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Disclosure of Interest None declared.

P006

INVESTIGATION OF IGA IMMUNE COMPLEX CAPTURE BY FCRL4+ B CELLS IN PERIPHERAL BLOOD AND SYNOVIAL FLUID

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Career situation of first and presenting author Student for a master or a PhD.

Introduction Increasing evidence points to a mucosal origin of the autoimmune process in the development of rheumatoid arthritis. A B cell subset identified by surface expression of Fc receptor-like 4 (FcRL4) associates with inflammation in the mucosa associated lymphoid tissue.¹ Our group identified these cells in the synovium of RA patients.² They express high levels of RANKL and participate in the autoimmune response to citrullinated proteins.^{3–4} Recent *in vitro* work suggested that FcRL4 may be a low-affinity receptor for aggregated IgA.⁵ FcRL4 +B cells in RA SF express low levels of CD21 and high levels of CD11c, a phenotype they share with Age-Associated B cells (ABC). Very low numbers of ABC are found in blood of healthy individuals but their frequency increases with age however their exact role in RA is not yet understood.⁶

Objectives 1) Investigate the binding activity of IgA immune complexes to FcRL4⁺ B cells in tonsil, RA synovial fluid, and the peripheral blood of healthy individuals and RA patients. 2) Determine if FcRL4 can specifically capture IgA from the RA SF. 3) Examine the specificity of FcRL4 for secreted and serum IgA and for different IgA isotypes.

Methods SF, peripheral blood and tonsil mononuclear cells were labelled for FcRL4, IgA, IgG, and CD19 (PBMCs were also labelled for CD21 and CD11c) and analysed by flow cytometry. Cells pre-treated with a pH3 buffer to remove receptor-bound immunoglobulins were compared with untreated cells to distinguish IgA B cell receptor expression from receptor-bound IgA Immune complexes. An FcRL4 expressing cell line was incubated with RA synovial fluid and purified human IgA to assess FcRL4s specificity.

Results Receptor-bound IgA Immune complexes were observed on *ex vivo* RA SF and tonsil FcRL4⁺ B cells but not on FcRL4⁺ B cells (p=0.001). Intriguingly, this IgA capture was not observed in peripheral blood FcRL4 +ABC from HC or RA patients. Furthermore, the proportion of B cells with IgA BCRs was increased in tonsil and SF FcRL4 +B cells but not in peripheral FcRL4⁺ B cells, compared to FcRL4⁺ B cells. Using a cell line, we show that FcRL4 specifically binds IgA immune complexes from SF and shows a preference for IgA1 over IgA2 (p=0.02).

Conclusions FcRL4 is a receptor for IgA immune complexes in RA joints. RA SF and tonsil FcRL4 +B cells RA SF differ from peripheral blood FcRL4 +ABC in their *in vivo* capture of IgA immune complexes and in their frequency of IgA BCRs, suggesting distinct function and origin of these cells.

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P007

AUTOANTIBODIES' TITRE CHANGES DURING ANTI-BLYS TREATMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction Belimumab, a human monoclonal antibody anti-soluble B lymphocytes stimulator, is the only biological drug approved for Systemic Lupus Erythematosus (SLE). It reduces disease activity and blocks damage progression.^{1–2} Anyway, no definitive results have been published regarding its effect on autoantibodies' titre.

Objectives To analyse the modulation of anti-dsDNA, anti-ENA and anti-phospholipid antibodies' titre by Belimumab in patients affected by SLE.

Methods 50 SLE³ patients starting Belimumab were enrolled. Sera were collected at baseline (T0) and every 6 months until 24th month. Clinical features and disease activity index (namely SLEDAI-2K)⁴ were collected at any timepoints. Anti-dsDNA were analysed by radioimmunological method, anti-cardiolipin (aCL) and anti-β2 glycoprotein I (anti-β2GPI) were detected by home-made ELISA.^{4–5} Anti-ENA were detected by ELISA; positive sera were further characterized by ELISA to identify anti-Ro, anti-La, anti-ribosomal P protein (ribP), anti-Sm and anti-U1RNP specificities.

Results At T0 anti-dsDNA were positive in 86%, anti-ENA in 50%, a CL in 20% and antiβ2GPI in 28% of cases, respectively. A negative seroconversion was detected in 9/43 anti-dsDNA (21%); in 5/12 anti-beta2GPI IgG (40%) and in 3/10 aCL IgG (30%) sera, mostly at T6. Among anti-ENA specificities 6/10 (60%) anti-ribP and 3/17 (17,6%) anti-Sm positive sera became negative; while anti-Ro and anti-U1RNP antibodies resulted stable during treatment. A significant decrease of anti-dsDNA titre was observed at T6 (p 0,0011); T12 (p: 0,014); T18 (p: 0,0031) and T24 (p: 0,013). Anti-beta2GPI IgM isotype showed significant reduction at T6 (p: 0,0032), T12 (0,001), T18 (p: 0,002) and T24 (p: 0,011). ACL antibodies showed significant decrease only for IgG isotype at T18 (p: 0,001). Anti-ribP antibodies showed a significant titre decrease at T6 (p: 0,015) and T12 (p:0,0078), with complete negative seroconversion at T18. Anti-Sm antibodies significantly dropped down at T6 (p:0.032), than maintained a stable titre during time. A significant correlation between anti-dsDNA titre anti-ribP titre and between SLEDAI ratio (SLEDAI value/SLEDAI T0) and anti-ribP ratio (value/value T0) were found.

Conclusions Belimumab treatment induced a significant reduction of high-affinity anti-dsDNA, anti-Sm and anti-ribP antibodies titre. The decrease of anti-ribP titre correlates with anti-dsDNA titre and disease activity.