molecules during inflammation. The results support the rationale to for development of TNFR1 specific antagonists or TNFR2 agonists for the treatment of RA.

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THU0052 A CIRCULATING PROTEIN SIGNATURE CORRELATES WITH SYNOVIAL PATHOTYPES IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) is a disease characterised by high clinical variability and an underlying cellular and molecular heterogeneity. Efforts to find tools for the classification of the different disease phenotypes and patient stratification are essential to develop tailored therapies and improve its management. According to this, specific pathological phenotypes of synovial tissue (pathotypes) have emerged as associated with diverse clinical evolution and response to therapy.¹

Objectives: To identify signatures of circulating proteins associated with specific synovial pathotypes in RA patients.

Methods: A proteomic analysis was carried out on samples from patients enrolled in the Pathobiology of Early Arthritis Cohort. Ultrasound-guided synovial biopsies from these patients allowed their classification into three groups: lymphoid (L), myeloid (M) or fibroid (F), according to the pathotype. The study was performed using 54 serum samples at baseline. Sera were analysed by nanoliquid chromatography coupled to mass spectrometry using a SWATH strategy on a triple TOF (Sciex). The proteomic data were processed using ProteinPilot and PeakView. A two-stage support vector machine (TSSVM) with RBF kernel and 10 cross-fold validation for each meta-model was applied using the Classifyfire, e1071 and caret R packages.

Results: The proteomic analysis led to the identification and quantification of 229 proteins in all samples. A screening was performed on a group of 30 samples (Train set: 10 L, 10 M and 10 F). Data were pre-processed by PCA for dimension reduction. Then, application of machine learning tools led to the identification of a panel of 11 proteins whose different abundance is associated with a specific synovial phenotype (either L, M or F) in RA patients. As shown in the table 1, a very high accuracy and Kappa coefficient were achieved with this classification tool. The results were confirmed on an independent validation set of 24 samples (12 L, 8 M and 4 F) with also good performance. This protein signature allowed the correct classification of the samples into the three pathotypes with very high sensitivity and specificity (see table 1).

Abstract THU0052 – Table 1. Metrics of the classification performance of the 11-protein panel identified in this work as associated with the synovial pathotype of the patient. Cut-off for significance was p-value<0.05.

Train set				Classes in the train set			
				Fibroid		Lymphoid	
Accuracy	0.9667	95% CI	(0.8278–0.9992)	Sensitivity/	1.000/	1.000/	0.9091/
				Specificity	1.000	0.9524	1.000
				Pos/Neg	1.000/	0.9000/	1.000/
Kappa	0.95	P-Value	4.48E-09	Pred Value	1.000	1.000	0.9500
				Classes in the validation set			
Validation set				Fibroid		Lymphoid	Myeloid
Accuracy	0.875	95% CI	(0.6764–0.9734)	Sensitivity/	1.000/	0.8462/	0.8750/
				Specificity	0.9524	0.9091	0.9375
				Pos/Neg	0.7500/	0.9167/	0.8758/
Kappa	0.7907	P-Value	0.0005881	Pred Value	1.000	0.8333	0.9375

Conclusions: A signature of 11 circulating proteins has been identified as associated with synovial pathotypes in RA patients. The putative correlation of this signature with the clinical evolution and/or response to therapy of the patients remains to be elucidated.

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THU0053 ANTI-FRACTALKINE MONOCLONAL ANTIBODY AMELIORATES JOINT DESTRUCTION IN COLLAGEN-INDUCED ARTHRITIS MODEL BY INHIBITION OF OSTEOCLAST PRECURSOR CELL SURVIVAL AND MIGRATION

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Background: In the Phase 1/2 clinical study, E6011, a novel humanised anti-fractalkine (FKN) mAb demonstrated a promising efficacy in active RA patients who were inadequately controlled by MTX and/or TNF- α inhibitors (NCT 02196558). FKN is expressed on endothelial cells and fibroblast-like synoviocytes in synovium and also expressed on osteoblasts. CX3CR1 is expressed on monocytes/macrophages and osteoclast precursor cells (OPCs). Therefore, FKN-CX3CR1 interaction could play pivotal roles in migration, differentiation and activation of those cells. However, the precise mechanism(s) of FKN-CX3CR1 axis in RA, especially on joint destruction remains to be elucidated.

Objectives: We examined the roles of FKN-CX3CR1 axis in joint destruction, particularly focused on osteoclast precursor cells in *in vitro* and *in vivo* by using anti-mouse FKN mAb (anti-mFKN mAb).

Methods: DBA/1J mice were immunised with intradermal injections of bovine type II collagen to induce arthritis (CIA). Anti-mFKN mAb or control IgG were intraperitoneally injected twice a week. The clinical arthritis score was monitored, and joint destruction was evaluated by soft X-ray and histopathology. Plasma levels of joint destruction markers were assessed by ELISA. FKN expression in joint tissues were assessed by immunohistochemistry. Cell survival of bone marrow-derived OPCs without or with immobilised FKN was also assessed by FACS. In *in vivo*, OPCs were labelled by fluorescein and transferred to CIA mice to evaluate migration of OPCs into inflamed synovium. Anti-mFKN mAb or control IgG were injected before the cell transfer. The number of fluorescein-labelled OPCs that migrated into the CIA joint tissue were analysed.

Results: In both prophylactic and therapeutic treatments, anti-mFKN mAb clearly reduced the clinical arthritis score, soft X-ray score. Plasma levels of cartilage oligomeric matrix protein (COMP) and matrix metalloproteinase-3 (MMP-3) were also decreased after treatment with anti-mFKN mAb. Histological analysis revealed that anti-mFKN mAb inhibited synovitis, pannus formation, cartilage destruction, and that it suppressed bone damage with marked reductions in the number of tartrate-resistant acid phosphatase (TRAP)-positive cells. In *in vitro*, RANKL-induced osteoclast differentiation was enhanced by immobilised FKN, and anti-mFKN mAb suppressed FKN-dependent enhancement of osteoclast formation. FKN also enhanced cell survival of OPCs and eventually increased the number of OPCs. In *in vivo*, increasing expression of FKN was detected on endothelium in synovial tissue of CIA mice, and fluorescein-labelled OPCs migrated into the affected synovium. Anti-mFKN mAb clearly abrogated their migration into synovium.

Conclusions: Anti-mFKN mAb remarkably ameliorated the joint destruction with the marked reduction of osteoclasts by the inhibition of both OPC survival and OPC migration in inflamed joint tissues. These results strongly indicate that inhibition of FKN-CX3CR1 axis by a humanised anti-FKN mAb, E6011, is an attractive and affected joints-selective therapeutic strategy for the treatment of both inflammatory synovitis and joint destruction in RA patients.

Disclosure of Interest: None declared

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THU0054 LONG NON-CODING RNA GAPLINC PROMOTES PROLIFERATION AND INVASION OF FIBROBLAST-LIKE SYNOVIOCYTES AS MICRORNA SPONGING IN RA PATIENTS

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Background: Accumulating evidence suggested that long non-coding RNAs (lncRNAs) play diverse functional roles in many autoimmune diseases including