Objectives: By using Firalis' BIOPRED panel, an innovative targeted gene sequencing panel of 2155 mRNA targets associated with immune-inflammatory pathways, we identified candidate biomarkers that have the potential to stratify patients for personalized therapy.
Methods: Paxgene RNA samples obtained from 18 RA patients treated with Etanercept (n=11) and Tocilizumab (n=7) who had achieved remission (DAS28 < 2.6) were directly profiled without RNA extraction with BIOPRED panel, a targeted sequencing kit based on HTG EdgeSeq platform. Data were extracted using HTG Parser software and normalized using EdgeR method. Student T-test was applied to find out targets which are significantly regulated.
Results: In total, 37 mRNA targets are found to be significantly up- or down-regulated in Etanercept groups as compared to Tocilizumab group (p-value <0.05). 3 mRNA genes are found to be significantly upregulated with fold change of > 2 (p-value < 0.05) and 1 mRNA gene is found to be significantly downregulated with fold change of <0.5 (p-value < 0.05).
Conclusion: Our preliminary analysis shows that a panel of candidate predictive markers for biological specific (Etanercept) remission has the potential to stratify patients for personalized therapy in RA patients. Longitudinal studies are required with RA patients treated with all biologicals to validate this signature and explore further dimensions.
Disclosure of Interests: None declared
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SAT0637 THE DIAGNOSTIC VALUE OF SERUM IGG4 IN IGG4 RELATED DISEASES

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Background: IgG4–RD is a newly recognized autoinflammatory disease. Serum IgG4 is an important tool for the diagnosis of IgG4—RD. However, only a few articles have reported the value of serum IgG4 for the diagnosis ofIgG4–RD.
Objectives: To explore the diagnostic value of serum IgG4 in IgG4-related diseases,Whether 1350 mg/L as the cutoff concentration is suitable for Chinese people to identify IgG4-RD and other rheumatic immune diseases.
Methods: From October 2013 to December 2018,40 patients with IgG4-RD diagnosed in the rheumatic immunology department of people's hospital of Xinjiang Uygur Autonomous Region were collected.We also reviewed the of 90 other CTD patients and 40 healthy controls.The age, gender, diagnosis, serum IgG4 concentration and other data were collected. The cut off levels were determined by receiver operating characteristic (ROC) curve analysis
Results: The mean serum IgG4 concentration of 40 definite IgG4-RD was was significantly higher than that of other rheumatic immune diseases group and healthy control group. There was a significant serum IgG4 concentration difference between patients with IgG4-RD,Non-IgG4-RD and healthy control group(P<0.05 (Figure 1 . By the ROC curves of serum IgG4 levels in 170 patients. The optimal cutoff value of serum IgG4 for a diagnosis of IgG4-RD was 1440 mg/L, and the sensitivity and specificity were 90.0% and 80.8%, respectively. The area under the curve (AUC) was 0.926. When We using a ratio >0.07 as the cut-off for normal and the sensitivity and specificity were 90.0% and 77.7%, respectively. The area under the curve (AUC) was 0.925(Figure 2 .

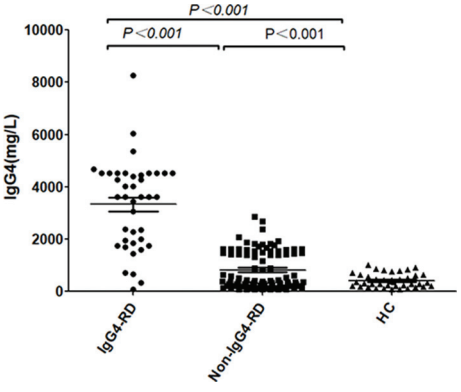

Figure 1. There were significant differences between IgG4-RD, Non-IgG4-RD and HC (P<0.05).

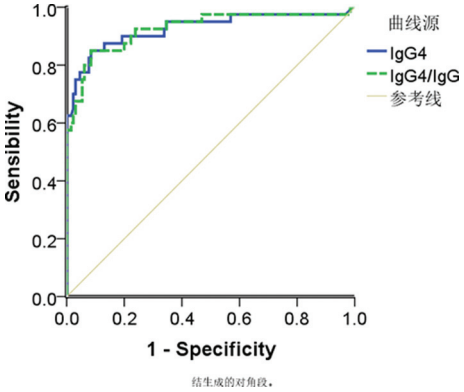

Figure 2. The ROC curve of IgG4 and IgG4/IgG ratio

Conclusion: The high levels of serum IgG4 are sometimes observed in not only IgG4-RD but also other rheumatic,malignancy diseases and common diseases. The cut of serum IgG4 is 1440mg/L,The usual cut-off value of 1350 mg/Lis useful for diagnosing whole IgG4-RD.

