We revealed a correlation between IgG aCL, IgG aβ2-GP1, IgG aAnV and TNF-α, IgG aCL and IL-6 in SLE patients, and only one between IgG aAnV and hs-CRP in RA patients. There wasn't any correlation between aPL and inflammatory mediators in the control group.
Univariate analysis has demonstrated an association of IgG aAnV with IMT (r=0,320, p=0,044) in SLE patients and positive association between TNF-α and IMT (r=0,362, p=0,028) in RA patients. Furthermore, we found an association between IL-6 and IgG aPT (r=0,426, p=0,038), TNF-α and IgG aCL (r=0,419, p=0,042) in SLE patients with carotid atherosclerosis. There wasn't any association between investigated parameters in the control group.
Conclusions: The association between inflammatory mediators and disease activity has been confirmed in ARD patients. Increased autoimmune activity has been verified both in patients with SLE and RA. It has been determined that IgG aAnV had more significance for IMT in patients with SLE, TNF-α - in RA patients. Our data can suggest that inflammatory mediators and antiphospholipid antibodies are involved in the atherosclerotic process in patients with ARD.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5306

AB0049 NF-κB-INDUCING KINASE REGULATES LTβR-DRIVEN NF-κB SIGNALING AND INFLAMMATORY ACTIVATION OF ENDOTHELIUM

P. Kucharzewka[1], C.X. Maracle[2], J.P. van Hamburg[2], K.C. Jeucken[2], H. Olsson[1], S.W. Tas[2]. *[1]Imed Ria, AstraZeneca, Mölndal, Sweden; [2]Department of Clinical Immunology & Rheumatology and Laboratory for Experimental Immunology, AMC, University of Amsterdam, Amsterdam, Netherlands*

Background: Sites of chronic inflammation, such as rheumatoid arthritis synovial tissue, are characterized by neovascularization and often contain tertiary lymphoid structures with characteristic features of lymphoid organs such as endothelial venules (HEV), and sometimes even true germinal centers. Ligation of the lymphotoxin (LT)-β receptor (LTβR) results in activation of both canonical and NF-κB-Inducing Kinase (NIK)-dependent non-canonical NF-κB signaling in endothelial cells (ECs) and plays a crucial role in lymphoid neogenesis. Non-canonical NF-κB signaling in ECs promotes inflammation-induced angiogenesis and triggers the development of the cuboidal HEV appearance. However, the relative contribution of the individual pathways to the acquisition of leukocyte traffic-regulating properties by ECs is less well understood.
Objectives: To identify the molecular pathways by which LTβR drives inflammatory activation of ECs to promote interactions with leukocytes.
Methods: Primary human ECs were treated with LTβ or LIGHT to activate LTβR. Induction of downstream signaling pathways was assessed by western blot analysis and NF-κB transcription factor ELISA. The expression of adhesion molecules, inflammatory cytokines and chemokines, such as CXCL1, CXCL5, CXCL8 and GM-CSF in ECs was measured by RT-qPCR and cytokine antibody arrays. EC interactions with leukocytes were determined by an adhesion assay, and EC barrier integrity was assessed by a permeability assay. To repress canonical NF-κB signaling pathway, a small molecule inhibitor of IKKβ was used, and inactivation of non-canonical NF-κB signaling was achieved with siRNAs targeting NFκB2. The role of NIK in LTβR signaling was investigated using small molecule inhibitors of NIK, siRNAs targeting NIK and adenoviral vectors encoding wild type and kinase-deficient NIK.
Results: LTβR triggering in ECs resulted in activation of both canonical and non-canonical NF-κB signaling pathways and induced the expression of inflammatory cytokines and chemokines (CXCL1, CXCL5, CXCL8, MCP-1, GM-CSF, CCL5). Consistent with inflammatory activation of ECs, LTβR ligation also induced adhesion of immune cells to activated endothelium and increased permeability across EC monolayers. IKKβ inhibition completely repressed LTβR-induced inflammatory activation of ECs, indicating that this process was mediated through canonical NF-κB signaling. Interestingly, inactivation of NIK with small molecule inhibitors and siRNAs significantly decreased LTβR-induced expression of inflammatory cytokines and adhesion of immune cells to endothelium, whereas silencing of NFκB2 had no effect. This suggests that the non-canonical pathway is dispensable for NIK-dependent activation of endothelial cells through the canonical NF-kB pathway. Further analyses, including silencing of NIK and NIK overexpression, demonstrated a role for NIK in activation of the canonical NF-kB pathway by amplifying IKK complex activity.
Conclusions: These findings suggest that in addition to its pivotal role in the non-canonical pathway, NIK can serve as an amplifier of the canonical NF-κB pathway and associated inflammatory responses in ECs mediated by LTβR ligation, which may play a role in development and maintenance of chronic inflammation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5498

AB0050 IMPAIRED ADIPONECTIN AND LEPTIN LEVELS DURING OSTEOARTHRITIS ONSET AND DEVELOPMENT IN STR/ORT MICE

R. Giambelli, S.K. Bernini, M. Perrella, A. Grotti, R. Cavagnoli, G. Samuelli, P. Garofalo, T. Zanelli, G. Caselli, L.C. Rovati. *Rottapharm Biotech, Monza, Italy*

