-2 CIRCUMVENTED MTOR SIGNALING IN T CELLS IN THE TREATMENT OF SLE

J. He[1], X. Sun[1], J. Li[1], R. Zhang[1], D. Yu[2], Z. Li[1]. *[1]Peking University People's Hospital, Beijing, China; [2]School of Biomedical Sciences, Monash University, Melbourne, Australia*

**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
**DOI:** 10.1136/annrheumdis-2017-eular.3482

## 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

J. Sun, S. Lundström, B. Zhang, R. Zubarev, J. Steuer, P. Gillgren, M. Rahman, S. Ajeganova, A. Liu, J. Frostegård. *Karolinska Institutet, Stockholm, Sweden*

**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
**DOI:** 10.1136/annrheumdis-2017-eular.5076

## AB0143 IMMUNOMODULATION FOLLOWED BY QUANTITATIVE TRANSCRIPTIONAL PROFILING TO CHARACTERIZE THE FUNCTIONAL ROLE OF THE SJÖGREN'S-ASSOCIATED NCRNA AC092580.4

J.A. Ice, I. Adrianto, A. Rasmussen, M. Joachims, A. Johnston, C. Montgomery, K. Sivils, C.J. Lessard. *Arthritis & Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, United States*

**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
**DOI:** 10.1136/annrheumdis-2017-eular.6872

## AB0144 PREGNANCY OUTCOMES IN IMMUNE-MEDIATED RHEUMATIC DISEASES: A RETROSPECTIVE LONGITUDINAL STUDY IN A TERTIARY HOSPITAL

J. Bernardo[1], I. Brito[1], H. Guimarães[2], M. Guimarães[3], R. Fonseca[1]. *[1]Rheumatology; [2]Pediatrics; [3]Gynecology and Obstetrics, Faculty of Medicine of the University of Porto, Porto, Portugal*

**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