wound healing response including myofibroblast differentiation and that humeral mediators found in the joint can promote myofibroblast production of ED-A FN. We additionally show that recombinant and plasmin-derived ED-A fragments can induce generation of pro-inflammatory mediators from FLS and MDM. This study supports targeting the formation of ED-A FN or the enzymatic fragmentation of FN to reduce pro-inflammatory responses in OA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2239

OP0326 EPIGENETICALLY-DRIVEN DISTAL EXPRESSION OF THE LNCRNA HOTTIP SHAPES INFLAMMATORY, ADHESIVE AND PROLIFERATIVE CHARACTERISTICS OF HAND SYNOVIAL FIBROBLASTS IN ARTHRITIS

M. Frank Bertoncelj[1], E. Karouzakis[1], K. Klein[1], A. Bratus[2], C. Kolling[3], O. Distler[1], A. Filer[4], R.E. Gay[1], C.D. Buckley[4], S. Gay[1], C. Ospelt[1].
[1]University Hospital Zurich, Schlieren; [2]Functional Genomics Center Zurich; [3]Schulthess Klinik, Zurich, Switzerland; [4]University of Birmingham, Birmingham, United Kingdom

Background: Rheumatoid arthritis (RA) and other types of inflammatory arthritis show a characteristic pattern of joint involvement. E.g. in RA there is a predilection for the small joints of hands and feet, whereas in spondyloarthropathy, single large joints are characteristically involved. We have recently shown that synovial fibroblasts (SF), which drive joint destruction in RA, display site-specific transcriptomes and functions, shaping unique microenvironments in different joints.

Objectives: To analyze the role of transcripts expressed in SF at specific joint locations in defining location-specific functions of SF, relevant to the pathogenesis of RA.

Methods: SF were isolated from hand, elbow, shoulder, feet, knee and hip joints of RA and OA patients undergoing joint replacement surgery and from knees of nonarthritic subjects with arthralgia. Transcriptomes and epigenomes of SF were determined by RNA-seq (Illumina HiSeq 2000, n=21), qPCR, ChIP-seq (H3K4me3, H3K27me3, H3K27ac, Illumina HiSeq 2500, n=7) and Infinium HumanMethylation450 BeadChip (n=12). Proliferative, adhesive and chemotactic properties of SF were studied by xCELLigence real time cell analysis and leukocyte chemotaxis towards supernatants of SF. The lncRNA HOTTIP was silenced in hand SF using LNA GapmeR oligos, followed by RNA-seq (n=2), pathway enrichment analysis (MetaCore, Thomson Reuters, FDR$<$0.05) and qPCR (n=5).

Results: HOTTIP was the most differentially expressed transcript in distal (hand) vs. proximal (shoulder) SF. HOTTIP was specifically transcribed in SF from hand and feet SF, but absent from other joints, inferring distal-specific function to this lncRNA. Hand-specific HOTTIP expression coincided with the enrichment of activating histone marks H3K4me3 and H3K27ac, absence of repressive H3K27me3 and decreased DNA methylation at the HOTTIP promoter in hand SF. In contrast, the HOTTIP promoter displayed abundant DNA methylation and H3K27me3 in knee and shoulder SF. Silencing of HOTTIP led to downregulation of 3275 genes and upregulation of 4326 genes (log ratio $>|0.5|$, $p<0.01$, FDR$<$0.05). Distal-specific homeobox A13, a known HOTTIP target, was repressed in HOTTIP-silenced SF. Pathway enrichment analysis of genes repressed by HOTTIP silencing showed enrichment for pathways regulating cell adhesion, cell cycle, angiogenesis and inflammation, including NF-kB activation and IL-6 signalling. Meanwhile, upregulated genes were enriched in fewer pathways, e.g. IL17 and Notch signalling. 110 genes that were differentially expressed in hand vs. shoulder SF were also altered by HOTTIP silencing, e.g. TNFRSF1B and MAP3K14. Hand SF showed enhanced proliferative and chemotactic, but decreased adhesive properties compared to shoulder SF.

Conclusions: The lncRNA HOTTIP, which is exclusively expressed in small, distal joints, via epigenetic mechanisms, is a regulator of inflammatory, proliferative and adhesive properties of SF. Such a functional specialization of arthritis relevant pathways in SF might represent an imprinted site-specific "risk" signature in SF, predisposing thereby to location-specific joint pathology, e.g. enhanced severity of hand arthritis in RA.

