(RKIP), an endogenous inhibitor of the extracellular signal-regulated kinase (ERK) pathway, has been implicated as a suppressor of metastasis and NF- κ B pathway in cancers².

Objectives: The NF- κ B and ERK pathways are considered to be one of the most important pro-inflammatory signalling pathways in RA. Therefore, RKIP might be a potential therapeutic target for RA. However, whether and how RKIP regulates RA is not fully understood. The present study was performed to examine whether and how RKIP are differentially regulated in RA.

Methods: The expressions of RKIP were assessed in synovial tissue, fluid and fibroblast-like synoviocytes (FLS) from patients with RA and osteoarthritis (OA) by immunofluorescence staining and western blotting. RA- or OA-FLS were infected with either a recombinant adenoviral RKIP overexpressing vector (Ad-RKIP) or shRNA-expressing vector (Ad-shRKIP). Control cells infected with a GFP-targeted recombinant adenoviral vector (Ad-shGFP) (figure 1C). And then, we investigated the effects of RKIP on the migratory activity and invasion rates of FLS by transwell migration and invasion assay.

Results: Here, we show that RKIP expression is inversely correlated with RA. The levels of RKIP were significantly decreased in fibroblast-like synoviocytes (FLS), synovial fluid and synovium of RA patients compare to OA patients. And also find that migration and invasion of RKIP in RA were significantly increased by the inhibition of RKIP compare to OA-FLS. Knockdown of RKIP in RA or OA-FLS resulted in a dramatic increase of MMP3 and IL6. We also found osteoclastogenesis of RAW cells were increased by the knockdown of RKIP.

Conclusions: Our data identify a role of RKIP in RA and suggest that further studies on the potential involvement of RKIP will be beneficial in better understanding the pathology of and providing a new target for treatment for RA.

REFERENCES:

- [1] Ospelt C. Synovial fibroblasts in 2017. *RMD Open* 2017;3(2):e000471.
- [2] Yesilkanal AE, Rosner MR. Raf kinase inhibitory protein (RKIP) as a metastasis suppressor: regulation of signaling networks in cancer. *Crit Rev Oncog*. 2014;19:447–454.
- [3] Noh HS, Hah YS, Ha JH, Kang MY, Zada S, Rha SY, Kang SS, Kim HJ, Park J, Byun J, Hahm JR, Shin JK, Jeong S, Lee Y, Kim DR. Regulation of the epithelial to mesenchymal transition and metastasis by Raf kinase inhibitory protein-dependent Notch1 activity. *Oncotarget* 2016;7(4):4632–46.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.5076

Spondyloarthritis – etiology, pathogenesis and animal models

AB0141 CERTOLIZUMAB PEGOL LIKE REDUCES INFLAMMATION AND BONE DAMAGE IN TMTNF TRANSGENIC MICE

E. Vieira-Sousa¹, S. Caetano Silva², B. Vidal², I. Lopes², H. Canhão³, J. E. Fonseca¹. ¹Rheumatology and Metabolic Bone Diseases Department, Hospital de Santa Maria, CHLN and Rheumatology Research Unit, Instituto de Medicina Molecular, Faculty of Medicine, University of Lisbon, Lisbon Academic Medical Centre; ²Rheumatology Research Unit, Instituto de Medicina Molecular, Faculty of Medicine, University of Lisbon, Lisbon Academic Medical Centre; ³CEDOC, EpiDoc Unit, NOVA Medical School, Lisbon, Portugal

Background: Transmembrane (tm)TNF (TgA86) mice is a transgenic line that spontaneously develops peripheral arthritis and spondylitis at 4 weeks of age, mimicking human spondyloarthritis (SpA).

Objectives: The aim of this work is to understand the effect of TNF blockade in this SpA-like phenotype mouse strain, focusing on histological inflammation and bone damage.

Methods: (tm)TNF (TgA86) mice were treated with a certolizumab pegol like product mice equivalent (Ab501), 100 mg/kg twice a week intraperitoneal, or with vehicle (phosphate buffer saline), for 12 weeks, in a therapeutic (10 weeks of age) and preventive (4 weeks of age) experimental settings. A semi-quantitative score for the severity of histologic inflammation and bone damage, in the paws (infiltration, lining cells, erosions and global), and in the spine (inflammation, intervertebral disc destruction, cartilage damage, bone erosion and ectopic chondrocytes/chondrocyte) was applied to haematoxylin and eosin stained slides.

