remodelling, its influence on bone stability and development of osteoporosis is not known.

Objectives: The objective of this project is the analysis of the role of miR-146a in bone metabolism.

Methods: Systemic bone, tibiae and femur, of wt and miR-146a deficient animals was assessed histologically and via μ CT analysis, over a period of 3 to 18 months of age. Serum cytokine levels were analysed by Elisa. mRNA expression levels in bone were analysed by qPCR. To induce osteoporosis, ovariectomy (OVX) induced bone loss was performed.

Results: When we analysed bone volume of long bones histologically as well as with μ CT analysis we detected significantly increased trabecular bone mass in miR-146a deficient compared to wt animals, starting at an age of 6 months. However, cortical thickness of systemic bones from miR-146a knock out animals was significantly reduced compared to control mice. Analysis of serum in aged miR-146a deficient animals displayed elevated activity of bone resorbing osteoclasts as amounts of CTX I in miR-146a^{-/-} mice were significantly increased compared to wt animals. Q-PCR analysis of important osteoclast as well as osteoblast marker genes in bones *ex vivo* displayed elevated expression of signature molecules of both cell types in aged miR-146a deficient mice, suggesting a regulatory role of miR-146a in both osteoclasts as well as osteoblasts. When we induced osteoporosis using the OVX disease model, histological analysis of long bones showed significant trabecular bone loss in ovariectomized wt mice. In contrast, we detected no trabecular bone loss in ovariectomized miR-146a knock out animals, suggesting that loss of miR-146a deficiency protects bone loss induced by oestrogen deficiency.

Conclusions: MiR-146a seems to control bone turnover and miR-146a deficient mice accrue bone over time. Moreover this miRNA has a negative influence on bone loss occurring during oestrogen loss induced osteoporosis. Therefore miR-146a could be possibly used as a therapeutic target in the treatment of osteoporosis.

Disclosure of Interest: None declared

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Rheumatoid arthritis – prognosis, predictors and outcome

SAT0073

ACPA AND RF AS PREDICTORS OF SUSTAINED CLINICAL REMISSION IN RHEUMATOID ARTHRITIS PATIENTS: RESULTS FROM THE ONTARIO BEST PRACTICES RESEARCH INITIATIVE (OBRI)

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Background: Positive anti-citrullinated protein antibody (ACPA) and rheumatoid factor (RF) are included among the 2010 ACR/EULAR classification criteria for rheumatoid arthritis (RA). Previous studies have shown that autoantibodies are positive predictors of response in RA patients treated with some biologics whereas other studies suggest worse prognosis if positive for ACPA and RF.

Objectives: The purpose of this study was to evaluate the interaction of RF and ACPA in predicting sustained clinical response in a large observational registry of RA patients followed in routine practice.

Methods: RA patients enrolled in the Ontario Best Practices Research Initiative (OBRI) registry, with active disease (≥ 1 swollen joint), available autoantibody information, and at least 1 follow-up assessment were included in the analysis. Sustained clinical remission was defined as CDAI ≤ 2.8 in at least 2 sequential visits separated by at least 3 and maximum of 12 months. Time to sustained remission was assessed by plotting cumulative incidence curves and multivariate cox regression.

Results: A total of 970 (30%) out of 3251 patients in the registry were included, of whom 262 (27%) were anti-CCP^{neg}/RF^{neg}, 60 (6.2%) anti-CCP^{pos}/RF^{neg}, 117 (12.1%) anti-CCP^{neg}/RF^{pos}, and 531 (54.7%) anti-CCP^{pos}/RF^{pos}. At baseline, significant differences were observed between groups in age ($p=0.02$), CDAI ($p=0.03$), tender joint count ($p=0.02$), and HAQ-DI ($p=0.002$), with anti-CCP^{pos}/RF^{pos} and anti-CCP^{pos}/RF^{neg} patients being youngest and having the lowest disease activity and disability. No differences were observed in terms of biologic use (20.2% of patients).

