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 μCT 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 μCT 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 osteocalcium as well as oстеocalcium 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 deficient mice would be possible used as a therapeutic target in the treatment of osteoporosis.

Disclosure of Interest: None declared


SAT0073

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

J.E. Pope1, M. Movahedi2, E. Rampakakis3, A. Cesta3, J.S. Sampalis1, C. Bombardier2,5,6

1Saint Joseph’s Health Care, University of Western Ontario, London, Canada; 2Ontario Best Practices Research Initiative, Toronto General Research Institute, University Health Network, Toronto, ON, Canada; 3Ontario Best Practices Research Initiative, Toronto General Research Institute, University Health Network, Toronto, ON, Canada; 4Ontario Ministry of Health and Long-Term Care, Ontario Health and Long-Term Care, Ontario Ministry of Health and Long-Term Care (MOHLTC), Canadian Arthritis Network (CAN) and unrestricted grants from: Abbvie, Amgen, Celgene, Hospira, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi, and UCB; 5M. Movahedi Employee of: OBRI, E. Rampakakis Employee of: JSS Medical Research, A. Cesta Employee of: OBRI, J. Sampalis: None declared, C. Bombardier Grant/ research support from: OBRI was funded by peer reviewed grants from CIHR (Canadian Institute for Health Research), Ontario Ministry of Health and Long-Term Care (MOHLTC), Canadian Arthritis Network (CAN) and unrestricted grants from: Abbvie, Amgen, Celgene, Hospira, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi, and UCB; 6Consultant for: Dr. Bombardier holds a Canada Research Chair in Knowledge Transfer for Musculoskeletal Care and a Pfizer Research Chair in Rheumatology

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-CCPpos/RFneg 60 (6.2%) anti-CCPpos/RFpos 117 (12.1%) anti-CCPneg/RFpos and 531 (54.7%) anti-CCPneg/RFneg. 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-CCPpos/ RFpos and anti-CCPneg/RFpos 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-CCPpos, and was achieved by 34.5% of anti-CCPpos/RFpos patients, 43.3% of anti-CCPneg/RFneg patients, 31.6% of anti-CCPneg/RFpos patients and 32.4% of anti-CCPneg/RFneg 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=0.01). RF status (p=0.08), and both (p=0.004) (figure 1). ACPApos/RFneg (median: 3.7 years; 95% CI: 3.0–4.3) and ACPApos/RFpos (median: 3.4 years; 95% CI: 2.4–NE) patients achieved sustained remission earlier than ACPApos/RFneg 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 significant in anti-CCPpos/ RFpos vs. anti-CCPneg/RFneg 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.

Disclosure of Interest: J. Pope Grant/research support from: OBRI was funded by peer reviewed grants from CIHR (Canadian Institute for Health Research), Ontario Ministry of Health and Long-Term Care (MOHLTC), Canadian Arthritis Network (CAN) and unrestricted grants from: Abbvie, Amgen, Celgene, Hospira, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi, and UCB. M. Movahedi Employee of: OBRI, E. Rampakakis Employee of: JSS Medical Research, A. Cesta Employee of: OBRI, J. Sampalis: None declared, C. Bombardier Grant/research support from: OBRI was funded by peer reviewed grants from CIHR (Canadian Institute for Health Research), Ontario Ministry of Health and Long-Term Care (MOHLTC), Canadian Arthritis Network (CAN) and unrestricted grants from: Abbvie, Amgen, Celgene, Hospira, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi, and UCB; Consultant for: Dr. Bombardier holds a Canada Research Chair in Knowledge Transfer for Musculoskeletal Care and a Pfizer Research Chair in Rheumatology.


SA0074

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

C. Ruiz-Romero1, F. Picchi1, L. González-Rodríguez1, P. Fernández-Puente1, R. Hands1, V. Calamia1, M. Camacho-Encina1, C. Bessant2, C. Pitzaíl3, F. J. Blanco1

1Unidad de Proteómica-ProteoRed/ISCIII, Grupo de Investigación en Reumatología, InBiC – CHUC/AC, A Coruña, Spain; 2Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, UK; 3School of Biological and Chemical Sciences, Queen Mary University of London, London, UK

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 anti-rheumatic 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.

Disclosure of Interest: None declared


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 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 nanoion 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 Classifyfire, 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.

<table>
<thead>
<tr>
<th>Train set</th>
<th>Accuracy</th>
<th>95% CI</th>
<th>p-value</th>
<th>Kappa</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Pos pred value</th>
<th>Neg pred value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.9333</td>
<td>(0.7793</td>
<td>1.108e-05</td>
<td>0.8667</td>
<td>1.0000</td>
<td>1.0000</td>
<td>0.8667</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.9918</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Validation set</td>
<td>Accuracy</td>
<td>95% CI</td>
<td>p-value</td>
<td>Kappa</td>
<td>Sensitivity</td>
<td>Specificity</td>
<td>Pos pred value</td>
<td>Neg pred value</td>
</tr>
<tr>
<td>0.9583</td>
<td>(0.7888</td>
<td>0.0007722</td>
<td>0.9091</td>
<td>1.0000</td>
<td>0.9375</td>
<td>0.8889</td>
<td>1.0000</td>
<td></td>
</tr>
<tr>
<td>0.9989</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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


SAT0075

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

L.-F. Chen, J.-D. Ma, Y.-Q. Mo, X.-Y. Du, D.-H. Zheng, L. Dai, Department of Rheumatology, Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Guangzhou, China

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 score >0.5 units.

Results: Among 200 RA patients recruited, there were 163 (81.5%) female, with median disease duration 24 (11–64) months, median DAS28-CRP 4.9 (4.2–5.7). There were 29% patients showed one-year radiographic progression. The median MMP-3 was 2097.7 (108.6–430.0) ng/ml. RA patients without radiographic progression had significantly lower level of serum MMP-3 than those with radiographic progression at baseline and each visit (figure 1A, all p <0.001). 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). 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). There were 6.5%, 11.0%, 14.5%, 20.5% and 25.5% patients with 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).

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

Acknowledgements: This work was supported by National Natural Science Foundation of China (no. 81471597 and 81671162), Guangdong Natural Science Foundation (no. 2016A030313307 and 2017A030313576) and Guangdong Medical Scientific Research Foundation (no. A2017093 and A2017109).

Disclosure of Interest: None declared


SAT0076

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

F. Rivelise, A. Nerviani, D. Mauro, S. Pagani, F. Hurnby, C. Pitzalis. Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Barts and the London School of Medicine and Dentistry, London, UK

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.