Results: 14 (tm)TNF (TgA86) mice (6M/8F) at 10 weeks of age (therapeutic group), and 15 (tm)TNF (TgA86) mice (10M/5F) at 4 weeks of age (preventive group), were treated with Ab501; and 30 (tm)TNF (TgA86) mice with the respective vehicles, for a period of 12 weeks. A statistically significant reduction of the inflammatory infiltrate ($p < 0.001$), lining cells layers ($p < 0.05$), erosions ($p < 0.05$) and global inflammatory score ($p < 0.05$) of the paws, was observed in the Ab501

treated group, when compared to the vehicle group, both in the 10 and 4 weeks of age treatment groups. In the spine, statistically significant reductions of the inflammation ($p < 0.001$), intervertebral disc destruction ($p < 0.05$), cartilage damage ($p < 0.001$), bone erosion ($p < 0.05$), and ectopic chondrocytes/chondrocyte scores ($p < 0.001$) was also depicted in Ab501 treated group in comparison with vehicle.

Conclusions: The certolizumab pegol like product mice equivalent reduced histologic inflammatory infiltrate in paws and spine of (tm)TNF (TgA86) mice. Bone damage, as defined by erosions in the paws and spine and ectopic chondrocytes/chondrocyte formation in the spine, also significantly improved in (tm)TNF (TgA86) mice.

Acknowledgements: To Leonie M van Duivenvoorde and Dominique Baeten (Amsterdam Academic Medical Centre) for providing (tm)TNF (TgA86) mice for breeding and colony establishment. George Kollias from Flemming Institute for authorisation for the use this mice line.

This investigator-initiated study was supported (financial and product) by UCB.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.4312

AB0142 A REGULATORY CCR10+ CD8+ T CELL POPULATION DIFFERENTIATES PSORIATIC ARTHRITIS FROM PSORIASIS LIMITED TO CUTANEOUS INVOLVEMENT

E.F. Leijten^{1,2}, T.S. van Kempen^{1,2}, M.A. Olde Nordkamp^{1,2}, J.S. Mertens^{1,2}, C. Angiolilli^{1,2}, M.L. Boes^{2,3}, T.R. Radstake^{1,2}. ¹Department of Rheumatology and Clinical Immunology; ²Laboratory of Translational Immunology; ³Department of Pediatrics, UMC Utrecht, Utrecht, Netherlands

Background: Few studies have compared the immune cell phenotype or function from patients with psoriatic arthritis (PsA) to patients with psoriasis limited to cutaneous involvement (Pso). Head-to-head comparisons of the immune cells in PsA and Pso can provide essential insights into the link between epithelial/cutaneous disease and rheumatic disease.

Objectives: Compare the immune cell phenotype and function from patients with PsA compared to Pso.

Methods: PBMCs were collected from 23 healthy controls, 21 patients with psoriasis in whom psoriatic arthritis was excluded by a rheumatologist (Pso), 23 patients with psoriatic arthritis (PsA) and 16 patients with ankylosing spondylitis. The Pso and PsA cohorts were free from immunomodulatory therapy and matched for demographics and skin severity. Extracellular and intracellular immunophenotyping using a highly standardised flow-cytometric approach detected over 110 different myeloid and lymphoid cell populations. Lesional and non-lesional skin biopsies and synovial fluid samples were collected from a subset of patients.

Results: The circulating immune cell composition showed a remarkable overlap in Pso and PsA, and only one specific cell population was different: CCR10 + CD8 + T cells, being enriched in PsA PBMCs as compared to Pso PBMCs. Further phenotypic and functional evaluation characterised them as effector memory, CXCR3-CCR6-, co-expressing the skin homing markers CCR4 and CLA, but lacking the gut homing marker $\alpha\beta 7$. Upon re-stimulation, CCR10 + CD8 + T cells showed low IFN γ production, high IL-10 production and were enriched for FOXP3^{high}CD25+ phenotype. Their frequencies in PBMCs were unrelated to joint disease activity and were stable throughout joint disease fluctuations. Synovial fluid displayed low frequencies of CCR10 + CD8 + T cells whereas skin contained the most abundant CCR10 + CD8 + T cell frequencies. Lesional psoriasis skin displayed relatively fewer CCR10 + CD8 + T cells compared to non-lesional skin.

