RHEUMATOID ARTHRITIS SAMPLES IDENTIFY BIOMARKERS THAT ARE UPREGULATED PRIOR TO THE DIAGNOSIS OF RHEUMATOID ARTHRITIS

Sunil Nagpal1, Matthew J. Loza1, Suzanne Cole2, Brittney Scott1, Renee Laird2, Frederic Baribaud1, Anderson1, Navin Rao1, Mark Riddle3, Chad Porter2, Matthew J Loza Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Navin Rao Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Chad Porter: None declared, Brittney Scott: None declared

Background: Rheumatoid arthritis (RA) patients have autoantibodies reactive against several citrullinated peptides that develop 10-15 years before the clinical onset of disease. However, there is a more limited understanding of serological biomarkers of disease progression, specifically those that are upregulated in patients 6-18 months before the clinical diagnosis of RA. A discovery subset of these serum samples was assessed for soluble PD-1 (sPD-1), as well as 497 protein analytes measured by SomaLogic SOMAscan proteomic platform.

Results: Serum levels of sPD-1 increased over time from pre-diagnosis to RA but tended to decrease over time in ReA subjects and healthy controls. A composite score of 24 SOMAscan analytes associated with recently diagnosed RA increased in serum 6-8 months before RA diagnosis and, to a lesser extent, before ReA diagnosis. IFN-inducible chemokines (CXCL9, CXCL10, CXCL11) increased over time preceding RA but not ReA diagnosis. Acute phase proteins (CRP, SAA, haptoglobin) and MPP-3 increased before diagnosis in serum samples from both RA and ReA patients. These protein analytes represent potential new biomarkers of early RA.

Conclusion: Samples from the US DoD serum repository have identified novel biomarkers (sPD-1 and IFN-inducible chemokines) of early RA that are elevated within 8 months of disease diagnosis. These protein analytes may afford the opportunity to develop novel biomarker(s) for diagnosis and disease progression to early RA. An understanding of the role of these proteins could provide increased insight into RA pathogenesis prior to disease diagnosis.


SAT0104 INITIAL EVIDENCE FOR THE NEED OF A DUAL TREAT-TO-TARGET STRATEGY IN PATIENTS WITH RHEUMATOID ARTHRITIS

Claudia Oppenauer1, Martina Durecova2, Michael Zauner3, Martin Psch8, Susanne Urach4, Klaus Machold5, Daniel Aletaha6, Ricardo Ferreira7, Tanja Stamml1. Medical University of Vienna, Section for Outcomes Research, Vienna, Austria; 2Medical University of Vienna, Department of Medicine III, Division of Rheumatology, Vienna, Austria; 3Medical University of Vienna, Section for Medical Statistics, Vienna, Austria; 4Centro Hospitalar e Universitario de Coimbra, Coimbra, Portugal

Background: The treat-to-target (T2T) strategy has been established as a key concept in the management of patients with rheumatoid arthritis (RA) aiming to achieve remission or at least low disease activity [1]. However, it might be more important for patients to set individual treatment goals which are related to their specific life context. For this reason, Ferreira at al [2] recently proposed a dual T2T strategy including both biological remission and individual patient reported symptom remission. It is currently unclear how achieving biological remission and individual patient treatment goals overlap and whether patients who reach the T2T target also reach their individual treatment goals.

Objectives: To explore if achieving T2T biological remission and individual patient treatment goals overlap in RA patients with initially low, moderate, or high disease activity (LDA, MDA, HDA).

Methods: We recruited a consecutive convenience sample of patients with RA diagnosed according to ACR/EULAR criteria and with LDA, MDA, or HDA into this observational longitudinal study. Disease activity was measured with the Clinical Disease Activity Index (CDAI) and the individual patient goals were assessed with the Goal Attainment Scale (GAS) at baseline and after three to five months. The number and proportion of patients who reach the T2T target, but not their individual goals and vice versa were calculated.