Disclosure of Interest: M. Frank Bertoncelj Grant/research support from: euroTEAM, BTCure, IAR, Promedica, Georg und Berta Schwyzer Winiker Grant, E. Karouzakis Grant/research support from: BTCure, GSK, K. Klein Grant/research support from: BTCure, A. Bratus: None declared, C. Kolling: None declared, O. Distler Grant/research support from: Actelion, Bayer, Boehringer Ingelheim, Pfizer, Sanofi, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, ChemomAb, EpiPharm, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, Mepha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Serodapharm, Sinoxa, Speakers bureau: AbbVie, iQone Healthcare, Mepha, A. Filer: None declared, R. Gay Grant/research support from: euroTEAM, BTCure, GSK, IAR, C. Buckley: None declared, S. Gay Grant/research support from: euroTEAM, BTCure, GSK, IAR, C. Ospelt Grant/research support from: euroTEAM, BTCure, CABMM, IAR, Promedica

DOI: 10.1136/annrheumdis-2017-eular.2689

FRIDAY, 16 JUNE 2017

Patient engagement in research: best practices, benefits and challenges

OP0327-PARE YOUR RHEUM – GIVING YOUNG PEOPLE A VOICE IN RHEUMATOLOGY RESEARCH

K. Cresswell[1,2], S. Parsons[1,2], S. Stones[3], J.E. McDonagh[4,5,6], W. Thomson[4,5,6], L. Lunt[7]. *[1]Public Programmes Team, Central Manchester NHS Foundation Trust, University of Manchester; [2]Manchester Academic Health Science Centre; [3]Public Contributor; [4]Arthritis Research UK Centre for Genetics and Genomics, Centre for Musculoskeletal Research, University of Manchester; [5]NIHR Manchester Musculoskeletal Biomedical Research Unit, Central Manchester NHS Foundation Trust, University of Manchester; [6]Barbara Ansell National Network for Adolescent Rheumatology; [7]Arthritis Research UK Centre for Epidemiology, Centre for Musculoskeletal Research, University of Manchester, Manchester, United Kingdom*

Background: Between 2014 and 2016, the Barbara Ansell National Network for Adolescent Rheumatology (BANNAR) commissioned research to explore young people's rheumatology research priorities and beliefs about research involvement. The next phase of this work has been to establish a UK-wide research advisory group, Your Rheum, to involve 11–24 year olds with rheumatic and musculoskeletal diseases (RMDs) more effectively in shaping research.

Objectives: To describe our experiences of developing a UK-wide research advisory group, for young people with RMDs, using both face-to-face meetings and online involvement approaches.

Methods: From September 2016, we recruited young people to the group using several approaches: including the previous research study database, through BANNAR members, through UK charities, such as Arthritis Care and via social media. To tailor options for involvement, young people were recruited to contribute to both face-to-face meetings and via online channels.

Results: Eight young people attended Your Rheum's first meeting in October 2016, where they discussed how they would like the group to work. Thirteen young people have been engaged online via a closed Facebook group, monitored by the Your Rheum facilitator. Key challenges in establishing the group have included developing age-appropriate communication approaches to appeal to the range of ages involved, devising ways of ensuring online members remain engaged with the group, and finding appropriate tasks for the group to be involved with, that are both suitable and aligned with research project timings. This involves working closely with young people, health professionals and researchers.

Conclusions: There is both a need for young people's involvement in research and a desire from young people themselves to do so. Expansion of the online network and involvement activities will allow young people across the UK to have a valuable input into research, regardless of location.

References:

[1] What do young people with rheumatic conditions think about being involved in research? 2017, S.Parsons, W.Thomson, K.Cresswell, B.Starling, J.E.McDonagh (unpublished).

Acknowledgements: This abstract presents independent work funded by Arthritis Research UK BANNAR grant 20164 via the Centre for Adolescent Rheumatology at UCL.

Supported by the National Institute for Health Research Biomedical Research Unit.

We would like to thank all of the young people who took part in the YOURR study and are currently part of Your Rheum, the clinicians, PPI coordinators and other individuals who facilitated their involvement, members of the Barbara Ansell National Network for Adolescent Rheumatology and Arthritis Care.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5807

FRIDAY, 16 JUNE 2017

Latest advances in the treatment and management of psoriatic arthritis and the latest news on the use of biosimilars in RMDs

OP0328-PARE PATIENT SAFETY IN RELATION TO BIOSIMILARS – HOW CAN WE ACT AS A PATIENT ORGANIZATION?