Abstract AB0142 – Figure 1

Conclusions: CCR10 + CD8 + T cells have regulatory properties and differentiate Pso from PsA. Future studies are needed to uncover if aberrances in regulatory, cutaneous CD8 + T cells precede the transition to joint disease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.5237

AB0143

IMPLICATION OF OSTEONECTIN ON CARDIOVASCULAR RISK IN AXIAL SPONDYLOARTHRITIS: A SEROLOGICAL AND GENETIC STUDY

F. Genre¹, J. Rueda-Gotor¹, S. Remuzgo-Martínez¹, J. Irure-Ventura², A. Corrales¹, V. Mijares¹, V. Portilla¹, R. Blanco¹, L. Rodríguez-Rodríguez³, J. L. Hernández⁴, J. Llorca⁵, J.G. Ocejó-Vinyals², R. López-Mejías¹, M.A. González-Gay¹. ¹Epidemiology, Genetics and Atherosclerosis Research Group on Systemic Inflammatory Diseases, IDIVAL; ²Immunology Division, Hosp. Univ. M. de Valdecilla, Santander; ³Rheumatology Dept, Inst. de Inv. Sanitaria del Hosp. Clín. San Carlos (IDISSC), Hosp. Clín. San Carlos, Madrid; ⁴Bone Metabolism Unit, Dept. of Internal Medicine, Hosp. Univ. M. de Valdecilla, IDIVAL, Univ. of Cantabria, Reticef; ⁵Dept. of Epidemiology and Computational Biology, School of Medicine, Univ. of Cantabria, and CIBER Epidemiología y Salud Pública (CIBERESP), IDIVAL, Santander, Spain

Background: Cardiovascular (CV) disease and atherosclerosis are common causes of morbidity in axial spondyloarthritis (axSpA),¹ a disease characterised by changes in the osteoproliferative process. A dysregulation in the molecules involved in bone remodelling could also affect the atherosclerotic process, since both processes are linked.²⁻³ Osteonectin (ON), a key molecule in bone homeostasis,⁴ was associated to obesity, insulin resistance and diabetes.⁵

Objectives: Since the exact role of ON on CV risk in axSpA has not been elucidated yet, we evaluated its role in the development of subclinical atherosclerosis and its association with CV risk factors in axSpA patients at the serological and genetic level.

Methods: 171 axSpA patients fulfilling the classification criteria for axSpA^{6,7} and 84 controls were included in this study. Serum ON levels were measured by multiplex assays. Carotid ultrasound was performed to evaluate the presence of markers of subclinical atherosclerosis. Five ON polymorphisms (rs1054204 [G/C], rs11950384 [G/A], rs13182103 [A/G], rs11745387 [G/A] and rs4958487 [A/G]) were selected by tagging and genotyped using TaqMan assays.

Results: No difference was observed in ON levels between axSpA and controls. Serum ON and CRP levels at study positively correlated in axSpA ($p=0.008$). Higher ON levels were observed in men, smokers and patients with an atherogenic index indicative of dyslipidemia ($p=0.008$, 0.01 and 0.001 , respectively). No association was found between ON and subclinical atherosclerosis in axSpA. Interestingly, we disclosed that the presence of the A allele of rs13182103 and rs11950384 ON polymorphisms led to lower ON serum levels in axSpA ($p<0.05$). Furthermore, the presence of the A allele of rs13182103 was linked to a later diagnosis of axSpA when compared to those patients bearing the G allele ($p=0.002$).

Conclusions: Our results show that ON is linked to inflammation and CV risk factors in axSpA and suggest that the A allele of rs13182103 and rs11950384 ON polymorphisms may have a protective effect in axSpA, leading to reduced ON serum levels and later diagnosis of the disease. These data support an implication of ON in the development and progression of atherosclerotic disease in axSpA.

REFERENCES:

- [1] Joint Bone Spine 2014;81(1):57–63.
- [2] Clin Chim Acta 2015;438:401–14.
- [3] Arterioscler Thromb Vasc Biol 2001;21(12):1998–2003.
- [4] J Bone Miner Res 2015;30(4):723–32.
- [5] Int J Clin Exp Med 2015;8(10):19290–6.
- [6] Ann Rheum Dis 2009;68:777–83.
- [7] Arthritis Rheum 1984;27:361–8.