Results: We enrolled 162 patients in the study (131 [80.9%] women, median age 59.0, IQR 49-71), 101 patients (62%) had a follow up visit with no missing data after three months. Of these, 48 (47.6%) patients had LDA, 43 (42.6%) had MDA, and 10 (9.9%) had HDA at baseline. 62 patients (61.4%) reached remission (14.7%) or stayed in LDA, 43 (42.6%) had MDA, and 10 (9.9%) had HDA at baseline. 48 (47.6%) patients achieved their individual goals (Table 1). 18 (17.8%) patients did not achieve their individual treatment goals, even if T2T was successful and 22 (21.8%) patients achieved their individual goals despite not reaching remission or LDA.

Conclusion: Our results indicate that most patients achieving T2T attain their individual treatment goals but a respectable part of T2T outcomes
had to be supplemented by the individual patient reported treatment goals.

REFERENCES


Table 1. Comparison of achieved T2T and individual patient goals

<table>
<thead>
<tr>
<th>T2T achieved, n (%)</th>
<th>Yes</th>
<th>No</th>
<th>Overall</th>
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<tbody>
<tr>
<td>Yes</td>
<td>44</td>
<td>22</td>
<td>66 (65.3)</td>
</tr>
<tr>
<td>(43.6)</td>
<td>(21.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>18</td>
<td>17</td>
<td>35 (34.7)</td>
</tr>
<tr>
<td>(17.8)</td>
<td>(16.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>62</td>
<td>39</td>
<td>101 (100.0)</td>
</tr>
<tr>
<td>(61.4)</td>
<td>(38.6)</td>
<td></td>
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</tr>
</tbody>
</table>

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SAT0105

HAND DISABILITY IN RHEUMATOID ARTHRITIS: AN ENGINEERED GLOVE FOR THE COMPUTERISED QUANTIFICATION OF THE DAMAGE

Massimo Patane, Lucica Carmisciano, Emanuele Gotelli, Veronica Tomatis, Federica Goeigan, Elisa Alessandri, Massimo Ghio, Alessio Signori, Maurizio Cutolo.

1Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, IRCCS Polyclinic Hospital San Martino, University of Genoa, Genoa, Italy; 2Biostatistics Unit, Department of Health Sciences, University of Genoa, Genoa, Italy

Background: Tenderness, swelling and loss of motility of the joints are the main determinants of the disability function (DF) of Rheumatoid Arthritis (RA) patients (RApts). The evaluation of DF is performed by Patient Reported Outcomes (PROs), like Health Assessment Questionnaire (HAQ). The lack of objective evaluation of DF is one of the most important “unmet needs” in RA. The Hand Test System (HTS, ETT) is an engineered glove, nowadays applied for neuroscience studies to evaluate hands motility with interesting perspectives of use in other clinical research fields.

Objectives: To quantify the DF of RApts by the analysis of speed and right execution of fingers opposition movement in both hands, evaluated by HTS. To verify the correspondence with the HAQ.

Methods: In this pilot study 14 consecutives RApts (3 males, 11 females, age 61 ± 11.5 years, mean duration of disease 11.21 ± 5.07 years), classified according to 2010 ACR/EULAR criteria, and 13 healthy controls (HC – 7 males, 6 females, age 50 ± 15 years) were enrolled from the RA clinic. After consent, all participants undergone HTS test that recognizes the touches between the finger tips during the opposition movement of the hands in standard sequences of movements, after dressed the glove. A multiple finger evaluation (MFE) and a single finger evaluation (SFE) were performed using a dedicated software that provided the physicians the following quantitative parameters: Touch Duration (TD), Inter Tapping Interval (ITI) and Movement Rate (MR). Average time for hand 2 minutes. RApts compiled the HAQ and a tender and swollen joint count of the hands was performed. Continue variables were summarized as mean and standard deviation (SD) or median and interquartile range (IQR), discrete variables were summarized with count and percentage. Variables with skewed distribution was converted to natural logarithm. T-test was used to compare log glove parameters between groups. Pearson’s r and p value were used to report the correlation between log-converted glove parameters and HAQ score.