L.M. Thomsen. *Danish Rheumatism Association, Gentofte, Denmark*

Background: During the last years two biosimilars has been approved by the national authorities in Denmark, and implemented in the treatment of patients with arthritis. When the first biosimilars were approved in 2015, the hospitals in Denmark decided to shift native patients from the original drug to the new biosimilar. This decision caused considerable insecurity among the patients, who were afraid of biosimilars and their effectiveness and safety profile. Therefore the Danish Rheumatism Association decided to implement an effort to create better patient information and safety for patients, who had to start with a biological drug or shift from one biological drug to another or to a biosimilar.

Objectives: The purpose of the effort was to increase patient safety and to ensure that patients received independent patient information within biological drugs.
Methods: First the Association conducted a small study of how the shift of drug had taken place in the different regions. Most patients experienced that they were told by the doctors to shift to biosimilars, and furthermore they experienced a lack of information about the new biosimilars. On a national level, nearly all patients on a biological drug are registered in a national database. It is registered in the database and hospital records which drug the patient are prescribed, but it is not registered on a batch-level.
In order to change these conditions the Association started a dialog with the politicians and the authorities on a national level and the hospital-administrations on a regional level. The purpose was to improve the registration of the drugs on batch-level, to improve more independent patient information and to improve the involvement of the patient in the decision making process. The dialog was on a general level, but with several patient-stories from each region.
Results: A new national plan for better monitoring and information about biologic and biosimilars was launched in august 2015 and carried out in 2016. The plan consists of four parts: 1) Monitoring biological drugs and biosimilars on batch level, 2) Information campaign to health professionals and patients, 3) Digital solutions and easy reporting of side effects from health professionals and patients, 4) Focus on monitoring patient safety by the authorities. The Danish Rheumatism Association has participated in the work to implement the plan. In addition to the national plan the hospitals on a regional level, has invited the Rheumatism Association to participate with a representative in the working group, where national recommendations for the use of biological drugs are being made in an attempt to involve the patient perspective more. The content of the national plan and the involvement in the work with national recommendations, will be elaborated and discussed from the patients perspective throughout the presentation.
Conclusions: The implementation of biosimilars created great insecurity among patients. Therefore, the Danish Rheumatism Ass. decided to make an effort to create better patient information and safety for the patients. Through dialog with politicians, national authorities and hospital-administrations, we managed to get a national plan for better monitoring and information about biologic and biosimilars, and to be involved in the work with national recommendations for these drugs. The national plan and work with national recommendations will be elaborated in the presentation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3716

FRIDAY, 16 JUNE 2017

Switching T on and off: how T cells drive and regulate chronic inflammation

OP0329 INVOLVEMENT OF T HELPER 17 CELLS IN INFLAMMATORY ARTHRITIS DEPENDS ON THE HOST INTESTINAL MICROBIOTA

H. Evans-Marin[1], R. Rogier[2], J. Scher[1], D. Roeleveld[2], M. Koenders[2], S. Abdollahi-Roodsaz[1,2]. *[1]Medicine, New York University School of Medicine, New York, United States; [2]Rheumatology, Radboud university medical center, Nijmegen, Netherlands*