Sustained remission was 10% more likely if anti-CCP^{pos}, and was achieved by 43.5% of anti-CCP^{pos}/RF^{pos} patients, 43.3% of anti-CCP^{pos}/RF^{neg} patients, 31.6%

of anti-CCP^{neg}/RF^{pos} patients and 32.4% of anti-CCP^{neg}/RF^{neg} patients ($p=0.01$). Significant differences were observed in the time to achieving sustained clinical response from enrolment in the OBRI based on anti-CCP status ($p<0.001$), RF status ($p=0.06$), and both ($p=0.004$) (figure 1). ACPA^{pos}/RF^{pos} (median: 3.7 years; 95% CI: 3.0–4.3) and ACPA^{pos}/RF^{neg} (median: 3.4 years; 95% CI: 2.4–NE) patients achieved sustained remission earlier than ACPA^{neg}/RF^{neg} patients (median: 5.1 years; 95% CI: 3.7–6.2), respectively (figure 1).

Multivariate cox regression adjusting for baseline CDAI score, age and sex also showed differences between groups; statistically significance in anti-CCP^{pos}/RF^{pos} vs. anti-CCP^{neg}/RF^{neg} patients (HR [95% CI]: 1.30 [1.01–1.67]; $p=0.04$).

Abstract SAT0073 – Figure 1. Cumulative incidence of first sustained remission by ACPA/RF status

Conclusions: These results suggest that anti-CCP but not RF positivity may be associated with a higher chance of remission, possibly due to an improved treatment response.

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SAT0074

IDENTIFICATION OF A PROTEIN PANEL USEFUL FOR THE PREDICTION OF RESPONSE TO METHOTREXATE IN RHEUMATOID ARTHRITIS PATIENTS

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Background: The treatment of rheumatoid arthritis (RA) aims to control a patient's signs and symptoms, prevent joint damage, and maintain his/her quality of life. Among the best known disease-modifying antirheumatic drugs, Methotrexate (MTX) is one of the most effective and widely used medications. It is used as a general first-choice drug, although some patients will not respond to this treatment and it is not free from side effects.

Objectives: To identify circulating proteins that could be useful as predictors of the patient's response to MTX.

Methods: Serum samples from patients enrolled in the Pathobiology of Early Arthritis Cohort (PEAC) were collected before treatment with MTX. Response to therapy was determined after 6 months by calculating the initial and final DAS28 of the patients. Their classification was performed following the EULAR response criteria. Sixty samples at baseline from this cohort (30 good responders and 30 non-responders) were depleted from the 14 most abundant proteins by affinity chromatography to remove background. Then, they were analysed by reversed-phase nanoliquid chromatography coupled to mass spectrometry using a SWATH strategy in a tripleTOF MS (Sciex). The quantitative data obtained in this proteomic analysis were processed using the ProteinPilot 5.0.1 and PeakView 2.1 software (Sciex). Machine learning analyses were performed on a train set of 30 samples (15 responders and 15 non-responders) via support vector machine (SVM) using the Classyfire, e1071 and caret R packages. Results were verified in an independent set of 24 samples by a two-stage support vector machine (TSSVM) with RBF kernel and 10 cross-fold validation for each meta-model.

Results: The proteomic analysis led to the identification and quantification of 229 proteins that were common between the screening and validation sets. Independent screening and validation data sets were preprocessed by PCA for dimension reduction and analysed by machine learning tools, leading to the definition of a panel of 8 proteins (one of them involved in MTX metabolism) differentiating the groups of responders and non-responders to MTX with strong agreement (Kappa >0.80), very high accuracy and good relevant metrics (table 1).

Abstract SAT0074 – Table 1. Metrics of the classification performance of the 8-protein panel identified in this work to predict response of the patient to MTX. Cut-off for significance was p-value <0.05.

Train set							
Accuracy	95% CI	p-value	Kappa	Sensitivity	Specificity	Pos pred value	Neg pred value
0.9333	(0.7793 - 0.9918)	1.108e-05	0.8667	0.8824	1.0000	1.0000	0.8667
Validation set							
Accuracy	95% CI	p-value	Kappa	Sensitivity	Specificity	Pos pred value	Neg pred value
0.9583	(0.7888 - 0.9989)	0.0007722	0.9091	1.0000	0.9375	0.8889	1.0000

Conclusions: We have defined a panel of circulating proteins useful to predict the response to MTX therapy in rheumatoid arthritis patients.