Background: Obesity is a risk factor for osteoarthritis (OA). In obese subjects OA develops not only in weight-bearing joints but also in non-weight-bearing joints, suggesting that dysregulated metabolism in obese patients may promote OA onset.
As obesity evolves many physiological parameters are dysregulated, including the levels of adipokine hormones such as leptin and adiponectin. For this reason, it has been suggested that adipokine levels in serum and synovial fluid are associated with a worsening of synovial inflammation and OA progression in these patients(1).
In vivo and in vitro studies show that high levels of leptin induce the synthesis of metalloproteases involved in cartilage degradation(2). Conversely, dietary-induced weight loss is associated with increased adiponectin serum levels and reduced loss of tibial and femoral cartilage volume, suggesting a protective role of adiponectin in OA.
STR/ort mice are an animal model of spontaneous OA characterized by early pathology development (at about 20 weeks) and dysregulated metabolism(3). Notably, these mice have adiponectin serum levels lower than those found in control mouse strains(4).
Objectives: To evaluate whether adiponectin and leptin serum levels are associated with OA development and/or progression in STR/ort mice.
Methods: First, we measured the time course of adipokine levels in STR/ort mice before the onset of OA (at 8, 14 and 20 weeks of age), and in age-matched CBA control mice. Then, we calculated the ratio leptin/adiponectin (L/A) in the serum of STR/ort mice during OA progression (at 20, 30 and 40 weeks). Blood samples were collected from caudal vein (time course) or from vena cava at sacrifice, when knee joints were collected, processed for histology and blindly scored according to OARSI and Mankin's methods.
Results: Adiponectin serum levels in STR/ort mice at 8, 14 and 20 weeks were significantly lower than in age-matched CBA mice. Instead, leptin serum levels in STR/ort mice were higher than in CBA strain at 14 and 20 weeks. Consequently, there was a relevant difference in the ratio L/A between the two strains, with greater L/A values in STR/ort mice at 14 and 20 weeks. (Table 1)
In STR/ort mice, the ratio L/A tended to further increase between 30 and 20 weeks (1.73±0.16 from 1.28±0.17, respectively), in parallel with the increase in OARSI scores of knee joints (11.1±1.5 vs 8.4±1.3). The histopathological score increased in STR/ort mice even between 30 and 40 weeks, but without a concomitant increase in the ratio L/A.

Adipokines levels (mean ± SEM)

Age (Weeks)	8	14	20
CBA (n=10)			
Adiponectin (µg/ml)	20.2 ± 0.7	16.0 ± 0.4	14.5 ± 0.3
Leptin (ng/ml)	1.5 ± 0.3	2.5 ± 0.3	3.1 ± 0.4
L/A	0.07 ± 0.02	0.16 ± 0.02	0.21 ± 0.03
STR/ort (n=14)			
Adiponectin (µg/ml)	9.2 ± 0.3**	7.3 ± 0.2**	6.0 ± 0.2**
Leptin (ng/ml)	3.3 ± 0.5	8.7 ± 1.3**	7.9 ± 1.1**
L/A	0.36 ± 0.05	1.15 ± 0.16**	1.28 ± 0.17**

**p<0.001 STR/ort vs CBA

Conclusions: We show for the first time that leptin serum levels and the ratio L/A in STR/ort mice are higher than in CBA mice, and that the ratio L/A in STR/ort mice increases as their histopathological scores worsen. We suggest that dysregulated levels of these adipokines may be associated or even precede OA development in this animal model.
References:
[1] King L.K. et al. Osteoarthritis and Cartilage, 2015.
[2] Bao J.P. et all. Mol Biol Rep. 2010.
[3] Uchida K. et al. Experimental Animals, 2009.
[4] Giambelli R. et al. Osteoarthtis and Cartilage Volume 24, Supplement 1, April 2016, Pages S85.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3083

AB0051 INTERLEUKIN-6 BLOCKADE WITH TOCILIZUMAB DECREASES METALLOPROTEINASE-9 ACTIVITY IN SYNOVIAL FIBROBLASTS STIMULATED WITH SYNOVIAL FLUIDS OF PATIENTS WITH RHEUMATOID ARTHRITIS OR SPONDYLOARTHRITIS

R. Blas[1], H. Tamashiro[2], A. Munarriz[3], R. Pardo-Hidalgo[4], M.S. Di Genaro[5,6]. *[1]Centro Médico MEDICI; [2]Clínica Bolivar; [3]Centro Médico CENYR, San Luis; [4]Centro de Rehabilitación Médica CER, San Juan; [5]National University of San Luis; [6]Laboratory of Immunopathology, Multidisciplinary Institute of Biological Investigations - San Luis (IMIBIO-SL), National Council of Scientific and Technical Investigations (CONICET), San Luis, Argentina*

Background: Fibroblast-like synoviocytes (FLS) exhibit a transformed aggressive phenotype characterized by increased secretion of pro-inflammatory cytokines and matrix metalloproteinases (MMPs). Early pathological mechanisms that explain the change to an altered phenotype in FLS of chronic inflammatory arthropathies remain largely unknown. The composition of synovial fluids (SF) is very complex and strongly influences the microenvironment of joints including FLS thus representing an inseparable element of the disease. The MMP-9 is a