Results: In MFE, glove parameters TD and ITI were significantly higher in RApts (TD 257.34 ± 123.93 ms, ITI 377.8 ± 211.35 ms) than HC (TD 172.25 ± 59.36 ms, ITI 177.98 ± 78.53 ms) (p = 0.004 and p < 0.001) and MR was significantly lower in RApts (1.51 ± 0.47 Hz) compared to HC (2.87 ± 0.9 Hz) (p <0.001). TD of RApts had a significant correlation with the total score of the HAQ (Pearson r = 0.79, p = 0.001). In SFE non-active fingers (NAF, not swollen and not tender) of RApts seemed to perform slightly better than a clinically active finger (AF) but significantly worse than average HC finger (ANOVA, p < 0.001).

Conclusion: HTS is a new easy and safe tool that seems to quantify in an objective manner the hand DF in RApts. The significant correlation found with HAQ underlines the value and veracity of self-assessment tools in clinical practice. Further studies are ongoing with larger number of RApts to validate its application to monitor the improvement or the worsening of RA in order to optimize pharmacological treatments. The study is now extended in other Rheumatic and Musculoskeletal Diseases.

REFERENCE


Disclosure of Interests: None declared

SAT0106

NOVEL SUBCLASS OF INTRAVASCULAR NON-CLASSICAL SYNOVIAL MONOCYTES ARE CRITICAL FOR RHEUMATOID ARTHRITIS

Anna Montgomery, Deborah Winter, Harris Perlmutter, Northwestern University, Medicine/Rheumatology, Chicago, United States of America

Background: There are at least three populations of circulating monocytes; classical, intermediate and non-classical. We demonstrated that circulating non-classical monocytes are required for the effector phase of arthritis and spontaneous models of arthritis in mice. While the vast majority of studies on monocytes have focused those in circulation, very little is known about the monocytes in the synovium.

Objectives: The aim of this study was to examine the heterogeneity of tissue monocytes with those circulation and determine their involvement in inflammation.

Methods: Female 8-10-week-old NRA1 +/-; CX3CR1ERTCox2GFP and C57Bl/6 mice were used in all studies. CX3CR1ERTCox2GFP were utilized for cell tracking studies and joint shielded bone marrow chimera via administration of tamoxifen (tam). Intravascular monocytes were identified using fluorescent anti CD45 antibody before perfusion. STIA was induced via I.V. KBNL sera. Monocyte populations were quantified by flow cytometry and FACS sorted for RNA-sequencing (RNA seq). Nonclassical tissue monocytes were identified CD45+CD11b+Ly6G-Tim4+CD64+Ly6clo and subdivided into intravascular (CD45-labeled, CD43+), trans-vascular (CD45-labeled CD43) and extravascular (no CD45-label). Human synovium was obtained from ultrasound guided synovial biopsies and CD45+ cells were FACSorted for single cell RNA seq.

Results: NRA1 +/- mice exhibit a 95% reduction in circulating Ly6c+ monocytes but retain Ly6c- cells in the joint and develop STIA. The transcriptional profiling of bulk populations of Ly6c+ cells in the synovium are distinct from those circulating in the blood. We then identified three populations of Ly6c+ monocytes in the joint; extra-vascular, trans-vascular cells, and intra-vascular cells using 18 color flow cytometry. Lineage tracking studies reveal that the origin of extra-vascular and trans-vascular synovial monocytes are from the embryo while the intravascular monocytes are derived post-natally. The intravascular monocytes are depleted with cladronate loaded liposomes while the extravascular and trans-vascular remain unaffected. Moreover, the intravascular monocytes rapidly expand during the first 1hour of STIA, increasing by 30x in population size. RA patients also display similar populations of non-classical monocytes using single cell RNA seq.

Conclusion: We have identified and described three previously uncharacterized populations of non-classical monocytes cells in the joint, an intra-vascular adherent, a trans-vascular population and an extra-vascular