Conclusions Here using an efficient strategy to express recombinant monoclonal antibodies from single B cells we demonstrated an elevated frequency of autoreactive naïve B cells in the circulation of SS patients supporting the existence of early defects in B cell tolerance checkpoints in SS.

A5.3 ALTERATIONS ON PERIPHERAL BLOOD B CELL COMPARTMENTS IN SYSTEMIC LUPUS ERYTHEMATOSUS: RELEVANCE FOR MONITORING LUPUS ACTIVITY AND THERAPY

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Background and Objectives Despite recent insights on abnormalities of blood B cell subsets in human systemic lupus erythematosus (SLE), a peripheral blood biomarker with useful clinical information about the occurrence of an active disease period hasn't yet been achieved. Moreover, the clinical relevance of anti-dsDNA antibodies and their utility for monitoring an individual patient remains a matter of debate. In this sense, we attempt to determine whether the degree of abnormalities of circulating B cell subsets correlates with SLE disease activity and constitute an useful tool for SLE patients monitoring.

Materials and Methods We analysed by flow cytometry the major circulating B cell subsets (immature, naïve, memory and plasmablast) and their expression profile of B cell related molecules (CD19, CD20, CD81 and BAFFR) in 43 SLE patients, 18 with active and 25 with inactive disease, according to the SLE Disease Activity Index 2000 (SLEDAI, 2k), as well as in 30 healthy individuals.

Results The results pointed to the existence of significant alterations on B cell homeostasis that are significantly correlated with disease activity. An overall decrease in absolute numbers of all B cell subsets was observed in SLE patients, with the exception of IgG-plasmablast that remained equal or even higher than in the control group, particularly in active disease. Additionally, a higher number of plasmablast expressing each Ig-heavy chain isotypes was found in patients with mucocutaneous involvement. Moreover, among memory B cells, an increased IgG and decreased IgM positive cells was observed in both SLE groups.

Furthermore, a decreased expression of CD19 observed in active disease and an increased BAFFR expression in inactive disease in the majority of B cell subsets, may contribute not only for breaking tolerance during B cell development, but also for enhancing plasmablast survival.

Conclusions In conclusion, flow cytometric monitoring of circulating B cell subsets, particularly focused on relative and absolute numbers of IgG plasmablasts, could provide a useful tool for monitoring disease activity, but also the therapy efficacy in patients with SLE.

A5.4 ANTI CARBAMYLATED PROTEIN ANTIBODIES (ANTI-CARP) ARE PRESENT IN ARTHRALGIA PATIENTS AND PREDICT THE DEVELOPMENT OF RHEUMATOID ARTHRITIS

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Background/Objective Recently, we discovered a new auto-antibody system in rheumatoid arthritis (RA): anti carbamylated

protein antibodies (anti-CarP). These antibodies have additional prognostic value in predicting joint destruction when compared to anti-citrullinated protein antibodies (ACPA). However, it is not yet known whether anti-CarP antibodies are present before the diagnosis of RA and whether they have predictive value for the development of RA. Therefore we studied whether anti-CarP antibodies are present in arthralgia patients and whether their presence associates with the development of RA.

Methods Sera of 340 arthralgia patients without clinical signs of arthritis and 32 healthy controls were measured for the presence of anti-CarP IgG antibodies. One hundred eleven arthralgia patients (33%) were IgM-rheumatoid factor (IgM-RF) positive/anti-cyclic citrullinated peptide 2 (aCCP2) negative and 229 (67%) were aCCP2 positive. Patients were followed for the development of RA (2010 criteria). The median follow up time was 36 months. Cox regression analysis was performed to compare the risk of developing RA between Anti-CarP positive and negative arthralgia patients in follow up time.

Results The arthralgia cohort consisted of 340 IgM-RF and/or aCCP positive patients. Anti-CarP antibodies were present in sera of 113 (39%) of the tested patients. A total of 120 patients developed RA after a median (IQR) of 12 (6–24) months. The presence of anti-CarP antibodies was associated with the development of RA in the whole arthralgia cohort even after correction for RF and aCCP2 status (HR: 1.56; 95%CI: 1.06–2.29; p = 0.023), as well as in the aCCP2 positive subgroup (OR: 2.231; 95%CI: 1.31–3.79; p = 0.003).

Conclusions Anti-CarP antibodies were present in arthralgia patients and their presence predicted the development of RA independent of aCCP2 antibodies.

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A5.5 ANTIBODIES AGAINST DOMAIN I OF β 2 GLYCOPROTEIN I IN ANTIPHOSPHOLIPID ANTIBODY SYNDROME

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Background and Objectives antibodies anti-phospholipids (aPL) react to proteins bound to PL, mainly β 2glycoprotein I (β 2GPI). Antibodies against β 2GPI (a β 2GPI) exert a pathogenic role and represent a risk-factor for clinical manifestations of anti-phospholipid syndrome (APS). However, some a β 2GPI-positive subjects never develop APS-related clinical manifestations. This observation may be explained by the heterogeneity of a β 2GPI population, with auto-antibody subgroups targeting different β 2GPI epitopes. In particular, antibodies anti-domain I (aDI) but not domains IV and V (aDIV/V) of β 2GPI have been associated with thrombotic events. Therefore, the aim of this study was to assess the prevalence of aDI and aDIV/V IgG in a cohort of aPL-positive patients.

Material and Methods 58 patients with a diagnosis of primary APS (PAPS) according to the 2006 Sydney criteria have been included in this study. 38 PAPS patients (65.5%) presented with venous and/or arterious thrombotic events while 20 subjects (34.5%) had obstetric manifestations only. 15 aPL asymptomatic carriers were also recruited. All samples had been tested for LA and for aCL and a β 2GPI with home-made assays according to international guidelines. In the thrombotic PAPS group, 35/38 subjects (92.1%) were a β 2GPI IgG positive; a β 2GPI IgG positivity rate was 85% in the obstetric PAPS group (17/20 women); 80% of the asymptomatic aPL carriers displayed a β 2GPI IgG. IgG specificities against whole β 2GPI, DI and DIV/V have been evaluated with a novel solid-phase chemiluminiscent assay (BioFlash and ELISA, INOVA Diagnostics).