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>.

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

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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 mixed CG leads to the formation of immune complexes that can precipitate and result in vasculitis.

Objectives The purpose of this study was to update information on CG biological characteristics in a large population recruited from all clinical departments of a French University Hospital.

Methods This retrospective study was conducted from January 2010 to December 2016. Patients included had at least one serum sample for CG detection and characterization: CG isotype and clonality, concentration and RF (IgM anti-IgG) in the cryoprecipitate; and serum complement exploration. Associated pathologies were determined by biological markers of gammopathy, viral infection and autoimmunity.

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/O05 MOLECULAR MIMICRY AND AUTOIMMUNITY: ANTI-P. GINGIVALIS ANTIBODY RESPONSE IN ACPA-POSITIVE RHEUMATOID ARTHRITIS

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

Introduction The presence of anti-citrullinated protein antibodies (ACPAs) is a hallmark of rheumatoid arthritis (RA). ACPAs specifically recognize citrullinated epitopes, a result of a post-translational modification catalyzed by peptidyl arginine deiminases (PAD). Based on the unique feature of the periodontal bacteria *Porphyromonas gingivalis* (*Pgingivalis*) to express P. PAD 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. PAD peptide (CPP3) 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

detected in 50% of ACPA-positive RA, 20% of ACPA-negative RA, and in 37% of non-RA controls ($p < 0.0001$). Notably, this antibody response was citrulline-specific, as the antibody response against the arginine-containing control peptide RPP3 was significantly lower in all subsets ($p < 0.0001$). Among 55 mAbs from gingival tissue, 14 (25%) unique clones were CPP3-reactive, of which 4 showed cross-reactivity with RPP3. Interestingly, 4 out of 14 (29%) CPP3-reactive clones also bound citrullinated peptides derived from human α -enolase, filaggrin and histone 4, demonstrating cross-reactivity between a bacterial epitope and human epitopes on a monoclonal level.

Conclusions This study shows that a substantial proportion of systemically healthy individuals possess ACPAs directed against *P. gingivalis*, and these ACPAs also bind epitopes on human proteins. Based on our data, we propose that the ACPA response may be triggered by *P. gingivalis* via an antibody response against CPP3, which cross-reacts with human citrullinated proteins by mechanisms of molecular mimicry.

Disclosure of Interest None declared.

P043

INFECTION WITH CITRULLINATING PORPHYROMONAS GINGIVALIS CAN INDUCE AUTOIMMUNITY TO HUMAN RIBOSOMAL PROTEINS

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Career situation of first and presenting author Young investigator.

Introduction *Porphyromonas gingivalis* (P. g.) is involved in triggering self-reactive immune responses when citrullinating bacterial or human proteins. However, first evidence to link anti-ribosomal T and B cells responses to rheumatoid arthritis (RA) has been published but the mechanism is still not clear.¹ Infection based autoimmunity induced by citrullination of human proteins with P. g. peptidyl arginine deiminase from RA patient (RA-PPAD) and crossreactivity binding induced by P. g. was investigated using affinity purified RA patient antibodies and a monoclonal antibodies to cit-RA-PPAD.

Objectives Antibodies to RA-PPAD isolated from an RA patients (RA-PPAD) was first time linked to target specific citrullinated ribosomal proteins.

Methods Screening of RA sera was conducted on 37.830 unique human proteins on protein microarrays (<http://www.engine-gmbh.de>) with 30 RA sera. The autoantibody response to 840 different proteins was recorded and bioinformatically evaluated. Protein arrays were citrullinated with PAD2,4, rabbit PAD and RA-PPAD. Sera and affinity purified antibodies were used to detect reactivity to 840 autoantigens.

Results A human protein microarray consisting of 840 indentified autoantigens from RA patients was modified by human PAD2 and PAD4, rabbit PAD, and RA-PPAD from P. g. Using cit specific monoclonal antibodies we identified the ribosomal proteins (RP), RPL18a, RPS27a, modified by PAD2, RPL18a and MRPS11 modifies by Pad4, and RPL7L1 modified by rabbit PAD specifically targeted. In addition 6 RA patient sera and 3 osteoarthritis (OA) control sera were used to identify the citrullinated RA-PPAD specific modified autoantigens not targeted when modified by human PAD2 or PAD4 or rabbit

Pad. We identified the RA-PPAD citrullinated ribosomal Proteins RPL3, RPL21, RPS24, RPL9, RPL15, RPS24.RPS3a, MRPL28 specifically targeted by RA patients. This identifies ribosomal proteins as major specific RA-PPAD citrullination targets. Moreover, affinity purified antibodies bound to native and citrullinated RA-PPAD from 6 RA patient sera and 3 OA patient sera were tested for crossreactivity on citrullinated human proteinarray. Antibodies to citrullinated ribosomal proteins MRPS11, RPL21, RPS3a, RPL18a, RPS27a, MRPL28 were detected in the RA group but not in the OA control group.

Conclusions Failure of *Porphyromonas gingivalis* clearance in RA patients leads to infection induced enzymatic mimicry based autoreactivity targeting evolutionary conserved human ribosomal proteins. Autoimmunity to ubiquitous self-antigens may trigger localized tissue damage in RA.

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P044

EFFECT OF SPECIALIZED 6-MONTH ADL TRAINING WITH SUBSEQUENT A 6-MONTH FOLLOW-UP PERIOD IN PATIENTS WITH MYOSITIS – PRELIMINARY DATA

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

Introduction Idiopathic inflammatory myopathies (IIM) are accompanied by muscular weakness caused by inflammation and immune changes in affected muscles, resulting in reduced quality of life. The aim of our study was to determine the effect of ADL training on muscle strength and endurance and quality of life of IIM patients.

Objectives The study included a total of 50 IIM patients who fulfilled the Bohan and Peter 1975 criteria and had skeletal muscle involvement. 27 patients were recruited into the intervention group (IG) and 23 patients into the control group (CG). Both groups received an educational material for home exercise, but only the IG underwent a 6 month intervention with a subsequent 6 month follow-up period.

Methods Patients were assessed by a physician and a physiotherapist blinded to intervention at months 0, 3, 6, and 12, and parameters evaluating quality of life, muscle strength and endurance were recorded. Patients also filled out PRO (patient reported outcomes) questionnaires and provided blood for routine laboratory analysis and bio-banking. Data analysis was performed between groups and within the group.

Results Compared to the observed statistically significant deterioration in the CG over the intervention period of 0–6 months, we found a statistically significant improvement in the IG in objectively assessed strength and endurance of muscles as well as in subjectively assessed functional abilities