The mean levels of IgG aCL, IgM aCL, and aPT were comparable in patients with SLE and RA. However, the mean levels of IgG aCL in RA patients were higher than in SLE patients. This may indicate an increased autoimmune activity.

Simultaneous elevation in four types of aPL levels was observed in 4.4% patients with RA, in 2.5% - with SLE; simultaneous elevation in three types of aPL was revealed in 11.1% patients with RA, in 17.5% - with SLE; two types of aPL were increased in 35.8% patients with RA and 27.5% - with SLE. Only one type of elevated aPL levels (12.9%) was indentified in the control group.

Conclusion: Thus, patients with RA are characterized by a wide range of aPL. Qualitative and quantitative changes in the levels and types of autoantibodies in patients with RA have been established similar to those in SLE patients.

In patients with autoimmune rheumatoid pathogeny, the presence of simultaneously elevated several types of aPL have been proved.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.5796
protein or 1000ng/ml of human IgG1 as a control for 12h. Gene expressions were detected by microarray assay.

Results: Microarray data analysis revealed that DR3 up-regulated or down-regulated the expression of various genes in RA-FLS (Figure). The function of regulated genes included protein-l-isoaspartate (D-aspartate) O-methyltransferase activity, carbohydrate-O-methyltransferase activity, protein carbonyl O-methyltransferase activity, regulation of cilium assembly, O-methylytransferase activity, regulation of plasma membrane bounded cell projection assembly, regulation of cell projection assembly, regulation of organelle assembly, protein methyltransferase activity, and S-adenosylmethionine-dependent methyltransferase activity. The most up-regulated 2 genes by DR3 were KIAA1109 (KIAA1109), and adhesion G protein-coupled receptor A3 (ADGRA3). The most down-regulated 2 genes by DR3 were RNA exonuclease 2 (REXO2), and family with sequence similarity 120A (FAM120A).

Conclusion: In this study, we first revealed the expression profiles of genes regulated by DR3 in RA-FLS. KIAA1109/TENR/ILO2/IL21 gene is strongly associated with RA in European descent populations [3]. ADGRA3 is a member of G protein-coupled receptors (GPCRs). GPCRs associates with the regulation of cytoskeletal organization, the cell adhesion and migration, cell proliferation and apoptosis, and cell differentiation [4]. Loss of REXO2 affects cell growth and morphology [5], and REXO2 was identified as a target gene for inflammatory bowel disease-associated variants [6]. FAM120A regulates activity of Src kinase to protect cells from oxidative stress-induced apoptosis [7]. DR3 regulates the gene expressions of various key molecules in RA-FLS and may affect the pathogenesis of RA by regulating gene expression of RA-FLS.

References:

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.1346

AB0091
PD-1 AND GAL3 REGULATE OSTEOCLAST DEVELOPMENT IN RHEUMATOID ARTHRITIS
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Background: Bone erosions in rheumatoid arthritis (RA) is a major complication. Despite improved treatment, erosions still occur and progress. Therefore, a continuous investigation of the interplay between bone regulation and immune activity is necessary. Co-inhibitory receptors, like CTLA-4, participate in modulating osteoclast activity1, and blocking these receptors in cancer treatment results in autoimmune disease2. Programmed death 1 (PD-1) is a central co-inhibitory receptor, also present in a soluble (s) form. We have previously shown that sPD-1 is associated with disease activity and reduced bone erosions in RA3. PD-1 and its ligands are glycosylated and the glycosylation affects signaling through the PD-1 pathway4. Galectins (Galectins) bind to specific glycosylation patterns on glycoproteins by their carbohydrate recognition domain. Galectin-3 can bind to multiple immune receptors shaping the immunological response5.

Objectives: To investigate if PD-1 and GAL3 modulate osteoclastogenesis in RA.

