monoculture (IL-1β (75%), activin A (22%), activin A and IL-1β (101%), follistatin and IL-1β (67%)).

Conclusions The autoregulatory cycle of activin A and follistatin is active in HUVECs, but not in RA SF. In direct coculture of HUVECs and RA SF, the effects of HUVECs appear to overwhelm resulting in a significant reduction of IL-1β in the presence of follistatin.

Disclosure of Interest None declared.

P081/O20

LASP1 REGULATES CELL-TO-CELL CONTACT FORMATIONS OF FIBROBLAST-LIKE SYNOVIOCYTES IN RA

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Introduction In rheumatoid arthritis (RA), fibroblast-like synoviocytes (FLS) undergo a stable transformation resulting in an aggressive, tumour-like phenotype that mediates cartilage damage by increased levels of MMPs and adhesion molecules such as β1 integrins. In this context, the tumour-associated protein Lasp1 is of interest because it modulates actin organization and focal adhesion turnover.

Objectives The effects of Lasp1 deficiency on RA-FLS cell-to-cell contact formations, the disease course and joint destruction have been investigated in this study.

Methods Lasp-1 expression was analysed in RA synovial tissue and in murine models of arthritis (hTNFtg mice and G6PI mouse model). Hind paws were analysed by using WB analyses and immunofluorescence stainings, primary FLS were isolated and cultivated, respectively. Furthermore, Lasp1+/− mice were interbred with hTNFtg mice and offspring were analysed for the progression of joint destruction by clinical evaluation and histopathology. Migration characteristics of FLS derived from wild type (wt), Lasp1+/−, hTNFtg and Lasp1−/-hTNFtg mice were analysed by live cell imaging. Additionally, we used an in vitro 3D organ culture system for functional analyses.

Results Upregulated Lasp1 levels in RA synovial tissue and FLS were observed. In line with the human data, increased levels of Lasp1 were found in murine FLS derived from hTNFtg mice and the chronic G6PI mouse model. Lasp1 was located in structures of cell-matrix as well as cell-to-cell contacts. The loss of Lasp1 led to clear alterations in adherens junction formation indicating by altered β-catenin pattern. In vivo evaluation of Lasp1−/-hTNFtg mice revealed a milder arthritis score, less cartilage degradation and reduced FLS attachment to articular cartilage compared to hTNFtg mice. In vitro migration assays using live cell imaging demonstrated alterations in spreading morphology and cell-to-cell contact turnovers and a significantly reduced migration rate of Lasp1−/- FLS and Lasp1−/-hTNFtg FLS compared to controls (~69.11% after 24 hour). Histological sections of the 3D matrices demonstrated that wt FLS formed an organised synovial structure comparable with healthy synovial tissue in vivo, whereas in matrices with hTNFtg FLS this synovial architecture was absent. Interestingly, Lasp1 deletion in the hTNFtg background resulted in an organised cellular lining layer comparable with wt FLS matrices.

Conclusions Lasp1 represents an interesting target involved in RA-caused joint destruction, because its loss resulted in significantly reduced cartilage destruction in vivo and RA-FLS interactions and migration rates in vitro.

Disclosure of Interest None declared.