by B cells through affecting monocytes. IL-6 and/or IL-10 may intermediate the effect. Our findings strongly suggest that BAFF signaling via BR3 is a possible therapeutic target for drug discovery to treat pSS or other intractable autoimmune diseases which accompany hypergammaglobulinemia. Moreover, these compounds may provide novel tools to explore the pathological mechanism of the development of these autoimmune diseases.

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THU0056 FREE FATTY ACIDS PROMOTE INFLAMMATION VIA OSTEOBLASTS AND OSTEOCLASTS FROM PATIENTS WITH RHEUMATOID ARTHRITIS OR OSTEOARTHRITIS

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Background: Various inflammatory cardiovascular and metabolic diseases such as atherosclerosis, coronary heart diseases and type 2 diabetes are associated with chronically elevated free fatty acid (FFA) levels. With inflammation being a factor in pathological bone loss, FFA may also be contributors to bone loss in osteoarthritis (OA) and/or rheumatoid arthritis (RA).

Objectives: To investigate whether FFA have an influence on osteoblasts and osteoclasts from patients with RA or OA, in a way that may alter bone degradation in these diseases.

Methods: Primary osteoblasts (OB) were isolated from cancellous bone of OA and RA patients undergoing knee joint surgery. Osteoclasts (OC) were differentiated from peripheral blood mononuclear cells (PBMC). OB and OC were stimulated with the saturated FFA palmitic acid (PA) and the unsaturated FFA linoleic acid (LA) (100 μM each). Immunoassays were used to quantify protein secretion. mRNA expression levels were quantified by real-time PCR. Mineralization activity was quantified using Alizarin Red S staining, differentiated OC were quantified by counting TRAP-positive multinuclear cells (>2 nuclei). Toll-like receptor (TLR) 4 and TLR2 were blocked by neutralizing antibodies.

Results: When stimulated with FFA, OB from RA and OA patients secreted higher amounts of the proinflammatory cytokine IL-6 (up to 9-fold) and the chemokines IL-8 (up to 221-fold), GRO-a (from below detection level to detectable levels) and MCP-1 (up to 16-fold). Differences in the degree of response were more dependent on the patient than the disease. RANKL as well as OPG, OB-secreted modulators of OC differentiation, as well as OB differentiation markers (e.g. osterix, osteocalcin) were not influenced by FFA on mRNA or protein level. The effect of FFA on mineralization activity of OB varied between patients, yet overall there was no significant difference between FFA-treated and untreated OB. Expression of the two Wnt signaling molecules, axin-2 and b-catenin, was not changed by PA or LA, suggesting no involvement of the Wnt signaling pathway in the effects observed by FFA in OB. On the other hand, TLR4 blockade significantly reduced PA-induced IL-8 secretion by OB (by 93%), while blocking TLR2 had no effect. In both RA and OA OC, IL-8 secretion was significantly enhanced by PA and LA, with a clear time-dependency within the differentiation process for RA OC but not for OA OC. The number of TRAP positive multinuclear cells decreased for RA OC by approx. 50%, which was in agreement with the reduced TRAP secretion by a factor of 2–3 at d14. mRNA expression of various osteoclast activity markers (CLCN7, CTSK, TCIRG) was not altered.

Conclusions: Inflammation is promoted by FFA via both OB and OC from patients with RA or OA, thus possibly indirectly contributing to bone loss while no direct effect on OB/OC activity could be observed. In OB, these effects are probably mainly mediated by TLR4, while TLR2 and Wnt pathways do not play a role.

Disclosure of Interest: None declared

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THU0057 LIPID PROFILING OF PLASMA IN RHEUMATOID ARTHRITIS PATIENTS BY LIQUID CHROMATOGRAPHY–TANDEM MASS SPECTROMETRY

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Background: Previously it has been described that lipid and lipid mediators are present in synovial fluid from patients with rheumatoid arthritis (RA). It is, however, currently unknown to what extent these lipid mediators are involved in disease pathophysiology.

Objectives: The aim of this study is to clarify which lipid mediators in plasma correlate with disease activity of RA.

