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

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

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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.

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Patient engagement in research: best practices, benefits and challenges

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

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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:

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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?

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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.