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SAT0638 INCREASED LEVELS OF CIRCULATING EXTRA CELLULAR LONG NON-CODING RNAS MALAT1, MEG3 AND NEAT1 IN PATIENTS WITH RHEUMATOID ARTHRITIS AND THEIR IMPACT ON DISEASE ACTIVITY MEASURES

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Background: Deregulations of long non-coding RNAs (lncRNA) have been lately implicated in autoimmune diseases(1) including Rheumatoid arthritis (RA). However, their specific roles in disease pathogenesis, extra-cellular manifestations and clinical impact in RA remain largely unknown.
Objectives: To identify the intra- and extra-cellular expressions of lncRNAs, MEG3, MALAT1, NEAT1, in RA and their impact on disease activity.
Methods: Blood samples were collected from 82 active RA patients (DAS28-CRP: 4.7±0.2) and 15 age-sex matched healthy individuals. Knee synovial fluids (SF) were collected from 24 RA patients (among 82) and 10 osteoarthritis patients (as control). Sera were separated for cytokines

measurements. RNA, isolated from peripheral blood mono nuclear cells (PBMCs), plasma and synovial fluid were quantified by spectrophotometry. Levels of MALAT1, MEG3 and NEAT1 were determined using specific primers and real time PCR, 18S rRNA was the endogenous control. Fold changes were calculated using standard $2^{-\Delta\Delta Ct}$ method. Multivariate analysis was performed to analyze associations between the dependent variable (DAS28-CRP) and the predictor variables (CRP, MALAT1, MEG3 and NEAT1). Confidence interval of 95% ($p \leq 0.05$) was considered statistically significant for all analyses.

Results: All patients recruited were anti-CCP positive (122.5 ±28.3 IU/ml) and RF positive (166.5 ±37.3 IU/ml). Their systemic inflammation were high compared to controls ($p<0.05$) as reflected in serum CRP (47.4 ±26.2 mg/L), TNFα (140±29 pg/dl) and IL17 (270±33 pg/dl). Levels of MALAT1, MEG3 and NEAT1 were increased in the PBMCs ($p<0.05$) of RA patients compared to controls. Similar increases of these lncRNAs were seen in plasma and in SF. Spearman's correlation were performed with the fold changes of lncRNAs in PBMC, DAS28-CRP and its components. MEG3 significantly correlated with tender joint count (TJC) ($r=0.75$, $p=0.002$) whereas NEAT1 correlated with both TJC ($r=0.571$, $p=0.002$) and DAS28-CRP ($r=0.943$, $p=.001$). Multivariate analysis was performed with NEAT1 and MEG3 as the predictors and DAS28-CRP (model 2) as outcome and co-efficient of determinant (r^2) was compared to that of CRP as the predictor and DAS28-CRP as the outcome (model 1). Model 1 was made to set a cut-off mark for model 2. The r^2 for model 1 (0.862) was greater than that of model 2 (0.656) indicating the expressions of NEAT1 and MEG3 accounted more for variability in DAS28-CRP scores (86.2%) than CRP (65.6%). In model 2, β co-efficient of NEAT1 (β=0.868) was greater than that of MEG3 (β=0.397) suggesting a greater impact of NEAT1 on DAS28-CRP scores. The lncRNAs in plasma and in synovial fluids had shown similar trends.

Conclusion: Increased in lncRNAs in extra cellular fluid suggests their systemic regulation on RA pathogenesis. Increased predictability of DAS28-CRP by NEAT1 and MEG3 compared to CRP indicate their potentiality of being probable markers in monitoring disease activity. However, validation of this finding in larger cohort is necessary.

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SAT0639 ACTIVE JAK/STAT SIGNALING IN CIRCULATING LEUCOCYTES DEFINES DISTINCT IMMUNOLOGIC ENDOTYPES OF RHEUMATOID ARTHRITIS

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Background: In rheumatoid arthritis (RA) stratification is considered an important step towards the development of patient-tailored therapeutic concepts. The fact that less than 50% of RA patients experience a substantial improvement in response to any single biologic therapy has brought up the idea that yet unidentified subtypes of RA (endotypes) might exist. This concept is in line with distinct microscopic patterns of synovitis found in biopsies of RA joints.[1] Furthermore, a subset of RA patients has leucocytes with interferon driven gene expression, whereas the majority of RA patients does not[2]. Interferons activate receptor associated Janus kinases leading to phosphorylation of STAT1 and STAT2. Other STAT family members are activated by cytokines such as IL-6 (STAT3) or IL-15 (STAT5). Therefore, the phosphorylation pattern of the different STAT molecules in circulating leucocytes might mirror the specific cytokine milieu of a given patient.