Background: Intestinal microbiota have been associated with psoriatic and rheumatoid arthritis. One of the major effects of microbiota is the induction of mucosal T helper 17 (Th17) cells. We therefore reasoned that the efficiacy of Th17-targeted therapies in arthritis may depend on the host microbiota. Previous studies focused on the role of the cytokine interleukin-17A (IL-17), rather than Th17 cells, by using IL-17 inhibitors or IL-17-deficient mice. Therefore, the role of Th17 cells, which produce multiple pro-inflammatory mediators in addition to IL-17, is not yet fully understood.
Objectives: The aim of this study was to determine the role of Th17 cells, beyond the cytokine IL-17, in arthritis, and to investigate whether Th17 cells are differentially involved in arthritis depending on the microbiota present.
Methods: We established conditional Th17-deficient mice, which exhibit a CD4-Cre-induced floxing of a part of the Rorc allele that encodes the Th17 master regulator RORγt. We compared the development of collagen-induced arthritis in Th17-deficient (CD4-Cre$^+$ Rorc$^{flox/flox}$) and -sufficient (CD4-Cre$^-$ Rorc$^{flox/flox}$) littermate mice, either colonized with known Th17 cell inducers segmented filamentous bacteria (SFB) or harboring the SFB-free Jackson microbiota. The abundance of Th1 and Th17 cells and the production of IL-17, IFNγ and GM-CSF were quantified by flow cytometry and multiplex cytokine assay.
Results: CD4-Cre$^+$ Rorc$^{flox/flox}$ mice had significantly lower Th17, but similar Th1 cell abundance, in intestinal lamina propria compared with Cre$^-$ littermate controls. Surprisingly, the total amount of IL-17A production by all lamina propria cells during arthritis was rather increased in Th17-deficient mice, with CD8$^+$ T cells and Gr1$^+$ neutrophils being the main alternative sources of IL-17. Despite this increased total IL-17 levels, conditional Th17-deficient mice developed a less severe arthritis compared with Th17-sufficient mice when intestinal microbiota comprised SFB. This suggests a role for Th17 cells in inflammatory arthritis distinct from IL-17. Accordingly, synovial inflammation, cartilage destruction and proteoglycan depletion were reduced in SFB-colonized Th17-deficient mice. While the production of IL-17 by joint-draining lymph node cells stimulated with PMA and ionomycin was similar between Th17-sufficient and –deficient mice, cells from the latter group produced significantly less IL-17 upon antigen-specific stimulation with type II collagen. Furthermore, the production of GM-CSF, another Th17 cell-derived cytokine, was significantly lower in the lymph nodes of Th17-deficient mice, an effect associated with the protection against arthritis. Importantly, substitution of the intestinal microbiota with SFB-free Jackson microbiota resulted in the loss of Th17 cell dependency of arthritis as Th17-sufficient and –deficient mice showed similar disease progression under this condition.
Conclusions: These data suggest that Th17 cells may mediate inflammatory arthritis partly through IL-17-independent mechanisms. Our observations also suggest that the involvement of Th17 cells in arthritis depends on the microbiota subset present in the host. Therefore, a microbiome-guided stratification of rheumatoid or psoriatic arthritis patients might improve the efficacy of Th17 (or IL-17)-targeted therapies.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5522

OP0330 FRA2 OVEREXPRESSION LEADS TO SYSTEMIC AUTOIMMUNITY BY DECREASING IL-2 RESPONSIVENESS AND THYMIC TREG DEVELOPMENT

F. Renoux[1], M. Stellato[1], D. Impellizzieri[2], A. Vogetseder[3], R. Huang[4], A. Subramaniam[4], C. Dees[5], J.H.W. Distler[5], G. Kania[1], O. Boyman[2], O. Distler[1]. *[1]Department of Rheumatology; [2]Department of Immunology, University Hospital Zurich, Zurich; [3]Pathology, Luzerner Kantonspital, Lucerne, Switzerland; [4]Immune Mediated Diseases, Sanofi-Genzyme, Framingham, United States; [5]Department of Internal Medicine 3, University of Erlangen-Nuremberg, Erlangen, Germany*

Background: Fos-related antigen 2 (Fra2) is a transcription factor belonging to the Fos family proteins which is part of the AP-1 transcription complex. We recently described a Fra2 transgenic (tg) mouse model which develops a multi-organ inflammatory phenotype affecting skin, lungs, thymus, liver and salivary glands. We have observed abnormalities in the T cell compartment, particularly in regulatory T (Treg) cells, which led us to hypothesize that Fra2 tg mice develop a T cell driven autoimmune phenotype.
Objectives: To demonstrate the autoimmune phenotype of Fra2 tg mice and to characterize the mechanisms leading to Treg cell abnormality.
Methods: We used previously generated Fra2 tg overexpressing mice. T lymphocyte populations were analyzed by flow cytometry for expression of activation markers and secretion of cytokines. We transferred purified CD4+ T cells into Rag2-/- mice lacking T and B cells, and we generated Rag2-/-Fra2 tg mice. Bone marrow cells were transferred into lethally irradiated recipients to create Fra2-WT bone marrow chimeric mice.
Results: Fra2 tg mice backcrossed onto a Rag2$^{-/-}$ background did not develop inflammatory manifestations (n=6), demonstrating the dependence on T and/or B cells of the autoimmune phenotype. In line with this, the transfer of purified CD4$^+$ cells from 16 week-old Fra2 tg mice into Rag2$^{-/-}$ recipients was sufficient to transfer the disease phenotype (n=3). Analysis of T cell populations from Fra2 tg mice showed the presence of activated CD4$^+$ and CD8$^+$ cells in the spleen