foetuses exposed to maternal anti-Ro52 autoantibodies. Recent studies investigating other pathogenic autoantibodies (anti-interferon, anti-desmoglein) report that they arise as a result of somatic mutation. The aim of this study was to determine how anti-Ro52 autoantibodies originate.

Methods We traced the evolution of two anti-Ro52 autoantibodies isolated from circulating IgG-switched memory B-cells from a mother of two children with cardiac neonatal lupus. Each antibody was expressed as its immune form or pre-immune ancestor by reverting somatic mutations to germline sequence. Antibody reactivity against autoantigens Ro52, Ro60, La and dsDNA were tested by ELISA.

Results Both anti-Ro52 autoantibodies utilised the same heavy and light chain genes (*IGHV3-23* and *IGLV1-44*) but represented distinct clones based on differing complementarity determining region sequences. Anti-Ro52 autoantibodies exhibited a low frequency (3%–4%) of somatic mutations compared to the average rate of 8% in healthy switched memory B-cells. In contrast to other pathogenic autoantibodies, the pre-immune (germlined) anti-Ro52 autoantibodies showed specific binding to Ro52. However, Ro52 reactivity was higher for the mutated post-immune antibodies compared to their pre-immune counterparts demonstrating that autoreactivity was enhanced by affinity maturation.

Conclusions These data demonstrate that Ro52 reactivity is an intrinsic property of the germline antibody repertoire in a mother of children affected by neonatal lupus and indicate defects in central and peripheral tolerance pathways allow propagation of pathogenic autoantibodies.

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55   **RESPONSE GENE TO COMPLEMENT-32 PROMOTES PLASMA CELL DIFFERENTIATION AND ENHANCES LUPUS-LIKE CHRONIC GRAFT VERSUS HOST DISEASE**

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Background and aims Response Gene to Complement (RGC) −32 plays an important role in cell cycle activation. Our prior studies showed that RGC-32 promotes Th17 differentiation of CD4 T cells. We used wild-type (WT) and RGC-32 knockout (KO) mice to determine whether lack of RGC-32 impairs B cell differentiation and activation and alters autoimmune parameters in the chronic graft versus host disease (cGVHD) model of lupus.

Methods TLR-dependent and T dependent B cell differentiation to plasma cells (PC) was induced with LPS and with CD40mAb plus IL-4. cGVHD was induced with 100×10^6 Bm12 splenocytes injected into WT or RGC-32 KO recipients.

Results RGC-32 KO B cells failed to differentiate normally to PC as demonstrated by a 2-fold reduction in PC numbers generated after stimulation and impaired upregulation of Prdm1 and IRF4 mRNA. RGC-32 transcripts were upregulated in spleen cells from cGVHD mice and protein expression was detected in B cells and germinal centre (GC) cells. RGC-32 KO hosts displayed an attenuated autoimmune phenotype as demonstrated by decreased production of anti-dsDNA autoantibodies and proliferation of germinal centre B cells. In

addition a decreased number of IgG anti-dsDNA secreting PC and IRF4 and Prdm1 mRNA expression were found

Conclusions These results suggest that expression of RGC-32 in B cells is critical for optimal GC proliferation, PC differentiation and autoantibody production in a murine model of lupus. These data support the idea that RGC-32 blockade has the potential to attenuate autoimmune parameters of cGVHD and possibly reverse abnormalities in the T and B cell that contribute to lupus pathogenesis.

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56   **MICROMANAGING LUPUS NEPHRITIS: MIR17–92 MODULATES REGULATORY T CELL ACTIVITY BY TARGETING FOXP3 CO-REGULATORS**

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Background and aims Regulatory T (Treg) cells play a critical role in maintaining self-tolerance and controlling the magnitude of physiologic immune response. The Treg transcription factor forkhead box P3 (Foxp3) works in concert with other co-regulator molecules including Eos to determine suppressive phenotype of Treg. We identified miR17-92 cluster targeting Eos through bioinformatics approaches.

Methods We generated T-cell-specific miR-17–92 null (*mir17-92* -/-) mice by mating *mir17-92*flox/flox mutants to CD4-Cre + transgenic mice. Treg from *mir17-92* -/- mice will be isolated, followed by suppression assay to evaluate the role of the miR-17–92 cluster in Treg function. We applied pristane to induce lupus nephropathy in wild type and *mir17-92* -/- mice. We examined the up-stream promoter region of miR-17–92 for binding sites of down-stream mediators of IL-6 signalling, verified by chromatin immunoprecipitation assay.

Results The inflammatory cytokine IL-6 unregulated miR17-92 through HIF-1. MiR17-92 cluster.actively suppressed Eos expression. Knockdown of miR17-92 in Treg enhanced their suppressive activity. Mir17-92 T cell specific deficiency mitigated pristane induced-lupus nephropathy associated with diminished Th17 cells and autoantibody. Moreover, histological analysis revealed a lower mean renal histopathology score and less compliment deposition. Ectopic expression of miR-17 downmodulated the suppression functions of Tregs and provided Treg with partial effector activity via the derepression of cytokine genes.

Conclusions Our studies suggest that miR17-92 modulates Treg cell function by targeting Eos and potentially additional Foxp3 co-regulators, unveiling the future therapeutic potential of microRNA manipulation in lupus nephritis.