Methods: Plasma and synovial fluid (SF) samples were collected from patients with chronic (c) RA (>6 years of disease, n=14) SF and blood samples were obtained when patients presented with disease flare. Soluble PD-1 and GAL-3 were investigated by ELISA. GAL-3/PD-1 complexes were captured in an optimized ELISA using both GAL-3 and PD-1 antibodies. Surface plasmon resonance was used to evaluate the binding properties between GAL-3 and PD-1, on a Biacore 3000. Lactate was used to block the potential binding. Cells from the synovial fluid (SFMC) were differentiated into osteoclasts with M-CSF and RANKL. Recombinant human (rh) PD-1 and rhGAL-3 were added and osteoclast formation evaluated by TRAP in the supernatant.

Results: Soluble PD-1 and GAL-3 were present in both plasma and SF from cRA patient, and the ratio (PD-1/GAL-3) was increased in SF. PD-1/GAL-3 complexes were detected in both plasma and SF, with the highest concentration in SF. The binding between PD-1 and GAL-3 was confirmed by surface plasmon resonance analyses, with an estimated Kd of 5uM. Binding could be blocked by addition of lactate, confirming the binding to be glycan dependent. In SFMC osteoclast cultures, rhPD-1 and rhGAL-3 slightly decreased osteoclast formation evaluated by TRAP. However, combining mPD-1 and rhGAL3 further potentiated the reduction in osteoclast formation by 37%.

Conclusion: We confirm glycan dependent binding between the co-inhibitory receptor PD-1 and GAL-3. Both sPD-1 and GAL-3, and the PD-1/GAL-3 complexes, are upregulated in the inflamed joint at site of erosions. In vitro RA culture demonstrates that GAL-3 potentiates the function of PD-1 and reduces osteoclastogenesis. These findings indicate that the binding between Gal-3 and PD-1 could provide a novel target to control erosions in RA. Future in vivo studies on this interaction is needed.

References:

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.5375

AB0092
FIBRIN ADHESION IS A PANNUS-INDEPENDENT MECHANISM OF CARTILAGE DEGENERATION IN RHEUMATOID ARTHRITIS
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Background: Current concepts of cartilage destruction in inflammatory arthritis include pannus infiltration by inflamed synovial tissue as well as direct detrimental effects of inflammatory cytokines and proteinases. Fibrin maintains chronic inflammatory processes in arthritis but has never been shown to be directly involved in cartilage damage occurring in rheumatoid arthritis (RA).

Objectives: To investigate fibrin-mediated cartilage degradation and the possible underlying mechanisms in arthritis.

Methods: Human cartilage samples were obtained from patients with RA undergoing joint replacement and investigated by H.E. and immunohistochemistry for cartilage damage and fibrin deposition. Cartilage explants from RA patients were incubated in vitro with autologous synovocytes and assessed by immunohistochemistry for cell-adhesion and colocalization with fibrin. Experimental RA was studied in the RA murine model of adjuvant-induced arthritis (AIA), in wildtype (WT) and fibrinogen deficient (Fg−/−) mice. Cartilage damage and chondro-synovial adhesion were analyzed by safranin-O staining and fibrin deposition by immunohistochemistry. Fibrinogen expression (Fgα, Fgβ, Fgδ) was studied in murine primary chondrocytes and human primary chondrocytes by qRT-PCR. Cartilage explants were stained with alizarin-red staining and assessed for colocalization of calcific deposits and fibrin. Calcification of murine primary chondrocytes stimulated with secondary calciprotein particles (CPP) and treated with purified human plasma fibrinogen (100 µg/ml) was assessed by alizarin red staining and gene expression for chondrocytic differentiation (Agg, CollII, ColI0, Sox9, Runx2), calcification (AlpI, Ank, Anx5, PctI, Pht, PhtO2), and extracellular matrix remodeling (Aatam4, Aatam5, Mmp3, Mmp13, Comp) by qRT-PCR.

Results: Abundant fibrin deposition on cartilage co-localized and positively correlated with cartilage damage in knee joints of patients with RA. In the AIA model,