CIRCULATING FOLLICULAR HELPER T CELLS ARE THE EUROPEAN CONSENSUS FINDING STUDY GROUP

ARD Disclosure of Interest mice. Our data prompt us to consider new interpretation of matory to an alternative functional phenotype in arthritic modulation of arthritis. Reverse signaling is expected to result involvement of reverse signaling in the anti-TNF-mediated tion of inflammation during K/BxN serum-induced arthritis. macrophage polarization as a probable mechanism for modula-

secretion demonstrating an effect of reverse signaling on mac-
cytokines (IL12p70 and IL-6) and an early peak of IL-10 observed an inhibition of the secretion of pro-inflammatory of alternative macrophages (Arg1, EgR2, e-Myc). We also were measured by ELISA. BCL-6, Blimp-1, CXCL13 and IL-

Results In vitro, 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 vitro 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.

CIRCULATING 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


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


Career situation of first and presenting author Instructor. 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 reactiv-

ity with specific nuclear staining on HEP-2 cells that can be confounded with homogeneous 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
laboratories, whereas 5/38 reported homogenous ANA, one reported unknown pattern. Except for 4 out of 24 laboratories reporting anti-histone and 2 out of 33 laboratories reporting ACPA, both in low levels, no autoantibodies were reported. Consensus was that the sample contained pure anti-DFS70.

Conclusions ECFSG helps to keep awareness on differences between autoantibody assays. The anti-DFS70 ANA pattern was identified by most laboratories in a reagent that proved to be free of other autoantibodies. The anti-DFS70 standard will be available via http://asc.dental.ufl.edu/ReferenceSera.html#text.

"Lab representatives: Renaudineau Y, Brest; Frick M, Hannover; Shoenfeld Y, Sheba, Israel; Nozal Aranda P, Madrid; Tzioufas AG, Athens; Kozakova D, Piestany; Toubi E, Haifa, Israel; Franceschini F, Brescia; Hennessy L, Glasgow; Roux-Lombard P, Genève; Heijnen I, Basel; Karlsen R, Oslo; Jeremy W, Luxembourg; Bombardieri S, Pisa; Cucnik S, Ljubljana; Huber AR, Aarau; Rozendal C, Groningen; Goetz J, Strasbourg; Vencovsky J, Praha; Wójcieszowska B, Warsaw; Guertik K, Antwerp; Hänninen A, Turku; McHugh N, Bath; Steiner G Wien; Schreurs M, Rotterdam; Montes Cano MA, Sevilla; Elvin K, Stockholm; Nagy E, Budapest; Babai I, Tikva, Israel; Bonroy C, Gent; Burmester GR, Berlin; Andrejevic S, Belgrade; Kral V, Usti nad Labem; Csernok E, Tübingen; Jeremie W, Luxembourg; Bombardieri S, Pisa; Cucnik S, Ljubljana; Huber AR, Aarau; Rozendal C, Groningen; Goetz J, Strasbourg; Vencovsky J, Praha; Wójcieszowska B, Warsaw; Guertik K, Antwerp; Hänninen A, Turku; McHugh N, Bath; Steiner G Wien; Schreurs M, Rotterdam; Montes Cano MA, Sevilla; Elvin K, Stockholm; Nagy E, Budapest; Babai I, Tikva, Israel; Bonroy C, Gent; Burmester GR, Berlin; Andrejevic S, Belgrade; Kral V, Usti nad Labem; Csernok E, Tübingen; Probst-Mueller E, Zürich; Fischer K, Szczecin; Hacein-Bey-Abina S, Paris; Conrad K, Dresden; Humbel RL, Leudelange. Disclosure of Interest None declared.

P041 IMMUNOLOGICAL CHARACTERISTICS AND DISTRIBUTION OF CRYOGLOBULINS IN A COHORT OF 13000 PATIENTS OVER 6 YEARS

1MN Sarda*, 1,P Minucci, 2Immunogenomics and inflammation research Unit EA 4130, Lyon 1 University; 3Immunology Laboratory; 2Dpt of Immunology and Rheumatology, Clinical Immunology Unit, Hospices Civils de Lyon, LYON, France


Career situation of first and presenting author Assistant. 

