

AI-04 **HIGH TITER ANA NOT NECESSARILY A VALID CRITERION FOR LUPUS – PROPOSAL OF A MODIFICATION TO THE CRITERIA FOR CLASSIFICATION OF SLE**

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Background The 1997 Update of the 1982 American College of Rheumatology Revised Criteria for Classification of SLE includes two autoantibody criteria: #10, abnormal level of anti-native DNA, anti-Sm, or antiphospholipid; #11 positive antinuclear antibody (ANA). Thus, ANA positivity is counted as 1 of the 11 criteria and a person shall be said to have SLE if any 4 or more of the 11 criteria are present, serially or simultaneously, during any interval of observation. The immunofluorescence pattern observed in the ANA test provides a direct initial assessment of ongoing autoantibody response in candidate patients of many systemic autoimmune rheumatic diseases (SARD). As a follow-up to the International Consensus on ANA Patterns (ICAP) initiative (ANApatterns.org), which aims to promote harmonisation of ANA pattern nomenclature and provides guidelines for ANA interpretation, thereby optimising usage in patient care, the relevance of each ANA pattern is being re-evaluated.

Methods Collective issues on ANA nomenclature were raised among research, clinical, and diagnostic laboratories represented by two workshop participants and a working committee. Post-workshop exchanges arrived at consensus on a few, but clearly not all, issues. One focus is to establish an interpretative clinical description for each defined ANA pattern for clinical use based on current literature.

Results Consensus was achieved for 28 ICAP patterns designated with alpha-numeric code (AC-1 to AC-28) and summarised under a nomenclature and classification tree categorised in three major groups (nuclear, cytoplasmic, and mitotic patterns). An important observation is that, while the Homogeneous (AC-1) and Coarse Speckled nuclear (AC-5) patterns are linked to autoantibodies strongly associated with SARD, the Dense Fine Speckled (DFS) nuclear pattern (AC-2) virtually rules out a SARD diagnosis. A clear cut DFS pattern is usually present when anti-DFS70/LEDGF/P75 is the only predominant autoantibody in the serum sample. DFS is the most common pattern in high titer ANA-positive, apparently healthy, individuals. Although DFS has been reported in a wide variety of chronic inflammatory diseases, such as Hashimoto's thyroiditis, atopic dermatitis, interstitial cystitis, Vogt-Koyanagi-Harada syndrome, and in miscellaneous non-inflammatory diseases, it is not associated with SARD, even when present at very high titer.

Conclusions ICAP has clearly provided a common platform to address issues that are of great interest to the ANA community and closely linked to ANA in disease criteria. Evidently, well-defined anti-DFS ANA, confirmed by antigen-specific reflex testing, should not be considered a criterion for SLE – either in the ACR or 2012 SLICC classification criteria.

AI-05 **RESPONSE GENE TO COMPLEMENT-32 PROMOTES PLASMA CELL DIFFERENTIATION AND ENHANCES LUPUS-LIKE CHRONIC GRAFT VERSUS HOST DISEASE**

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Background Response Gene to Complement (RGC)-32 is an intracellular protein that plays a role in cell growth and promotes cell cycle activation and Akt phosphorylation. RGC-32 is also a downstream target of TGF- β in fibroblasts and renal proximal tubular cells and plays a role in renal fibrogenesis. In immune cells, RGC-32 is expressed by both T and B lymphocytes. Our prior studies showed that RGC-32 promotes Th17 differentiation of mouse CD4 T cells and is highly expressed in human IL-17 CD4 cells. Whether RGC-32 plays a role in the activation and differentiation of B cells and the development of autoimmunity is not known. We used WT and RGC-32 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.

Materials and methods B cells were cultured with lps, anti-CD40 mAb, IL-21 and IL-6, IL-4 or TGF β and RGC-32 mRNA and protein expression was determined. 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. Host B cell number and activation, anti-dsDNA Ab production, germinal centre (GC) B cell number and proliferation, PC number, expression of transcription factors IRF4 and Blimp1 were assessed at 2 and 4 weeks.

Results RGC-32 mRNA was upregulated in B cells by lps, anti-CD40 mAb, IL-21 and IL-6. RGC-32 KO B cells failed to differentiate normally to PC as demonstrated by a 2-fold reduction in PC numbers generated after lps and anti-CD40+ IL-4 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 GC cells. RGC-32KO hosts displayed an attenuated autoimmune phenotype as demonstrated by: 1) decreased production of anti-dsDNA autoAb. 2) decreased number and proliferation of GC B cells. 3) decreased number of IgG anti-dsDNA secreting PC and 4) decreased IRF4 and Prdm1 mRNA expression.

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 pathways that contribute to lupus pathogenesis.

AI-06 **DALAZATIDE, AN INHIBITOR OF THE KV1.3 CHANNEL ON ACTIVATED EFFECTOR MEMORY T CELLS, HAS IMMUNOTHERAPY POTENTIAL AGAINST SYSTEMIC LUPUS ERYTHEMATOSUS**

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