Objectives: To define endotypes of RA based on the phosphorylation patterns of the different STAT molecules in circulating leucocytes.

Methods: Cross-sectional study of 63 patients with established RA fulfilling the 2010 EULAR/ACR criteria (mean age: 64.5 ± 1.7 (SEM) years, female ratio: 0.79). Ten healthy subjects served as a control group. Flow cytometry was performed to detect the phosphorylated forms of STAT1-6 in Monocytes, Granulocytes, B cells, naïve-, effector-, and memory-T cells of the CD4+ and CD8+ lineage. All steps from blood draw to cell fixation were performed at 4°C to prevent auto-activation of leucocytes. The mean fluorescence intensity (MFI) of phosphorylated STATs in the different leucocyte populations was used for statistical analysis. MFIs were correlated with disease activity measured by the cDAI. MFIs of populations with elevated STAT phosphorylation not associated with disease activity were analyzed by unsupervised hierarchical clustering. The resulting groups were validated by principal component analysis. Finally, criteria for patient assignment to specific groups by MFI were generated by calculating ROC-curves.

Results: Pronounced e*x vivo* phosphorylation of STAT1-6 in any leucocyte population was detected in 20 of 63 (48%) RA patients but not in healthy subjects (n=10). Active STAT5 signaling in Monocytes, naïve CD4 + T cells and CD4+ effector T cells was significantly associated with disease activity. Unsupervised hierarchical cluster analysis of RA patients based on pSTAT MFIs not associated with disease activity resulted in 3 groups: 1) Patients with active STAT1 and STAT3 signal in Monocytes and Granulocytes (n=14/63, 22%), 2) Patients with active STAT5 signal in naïve CD8+ T cells, CD8+ effector T cells and CD4+ memory T cells (n=16/63, 25%) and 3) Patients without active STAT signal in any leucocyte population (n=33/63, 52%). cDAI, CRP, ESR, current treatment, RF and ACPA status did not differ significantly between the groups. To test if the assignment to a group changed over time, we performed a second analysis of STAT phosphorylation after 3-6 months. Eighty percent of the patients tested (12/15) were re-assignment to their initial group.

Conclusion: We identified three distinct RA endotypes based on active STAT signal. Whether patients within different endotypes respond differently to a given therapy will be subject to further research.

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SAT0640 SHEAR-WAVE ELASTOGRAPHY OF SKIN STIFFNESS IN SYSTEMIC SCLEROSIS: A FIVE-YEAR FOLLOW-UP STUDY

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Background: Measurement of skin involvement is essential for diagnosis and assessment of prognosis in systemic sclerosis (SSc). The mRSS is the gold standard measure of skin thickness. The mRSS has been criticised for being associated with high inter-observer variability and being too insensitive to detect relevant changes in skin thickness over time. Previously, our group demonstrated that shear-wave elastography (SWE) offers a potential for objective and quantitative assessment of skin involvement in SSc patients.[1] However, no studies have evaluated its sensitivity to change over-time.

Objectives: To assess changes in skin stiffness in SSc patients using SWE over-time.

Methods: This study included 19 SSc patients [89.5% females; age 57.5 years (10.3), 53% with limited form; disease duration 11.4 years (8.5)] at baseline and, 13 healthy controls [69.2% females; age 53.4 years (11.5). Skin stiffness was measured by SWE, using virtual touch image quantification, at the 17 sites corresponding to the mRSS, in each participant, at baseline and follow-up [a mean of 4.9 ((4.6-4.9) years later]. mRSS was performed at both time points. Differences between groups were analysed using the related-samples Wilcoxon Signed Rank test. Results are presented as median (interquartile range (IQR)).

Results: In SSc patients, skin stiffness measured by SWE decreased in a strongly significantly way ($p \leq 0.001$), over time at all skin Rodnan sites, except the fingers (table 1). Interestingly, the same was observed in controls for all sites, except the leg. The effects of normal ageing correspond to 30 to 60% of the changes observed in SSc. Local Rodnan