LONGITUDINAL PRE-DISEASE TO DISEASE SERUM SAMPLES IDENTIFY BIOMARKERS THAT ARE UPREGULATED PRIOR TO THE DIAGNOSIS OF RHEUMATOID ARTHRITIS

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Disclosure of Interests: 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.

Objectives: Identification of biomarkers that could classify patients 6-18 months before the clinical diagnosis of RA.

Methods: We identified 500 subjects with RA, 500 with Reactive Arthritis (ReA) (based on ICD9-CM code) as well as 250 age, gender and time-matched healthy control subjects from the Defense Medical Surveillance System (DMSS). For each subject, up to four serum samples were obtained from the Department of Defense (DoD) serum repository, 3 pre-disease diagnosis points and one immediately prior to or around disease diagnosis. 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 trended 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 (MIG), CXCL10 (IP-10), CXCL11 (I-TAC), and CXCL13 (BLC) increased over time preceding RA but not ReA diagnosis. Acute phase proteins (CRP, SAA, haptoglobin) and MMP-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.


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>
</tr>
</thead>
<tbody>
<tr>
<td>(%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient goal(s)</td>
<td>44</td>
<td>22</td>
<td>66 (65.3)</td>
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<tr>
<td></td>
<td>(43.6)</td>
<td>(21.8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>18</td>
<td>17</td>
<td>35 (34.7)</td>
</tr>
<tr>
<td></td>
<td>(17.8)</td>
<td>(16.8)</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>62</td>
<td>39</td>
<td>101</td>
</tr>
<tr>
<td></td>
<td>(61.4)</td>
<td>(38.6)</td>
<td>(100.0)</td>
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</tbody>
</table>

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ments. The study is now extended in other Rheumatic and Musculoskeletal Diseases.

REFERENCE


Disclosure of Interests: None declared


SAT0105

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

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Background: Tenderness, swelling and loss of motility of the joints are the main determinants of the disability function (DF) of Rheumatoid Arthritis (RA).

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

Methods: In this pilot study 14 consecutive RA patients (3 males, 11 females, age 61 ± 11.5 years, mean duration of disease 11.21 ± 5.07 years), classified according to 2010 ACR/EULAR criteria5, and 13 healthy controls (HC) 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 in standard gloves. The objective DF evaluation was performed in 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 fields3,4.

Objectives: To quantify the DF of RA patients 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 consecutive RA patients (3 males, 11 females, age 61 ± 11.5 years, mean duration of disease 11.21 ± 5.07 years), classified according to 2010 ACR/EULAR criteria5, 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 physician the following quantitative parameters: Touch Duration (TD), Inter Tapping Interval (ITI) and Movement Rate (MR), Average time for hand 2 minutes. RA patients compiled the HAQ and a tender and swollen joint count.

Conclusion: HTS is a new easy and totally safe tool that seems to quantify in an objective manner the hand DF in RA patients. 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 patients 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.

SAT0106

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

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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 NR4A1 -/-, Cx3CR1Ercx.zsGFP, and C57Bl/6 mice were used in all studies. Cx3CR1Ercx.zsGFP were utilized for cell tracking studies and joint shielded bone marrow chimeras via administration of tamoxifen (tam). Intravascular monocytes were identified using fluorescent anti CD45 antibody before perfusion. STIA was induced via I.V. KBxN sera. Monocyte populations were quantified by flow cytometry and FACS sorted for RNA-sequencing (RNA seq). Nonclassical tissue monocytes were identified CD45+CD11bLy6g+TIM4CD64Ly6c– and subdivided into intravascular (CD45-labeled, CD43–), trans-vascular (CD45-labeled CD43) and extravascular (no CD45-labeled). Human synovium was obtained from ultrasound guided synovial biopsies and CD45+ cells were FACSorted for single cell RNA seq.

Results: NR4A1 -/- 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