Disclosure of Interest: None declared

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SAT0075

ADDITIONAL TARGET OF NORMAL SERUM MATRIX METALLOPROTEINASE-3 IS A POTENTIAL BIOMARKER FOR LESS ONE-YEAR RADIOGRAPHIC PROGRESSION IN RHEUMATOID ARTHRITIS

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Background: Matrix metalloproteinase (MMP)-3 plays important roles in bone and cartilage destruction in rheumatoid arthritis (RA). Our previous study showed continuously elevated serum MMP-3 for 3–6 months predict one-year radiographic progression in RA (Arthritis Res Ther. 2015 17:289). However, whether serum MMP-3 normalisation is a biomarker for better outcome remains elusive.

Objectives: To explore the association of serum MMP-3 normalisation with clinical and radiographic outcome in RA.

Methods: RA patients with moderate to high disease activity (DAS28-CRP>3.2) were treated according to treat to target (T2T) strategy and followed up at regular intervals (0, 1 st, 3rd, 6th and 12th months). Demographic and clinical data were collected according to the 2017 EULAR recommendation and serum MMP-3 was detected by ELISA at each visit. X-ray assessment of hand/wrist was repeated at baseline and month 12 and radiographic progression was defined as a change of the Sharp/van der Heijde modified sharp score ≥ 0.5 units.

Results: (1) Among 200 RA patients recruited, there were 163 (81.5%) female, with median disease duration 24^(11–84) months, median DAS28-CRP 4.9 (4.2–5.7). There were 29% patients showed one-year radiographic progression.² The median MMP-3 was 209.7 (108.6–430.0) ng/ml. RA patients without radiographic progression had significant lower level of serum MMP-3 than those with radiographic progression at baseline and each visit (figure 1A, all p<0.001).³ There were 13.0%, 14.5%, 17.0%, 25.5% and 31.0% patients having normal MMP-3 at baseline and 1 st, 3rd, 6th and 12th months, respectively. There were significantly

lower percentage of RA patients with normal MMP-3 at baseline and each visit showed radiographic progression than those with elevated MMP-3 (figure 1B, all p<0.05).⁴ There were 8.5%, 13.0%, 20.0% and 25.5% patients who achieved therapeutic target and showed normal MMP-3 at 1 st, 3rd, 6th and 12th months, respectively. Among patients achieved therapeutic target, there were significantly lower percentage of normal MMP-3 patients showed radiographic progression than those with elevated MMP-3 (figure 1C, all p<0.05).⁵ There were 6.5%, 11.0%, 14.5%, 20.5% and 25.5% patients who had normal CRP and normal MMP-3 at baseline and 1 st, 3rd, 6th and 12th months, respectively. Among patients with normal CRP, there were significantly lower percentage of normal MMP-3 patients at 1 st, 3rd, 6th and 12th months showed radiographic progression than those with elevated MMP-3 (figure 1D, all p<0.05).

Abstract SAT0075 – Figure 1. Dynamic change of serum MMP-3 and indicators of disease activity and radiographic progression in RA.

A Comparison of disease activity and radiographic progression indicators between RA patients with and without radiographic progression. **B** Comparison of T2T achieving and the percentage of RA patients showing radiographic progression between normal and elevated serum MMP-3 groups at each visit. **C** Comparison of the percentage of RA patients showing radiographic progression among groups with or without T2T achieving and normal serum MMP-3. **D** Comparison of the percentage of RA patients showing radiographic progression among groups with or without normal CRP and normal serum MMP-3.

Conclusions: Additional target of normal serum MMP-3 may be a potential biomarker for less one-year radiographic progression.

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SAT0076

SYNOVIAL MAST CELLS AND RESPONSES TO SYNTHETIC AND BIOLOGIC DMARDS IN EARLY AND ESTABLISHED RHEUMATOID ARTHRITIS

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Background: Mast cells (MCs) are immune cells implicated in the pathogenesis of Rheumatoid Arthritis (RA), but their presence in synovia has not been assessed systematically and their association with disease progression and treatment response is unknown.

Objectives: To analyse MCs in the synovia of patients with early vs established RA in correlation with histological and clinical phenotype.