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 allowing propagation of pathogenic autoantibodies.

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.

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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 mir17-92flox/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, histologic analysis revealed a lower mean renal histopathology score and less complement deposition. Ecotropic 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.

Background and aims This study is aimed at elucidating the role of RGC-32 in B cells 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.

A higher frequencies of T helper 22 cells in patients with new onset active systemic lupus erythematosus

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.

Conclusions Activated Th17 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.