Objectives: We aimed to investigate the proportion and phenotype of peripheral blood ABCs in patients suffering from early drug naïve RA.

Methods: Newly presenting patients, naïve to immunomodulatory treatment, were recruited from the Newcastle Early Arthritis Clinic, and followed until diagnoses were confirmed. B-cell subsets in peripheral blood were detected and phenotyped using flow cytometry.

Results: Our work showed increased proportions of ABCs in seropositive RA compared to other inflammatory arthritis controls, highlighting a potential link between autoantibody production and ABCs. Moreover, patients with high disease activity had higher proportions of ABCs in peripheral blood. Interestingly, the FcRL4⁺, the proliferating Ki67⁺ and the T-bet expressing B cells were enriched in the ABC population compared to the other B cell subsets. Furthermore, ABCs expressed high levels of MHC class II and co-stimulatory molecules, as well as the activation marker, CD69.

Conclusions: These data supports a possible pathogenic role of ABCs in RA, potentially via autoantibody and T cell stimulatory ability, but further characterisation of this subset and functional studies are needed.

Disclosure of Interest: None declared

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THU0034 SALMONELLA TYPHI VI IGG AS A MARKER OF IMMUNOSUPPRESSION IN RHEUMATIC DISEASE

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Background: Measurement of vaccine response may be used as a diagnostic tool to aid determination of antibody deficiency. The IgG response to pneumococcal polysaccharide vaccination (PPV) is currently used to assess T cell independent responses, however additional polysaccharide vaccines are under evaluation. In patients with rheumatic diseases (RD) treatment regimens can result in immunosuppression and subsequently secondary immune deficiency (SID).

Objectives: To measure the IgG response to Typhi Vi vaccination (TV) in RD patients presenting with antibody deficiency. To correlate immunosuppression with TV responses, as well as TV responses to clinical presentations, B cells and total IgG. Further, we interpret the responses in combination with the responses to PPV.

Methods: 35 RD patients were referred for immunological evaluation at Hospital Clínico San Carlos, Madrid, Spain. The responses to TV and PPV were measured using commercial human anti-*Salmonella* Typhi Vi IgG and pneumococcal capsular polysaccharide (PCP) IgG ELISAs kits. A TV responder was defined as achieving ≥ 32 IU/mL (lower limit of the normal range), a PCP IgG responder (>50 mg/L). B cells were measured by flow cytometry (responder $\geq 6.6\%$) and total IgG by nephelometric assay (responder ≥ 600 mg/dL). For all measurements (+) indicates a responder and (-) indicates a non-responder.

Results: A greater percentage of TV- patients previously received non-biological treatment (79% vs 43%), specifically steroid treatments (68% vs 28%) and biological treatments (particularly CD20 and TNF alpha targets; 46% vs 14%). At presentation, TV non-responsiveness was associated with a higher frequency of upper respiratory tract infections (75% vs 57%), serious bacterial infections (21% vs 14%) and required slightly higher antibiotic usage (93% vs 71%).

Stratification of the RD patients using the response to the TV and PPV identified four groups of activity: TV+/PCP+, TV-/PCP+, TV+/PCP- and TV-/PCP-. In the presence of a normal response to PPV, the failure to respond to TV (TV-/PCP+) correlated with a higher frequency of previous non-biological treatment (84% vs 43%), biological treatment (47% vs 14%), steroids treatment (68% vs 29%) and were currently undergoing treatment (84% vs 29%, $p=0.01$) compared to those who responded to TV (TV+/PCP+). At presentation TV-/PCP+ patients had a greater incidence of upper respiratory tract infections (74% vs 57%), serious bacterial infections (16% vs 14%) and antibiotic usage (95% vs 71%). Non-responders to both vaccinations (TV-/PCP-) had a higher incidence of serious bacterial infections (25% vs 16%) and pneumonia (50% vs 32%) when compared to the TV+/PCP- group. When correlated with B cell number, 58% of B cells had a concentration of TV antibodies <32 U/mL.