Methods: We obtained blood from RA patients registered in the KURAMA (Kyoto University Rheumatoid Arthritis Management Alliance) cohort. None of the patients was treated with glucocorticoids or NSAIDs, both of which could affect lipid metabolism. Targeted lipidomics, using a LC–MS/MS (liquid chromatography–tandem mass spectrometry) platform was used for the identification of lipids present in the patients' plasma. SDAI (simplified disease activity index) was examined in this cohort and lipidomics profiling and disease status were combined. Data were statistically analyzed by Spearman's rank correlation coefficient test or multivariate regression analysis.

Results: Twenty-six RA patients were enrolled; female ratio: 84%, mean age: 63.0 years old, mean disease duration: 18.7 years and mean SDAI 5.26. In this group, patients age was significantly correlated with SDAI (p value =0.005, Spearman's rho =0.552). By LC-MS/MS analyses, 23 lipid components were identified and quantified. Multivariative regression analysis (Standard Least Squares) revealed that 19,20-diHDPA (Dihydroxydocosapentaenoic acid) and 14,15-diHETE (Dihydroxyeicosatetraenoic acid) significantly explained SDAI score independently of sex and age.

Among the composite measure for SDAI, the best correlated component with TJC (tender joint count) was LA (Linoleic acid, p=0.002, rho = -0.611), that with patient VAS (visual analogue scale) was 19,20-diHDPA (p=0.032, rho =0.440), and that with CRP was DHA (Docosahexaenoic acid, p=0.021, rho = -0.452).

Additionally, principal component analysis was carried out. In the first primary component (PC1), absolute eigenvecotor values of AdA (Adrenic acid), ALA (Alpha-linolenic acid), DHA, DPA (Docosapentaenoic acid) and LA are more than 0.25, among which DHA was strongly correlated with PC1 (p<0.0001, rho =0.902). PC1 positively and significantly explained TJC count independent of sex and age.

Table. Parameter Estimates by Standard Least Squares (Role variant = SDAI)

	Lower 95%	Upper 95%	Std. Beta	p value
Intercept	-39.2	-6.63	0	0.008
19,20-diHDPA	4.54	16.55	0.707	0.003
14,15-diHDPE	-26.4	-6.24	-0.62	0.003
Age	0.08	0.56	0.455	0.013
Sex				0.475

Conclusions: Since 19, 20-diHDPA (metabolized from DHA) and 14,15-diHETE (from EPA, eicosapentaenoic acid) are both generated by cytochrome P450-catalyzed epoxidation followed by conversion to the vicinal diols by epoxide hydrolase, such kind of enzymes might be key molecules connecting lipid metabolism and RA. Although a replication study is inevitable, a certain kinds of lipid and lipid mediator profiles may be associated with disease activity, especially analgesic descriptors such as tender joint count.

References:

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THU0058 S100A11 PROTEIN IS UP-REGULATED IN PATIENTS WITH IDIOPATIC INFLAMMATORY MYOPATHIES AND IS ASSOCIATED WITH DISEASE ACTIVITY

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Background: S100A11 (calgizzarin) is a member of the S100 protein family that participates in regulating number of biologic functions and is associated with oncogenesis and inflammation. Recent data suggest involvement of S100A11 in myocardial damage.

Objectives: The aim of our study was to analyze the expression of S100A11 in patients with idiopathic inflammatory myopathies (IIMs) and its potential association with disease activity parameters and IIMs-related clinical features.

Methods: immunohistochemistry in patients with polymyositis/dermatomyositis (PM/DM, n=5/6) and control individuals with myasthenia gravis (MG, n=5). S100A11 in plasma was measured by ELISA (Biovendor) in 112 patients with IIMs (PM, n=41; DM, n=41; and cancer associated myositis (CAM), n=30) and in 42 healthy controls (HC). Patients with PM/DM fulfilled Bohan and Peter diagnostic criteria and CAM was defined as cancer occurring within 3 years of the diagnosis of myositis. Clinical disease activity was assessed by myositis disease activity assessment (MYOACT), physician and patient's global activity using visual analogue scales (VAS), manual muscle testing (MMT) and health assessment questionnaire (HAQ). Muscle enzymes CK, LD, ALT, AST and CRP were measured by routine laboratory techniques. Autoantibodies were detected by immunoprecipitation.