Introduction Cryoglobulins (CG) are immunoglobulins (Ig) that precipitate in vitro at cold temperature and dissolve at 37°C, they are classified in 3 types. Type I CG are monoclonal Ig of IgM or IgG isotype. Type II and III are mixed CG: type II CG associate a monoclonal with polyclonal Ig, type III CG associate polyclonal Ig. Rheumatoid factor activity (RF) of CG associate a monoclonal with polyclonal Ig, type III CG

Results A total of 13439 patients were included, 1675 (12.5%) of whom had positive CG. In case of negative CG detection, 2213 patients were retested and CG was detected on the new sample for 196/2213 patients (8.9%). Type I CG was found in 9.3% (155/1675), type II CG in 47% (788/1675), and type III CG in 43.7% (732/1675) of patients. In type I CG, IgM CG was more frequent than IgG CG, but in lower concentration (p=0.02). For mixed CG, 34.8% of HCV+ tested patients had CG, less than 5% of CG was associated with HBV+ or HIV+ serology. Mixed CG were found in 25.4% of patients with anti dsDNA, anti-SSA60 or anti-CCP autoantibodies (Ab). Mixed CG were positive for 87/333 (26.1%) patients with anti-dsDNA Ab, 74/447 (16.6%) patients with anti-SSA60 Ab, and for 19/155 (12.3%) patients with anti-CCP Ab. Both the cryoprecipitate and the serum were positive for RF in 21.6% of type II CG and 10.1% of type III CG. C3, C4 and/or CH50 decrease was found in 23.6% of serum with CG vs 3.2% of CG-negative serum (p<0.001).

Conclusions In this largest cohort even studied, with patients from all clinical specialties, CG distribution and characteristics were described with minimal selection bias. Despite strict pre-analytical conditions, negative CG detection must be repeated according to clinical context. Mixed CG are more frequently detected in patients positive for HCV or anti-dsDNA Ab. CG with RF activity form immune complexes that precipitate in vessels and activate complement system, responsible for cryoglobulinemic vasculitis.

Disclosure of Interest None declared.

P042/005 MOLECULAR MIMICRY AND AUTOIMMUNITY: ANTI-P. GINGIVALIS ANTIBODY RESPONSE IN ACPA-POSITIVE RHEUMATOID ARTHRITIS

1N Sherina*, 1,N Sipp, 1,L Israelsson, 2,E Le Maitre, 1,N Khramanova, 1,M Hansson, 2,K Eriksson, 1,Yucel-Lindberg, 1,V Malmström, 1,K Amara, 1,K Lundberg, 2Department of Medicine, 3Department of Dental Medicine, Karolinska Institute, Stockholm, Sweden

10.1136/annrheumdis-2018-EWRR2019.34

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

Introduction The presence of anti-citrullinated protein antibodies (ACPs) is a hallmark of rheumatoid arthritis (RA). ACPs specifically recognize citrullinated epitopes, a result of a post-translational modification catalyzed by peptidyl arginine deiminas (PAD). Based on the unique feature of the periodontal bacteria Porphyromonas gingivalis (P gingivalis) to express P. gingivalis, it has been suggested that ACPA-positive RA may be precipitated in the gum mucosa.

Objectives To address this hypothesis our aims were to investigate the antibody response against a citrullinated P P. gingivalis antibody response in ACPA-positive R PAD in patients with RA, chronic periodontitis (PD) and in controls. In addition, we generated monoclonal antibodies (mAbs) from gingival tissue B cells of RA patient aiming to investigate whether citrulline-specific B cells may reside in the gingiva.

Methods Gingival tissue-derived single CD19+ B cells from an ACPA-positive RA patient with PD were sorted by flow cytometry. Immunoglobulin variable region genes were sequenced and expressed to generate recombinant mAbs. CPP3-reactivity was analysed by ELISA in serum samples from 66 PD patients, 63 periodontally healthy controls (non-PD), 200 RA patients, and 120 non-RA controls, as well as in 55 mAbs. Differences in antibody levels were examined using Mann-Whitney U test for independent groups.

Results Anti-CPP3 antibody levels were low in non-PD controls, while 65% of PD patients showed elevated levels (p<0.0001). Significantly increased antibody levels were also