Acknowledgements: FG is a recipient of a Sara Borrell post-doctoral fellowship from Instituto de Salud Carlos III (ISCIII, Spain), co-funded by European Social Fund (ESF,CD15/00095). SR-M is supported by funds of RETICS Program (RD16/0012/0009,ISCIII,co-funded by European Regional Development Fund, ERDF). RL-M is a recipient of a Miguel Servet type I fellowship from ISCIII, co-funded by ESF(CP16/00033). VM is supported by funds of a Miguel Servet type I (CP16/00033)(ISCIII, co-funded by ERDF).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.5186

AB0144

NMR BASED SERUM AND SYNOVIAL FLUID METABOLOMICS REVEAL SIMILAR METABOLOMIC PROFILE IN PATIENTS WITH REACTIVE ARTHRITIS AND UNDIFFERENTIATED SPONDYLOARTHRITIS

R. Misra¹, D. Dubey², S. Ahmed³, S. Chaurasia¹, S. Chaudhary¹, A. Guleria², D. Kumar². ¹Clinical Immunology, Sanjay Gandhi Post Graduate Institute of Medical Sciences; ²Centre for Biomedical Research; ³Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India

Background: Reactive arthritis (ReA) and undifferentiated spondyloarthritis (USpA) have similar clinical picture, the former is preceded by mucosal infections and the latter do not meet criteria of well defined entity of seronegative spondyloarthritis (SSA). We have shown that both ReA and USpA have similar synovial fluid T cell response to salmonella antigens and cytokine profile.

Objectives: To investigate if the metabolic profiles of ReA in sera and synovial fluid are different from those of USpA

Methods: Standard definitions were used to classify patients as ReA² and USpA³. Metabolic profiles in sera and synovial fluid samples were measured using 1D ¹H NMR spectroscopy and analysed using CHENOMX® software. The quantitative profiles between the groups were compared using Partial Least Square-Discriminatory Analysis (PLS-DA) and Q² parameter was used to assess the metabolic differences between the groups.

Results: The study involved 19 ReA and 13 USpA patients with median age 26 (21–33.75) years. Of 32 patients: 7 (22%) were females, three (12%) had mono-phasic illness, 16 (64%) polyphasic, and six (24%) persistent arthritis (follow-up data was not available for 7). 27% had monoarticular, 59% oligoarticular and 14% polyarticular involvement. Six had inflammatory backpain, three had oral ulcers, one dactylitis, but none had mucocutaneous manifestations. Two had asymptomatic sacroiliitis on radiographs.

Compared to normal controls ($n=18$, median age=29 years, male:female=17:1), the sera of ReA/USpA patients were characterised by elevated levels of malonate, mannose, N-nitrosodimethylamine, and pyruvate, whereas 3-hydroxyisovalerate was decreased significantly (T-test p -value<0.001). PLS-DA analysis between sera and synovial fluid samples showed clear demarcation with higher pyruvate and acetoacetate and lower aspartate, methanol, ethanol, and methylsuccinate in synovial fluid samples compared to sera (t-test $p<0.01$). The PLS-DA analysis of sera showed little difference between ReA and USpA (figure 1) while that of synovial fluid showed Q² <0 for all models. Further no significant metabolic differences in sera/synovial fluid were found between HLA-B27 positive and negative groups (Q² <0 in all models).

Abstract AB0144 – Figure 1. (a) PLS-DA of sera of HLA B27 positive versus negative patients (b) PLS-DA of synovial fluid of HLA B27 positive versus negative patients

Conclusions: ReA and USpA have indistinguishable metabolomics profiles in sera and synovial fluid reflecting similar metabolo-inflammatory pathways involved.

REFERENCES:

- [1] Chaurasia S, Shasany AK, Aggarwal A, Misra R. 2016 Aug;185(2):210–8.
- [2] Braun J, Kingsley G, et al. Journal of Rheumatology 2000;27:2185–92.
- [3] Sieper J, Rudwaleit M, et al. Ann Rheum Dis. 2009 Jun;68(Suppl 2):ii1–44.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.6257