Conclusions: The response to TV correlated with underlying disease treatment and immunological presentation. Assessing the response to two polysaccharide vaccinations, TV and PPV, may provide a greater understanding of the T cell independent pathway and provide more clinical information for the clinician.

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THU0035 A CD8 ALPHA-NEGATIVE SUBSET OF CD4+SLAMF7+ CYTOTOXIC T CELLS IS EXPANDED IN PATIENTS WITH IGG4-RELATED DISEASE AND DECREASES FOLLOWING GLUCOCORTICOID TREATMENT

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Background: IgG4-Related Disease (IgG4-RD) is a fibro-inflammatory disorder characterised by tumefactive lesions, frequent elevation of serum IgG4 levels, and tissue fibrosis.¹ Glucocorticoids represent the treatment of choice to induce IgG4-RD remission but their effect on the cells orchestrating the disease remains unknown.¹ We recently described an unconventional population of clonally expanded CD4⁺SLAMF7⁺ cytotoxic T effector memory (T_{EM}) cells (CD4⁺CTLs) and causally linked it to IgG4-RD in view of their capacity to secrete pro-fibrotic molecules and to infiltrate affected organs.²⁻⁴

Objectives: In order to better clarify the mechanisms of action of glucocorticoids in IgG4-RD and the pathogenic relevance of CD4⁺ CTLs, we herein aim to describe the effects of corticosteroid treatment on CD4⁺ CTLs.

Methods: CD8 α , granzyme A, perforin, and SLAMF7 expression within the effector/memory compartment of CD45RO (T_{EM}) and CD45RA (T_{EMRA}) CD4⁺ T cells was quantified by flow cytometry in 18 active IgG4-RD patients at baseline and after 6 months of glucocorticoid treatment. Eighteen healthy subjects were studied as controls. Next-generation sequencing of the T-cell receptor α and β chain gene was performed on circulating CD4⁺CTLs in patients with IgG4-RD before and after treatment, and in affected tissues.

Results: Circulating CD4⁺ T_{EM} and T_{EMRA} cells were not expanded in IgG4-RD patients compared to healthy controls. CD4⁺SLAMF7⁺ T_{EM} cells (but not T_{EMRA} cells) were significantly increased among IgG4-RD patients. Within CD4⁺SLAMF7⁺ T_{EM} cells, CD8 α ⁺ but not CD8 α ^{low} cells were elevated in IgG4-RD patients. The same dominant clones of CD8 α ⁺CD4⁺SLAMF7⁺ T_{EM} cells found in the peripheral blood were also identified in affected tissue. Both CD8 α ⁺ and CD8 α ^{low} CD4⁺SLAMF7⁺ T_{EM} cells expressed cytolytic molecules. Clonally expanded CD8 α ⁺ but not CD8 α ^{low} CD4⁺SLAMF7⁺ T_{EM} cells decreased following glucocorticoid-induced disease remission.

Conclusions: A subset of CD8 α ⁺CD4⁺SLAMF7⁺ cytotoxic T_{EM} cells is oligoclonally expanded in patients with active IgG4-RD. This population contracts following glucocorticoid-induced remission. Further characterisation of this cell population may provide prognostic information and targets for therapeutic intervention.

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THU0036 ABATACEPT INCREASES REGULATORY B CELL EFFECT ON T CELL PROLIFERATION THROUGH THE PRODUCTION OF IL-10 AND TGF-BETA IN VITRO AND IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Abatacept is a CD152 agonist known to inhibit T cell proliferation but recent data suggest that it could act directly on B cells.¹⁻²

Objectives: To demonstrate the effect of Abatacept (versus IgG control) on regulatory functions of B cells on T cell proliferation in an established *in vitro* co-culture model. To evaluate its role, *in vivo*, by measuring the regulatory functions of B cells from rheumatoid arthritis patients before and after the Abatacept treatment.