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57   **A HIGHER FREQUENCIES OF T HELPER 22 CELLS IN PATIENTS WITH NEW ONSET ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS**

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Background and aims This study is aimed at elucidating the potential role of Th22 cells in patients with SLE.

Methods The frequencies of Th22, Th17, Th1 cells were determined by flow cytometry of peripheral blood by the chemokine receptors or/and the intracellular cytokine from a total of 25 patients with freshly diagnosed SLE and 13 age-/gender-matched healthy controls, and the values were compared with disease activity as determined by the Systemic Lupus Erythematosus Disease Activity (SLEDAI), serum complement factors (C3, C4), C-reactive protein (CRP), Erythrocyte sedimentation rate(ESR), Immunoglobulin(Ig), anti-double stranded (ds) DNA and anti-Smith (Sm) antibodies were measured.

Results We found increased Th22, Th17 cells in SLE patients compared with those in healthy controls. The elevated Th22 positive correlated with SLEDAI, ESR, IgG and IgA. Higher frequencies of Th22 and positive correlations between the percentage of Th22 cells and Revised Cutaneous Lupus Erythematosus Disease Area and Severity Index (RCLASI) were observed in patients with lupus skin disease.

Conclusions Our data suggests that both Th22 and Th17 may participate in the pathogenesis of SLE and Th22 may migrate to skin and promote inflammation in the lupus skin impairment.

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Background and aims Interstitial lung disease (ILD) is common in systemic lupus erythematosus (SLE) patients. These patients tend to have large amounts of autoantibodies. Blood memory Tfh17 cells represent efficient B cell helper cells with distinct capacities to induce IgG and IgA secretion and to regulate immunoglobulin isotype switching. Recent study found overall Tfh17 cells are highly presented in peripheral blood of SLE patients. However, it is not clear how different subsets of Tfh17 cell are distributed in broncholalveolar lavage fluid (BAL) and peripheral blood of SLE-ILD patients. The study is to determine the proportion of different Tfh17 cell subsets (activated Tfh17: CXCR3-CCR6+ICOS+PD-1++CCR7lo, quiescent: CXCR3-CCR6+ICOS-PD-1+CCR7int and CXCR3-CCR6+ICOS-PD-1-CCR7hi) among CD4+ T cells and levels of immunoglobulins in BAL and peripheral blood of SLE-ILD patients.

Methods 30 SLE-ILD patients were included. The lung disease were proved by high resolution CT scan. Patients underwent bronchoscopy and BAL were collected. Tfh17 cell profiles were determined using flow cytometry. Levels of immunoglobulins were detected by ELISA. Statistics were analysed by SPSS 22.0.

Results IgA and IgG levels were significantly higher in BAL than in blood. Activated Tfh17 in BAL was increased significantly (p=0.011) and both subsets of quiescent Tfh17 cells were decreased (p<0.05) compared to those in the blood. The activated Tfh17 was positively correlated with IgA level (r=0.871, p=0.039) in BAL and with IgG level (r=0.714, p=0.047) in blood.

Conclusions Activated Tfh17 is more abundant in BAL than in blood and switches from IgG correlation to IgA correlation, suggesting its role in the pathogenesis of SLE-ILD.

Antiphospholipid syndrome

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Background and aims The antiphospholipid syndrome (SAPL) is an autoimmune and thrombogenic pathology that the diagnosis is based on clinical and biological criteria. It can be isolated (primary SAPL) or associated with another auto-immune disease (secondary SAPL). The purpose of this work is to finalise the epidemiological, clinical, biological, characteristic.

Methods We led a retrospective and descriptive study of the patients followed in the service of internal medicine for SAPL between January 1990 and April 2014.

Results We brought together 62 cases (61 women and 1 man). The average age was 41 years.The peripheral thromboses were observed in 51.6%. The obstetric accidents were found at 26 patients dominated by repeated abortion (35.5%) and fetal death in uterus (16.1%). The cardiac infringement was dominated by valvular disease in 9.6%. The lung demonstrations were represented by a pulmonary embolism in 32.25% and a lung arterial high blood pressure in 19.3%. The neurological infringement was present in 29%. The SAPL was primary in 32% and secondary in 86%. The CAPS was found in 2 cases. The SLE was present in 59.7%. The immunological balance sheet revealed aCL in 77.4%, anti-ß 2GPI in 24.2% and anti-PT in 17.7%. a statistically significant correlation between the obstetric and vascular sign with the presence of aCL.

Conclusions The SAPL is an entity among which the knowledge and the understanding are in permanent evolution. It is necessary to think of it in front of any vascular reccurent thrombosis to a young subject.

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Background and aims To evaluate cardiac function in primary antiphospholipid syndrome (PAPS) patients using the echocardiogram with conventional and tissue Doppler evaluations.

Methods Nine PAPS patients (Sapporo criteria) were enrolled. Demographic and clinical data, co-morbidities, medication use and antiphospholipid antibodies were evaluated. All were asymptomatic regarding cardiovascular system. Exclusion criteria were history of heart failure, coronary artery disease, arrhythmia, valve abnormalities, age >70 years old, renal failure and severe hypertension. Seven age-, sex- and race-matched healthy subjects were included as control group.