Methods Thorough analysis of peripheral blood T-lymphocytes was made by flow-cytometry in a cohort of SLE patients treated with belimumab. SLE-disease activity was assessed by SLEDAI-2K score. BAFF was tested by ELISA. SPSS was used for statistical analysis.

Results The relative change of BAFF levels at 6 and 12 months from baseline showed linear correlation with the percentage of naïve B-cells (Pearson correlation=0.645, p=0.044 and 0.639, p=0.002, respectively) and of transitional B-cells (Pearson correlation=0.768, p=0.009 and 0.623, p=0.055, respectively). The percentage and absolute number of naïve B-cells showed a progressive decrease during time (ANOVA, p=0.013 and p=0.001 respectively). In terms of response prediction, a significant association of SLEDAI percentage improvement at 12 months with the decrease of total number of B-cells within the first 6 months of therapy was observed (Log regression r=0.707, p=0.05).

Conclusions BAFF inhibition induces B-cell number modifications in a SLE cohort. The reduction of total number of B-cells within the first six months shows predictive value for SLEDAI response after the first year of therapy.

Acknowledgements The authors are grateful to Carla Bosio and Alessandra Paletti, laboratory technicians at the Laboratory of Rheumatology and Clinical Immunology in Brescia, for their valuable collaboration. The authors wish to thank the nurses of the Rheumatology and Clinical Immunology Unit in Brescia for their support in blood collection.

Disclosure of Interest None declared.

P038 IN VIVO DEMONSTRATION OF TMTNF REVERSE SIGNALING: SIGNIFICANCE IN THE THERAPEUTIC RESPONSE TO ANTI-TNF AGENTS DURING MURINE ARTHRITIS

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Introduction Anti-TNF agents are widely used in rheumatoid arthritis (RA). Their effect on inflammation results from the neutralization of soluble TNF (sTNF), but also supposedly from the induction of reverse signaling through their binding to membrane TNF (mTNF). Despite possible clinical relevance, reverse signaling has been described only in vitro but has not been proven in vivo.

Objectives In this study we aim to demonstrate for the first time the existence of mTNF reverse signaling in vivo and its importance in anti-TNF response during arthritis.

Methods Triple transgenic mouse model (3TG), KO for TNFR1/TNFFR2 and KI for mTNF, thus secreting no sTNF was developed. To analyze reverse signaling, mice were injected...
either with etanercept (ETA, 10 mg/kg), an anti-mouse TNF antibody (MP6-XT22, rat IgG1, 10 mg/kg) or an anti-human IL17 antibody (seukinumab, SEC, 10 mg/kg) as a control. Daily clinical evaluation of K/BxN serum induced-arthritis was performed in 3TG as well as WT mice. Polarization of bone marrow-derived macrophages (BMDM) and cytokine production from non-arthritic WT and 3TG mice under the action of anti-TNF in vitro was evaluated by RT-qPCR, CBA and ELISA.

Results In vivo, the administration of anti-TNF (ETA or MP6-XT22) decreased arthritic scores in WT mice (p=0.005) as well as in 3TG mice (p<0.001), unlike SEC which had no effect, proving that anti-TNF binding of tmTNF decreased arthritis. In vitro effect of anti-TNF on BMDM from WT as well as 3TG mice induced a decrease in the expression of genes specific of inflammatory macrophages (CD38, GpR18 and FpR2), and an increase in the expression of genes specific of alternative macrophages (Arg1, EgR2, e-Myc). We also observed an inhibition of the secretion of pro-inflammatory cytokines (IL12p70 and IL-6) and an early peak of IL-10 secretion demonstrating an effect of reverse signaling on macrophage polarization and activation. This suggested a switch in macrophage polarization as a probable mechanism for modulation of inflammation during K/BxN serum-induced arthritis.

Conclusions Our work provides in vivo evidence for the involvement of reverse signaling in the anti-TNF-mediated modulation of arthritis. Reverse signaling is expected to result in the modulation of macrophage polarization from an inflammatory to an alternative functional phenotype in arthritic mice. Our data prompt us to consider new interpretation of the effects of anti-TNF in the treatment of RA.

Disclosure of Interest None declared.

CIRCLUATING FOLLICULAR HELPER T CELLS ARE INCREASED IN SYSTEMIC SCLEROSIS AND PROMOTE PLASMA BLAST DIFFERENTIATION THROUGH THE IL-21 PATHWAY WHICH CAN BE INHIBITED BY RUXOLITINIB

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Results We observed that cTfh cell numbers are increased in SSc patients compared with HC. Furthermore, the increase in cTfh cells was more potent in patients with severe forms of SSc such as diffuse SSc and in the presence of arterial pulmonary hypertension. cTfh cells from SSc patients present an activated Tfh phenotype, with high expression of BCL-6 and increased capacity to produce IL-21 in comparison to HC. In vitro, cTfh cells from SSc patients had higher capacity to stimulate the differentiation of CD19⁺CD27⁺CD38hi B cells and their secretion of IgG and IgM through the IL-21 pathway than cTfh cells from HC. Blocking IL-21 or using the JAK1/2 inhibitor ruxolitinib reduced the Tfh cells’ capacity to stimulate the plasmablasts and Ig production.

Conclusions Circulating Tfh cells are increased in SSc and correlate with SSc severity. The IL-21 pathway or JAK1/2 blockade by ruxolitinib could be a promising strategy in the treatment of SSc.

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Acknowledgements This work was supported by the Aterhit foundation and received grants from ‘Groupe Francophone de Recherche sur la Sclérodermie’ (GFRS).

Disclosure of Interest None declared

The European Consensus Finding Study Group on Autoantibodies 2017/18 Investigation. Characterisation of autoantibody content in a new international reference standard for dense fine speckled 70KD (DFS70) autoantibodies

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Career situation of first and presenting author. Introduction The European Consensus Finding Study Group on autoantibodies (ECFSG) a.k.a. the EULAR autoantibody study group has been active for 30 years.

Objectives To reach consensus about autoantibody measurements in clinical practice, and to evaluate upcoming autoantibody standard reagents concerning autoantibody content.

Methods ECFSG focus on evaluating difficult to interpret serum samples, where differences between assays can be clearly visible. Ten unknown samples are distributed yearly to European laboratories, and analyzed broadly. Results are collected with information about laboratory techniques used, and discussed in relation to clinical information on the donating patients during EWRR. The 2017/2018 investigation contained nine patient samples, and a not yet launched pooled standard for anti-dense fine speckled 70kD antibodies, an ANA reactivity with specific nuclear staining on HEp-2 cells that can be confounded with homogenous ANA, but that is not associated with autoimmune disease.

Results Acceptable consensus was reached for the clinical samples. Anti-DFS70 pattern was reported from 32/38