AB0044  ESTABLISHED RHEUMATOID ARTHRITIS PATIENTS HAVE INCREASED FREQUENCIES OF FOLLICULAR REGULATORY T CELLS IN PERIPHERAL BLOOD

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Background: Several studies have demonstrated that an immune dysregulation affecting both B and T cells occurs in rheumatoid arthritis (RA). Follicular helper T (Tfh) cells are crucial for B cell maturation, activation and class-switching as well as for germinal center (GC) formation, whereas follicular regulatory T (Tfr) cells can modulate the GC reaction by suppressing Tfh and B cells.

Objectives: The main goal of this study was to analyze the phenotype and frequency of circulating Tfh cell subsets in established RA patients.

Methods: Blood samples were collected from established RA patients with active disease, treated with methotrexate (n=32) and from a group of age and sex-matched healthy donors (n=11). Peripheral blood mononuclear cells (PBMC) were isolated and Tfh (CD4+CXCR5+CD45RO–) and Tfr (CD4+CXCR5+CD25+FoxP3+) cells, as well as their three major subsets [CXCR3–CCR6– (Th1-like), CXCR3–CCR6– (Th2-like) and CXCR3–CCR6+ (Th17-like)] were evaluated by flow cytometry.

Results: The frequency of circulating Tfh cells was similar between established RA patients and controls. Nonetheless, RA patients had a decreased frequency of Th1-like Tfh cells, and an increased frequency of Th2-like Tfh cells when compared to controls. No significant differences were observed in the frequencies of Th17-like Tfh cells between both groups. The frequency of circulating Tfr cells was significantly increased in RA patients in comparison to controls. Furthermore, Tfr cells from RA patients had significantly increased CD69 median fluorescence intensity (MFI) values when compared to controls. No significant differences were found in the percentages and MFI values of PD-1, ICOS, CD28, CTLA-4, CD40-L and HLA-DR expressed by Tfh and Tfr cells in RA patients when compared to controls.

Conclusion: Established RA patients have increased circulating frequencies of Tfr cells, with higher CD69 expression levels, when compared to healthy controls. These results suggest a pre-activation state of Tfr cells in RA and a potential role in modulating the GC reaction by suppressing Tfh and B cells.

Disclosure of Interests: None declared.

*RA Moura, J. E. Fonseca and L. Graca are joint senior authors.

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Disclosure of Interests: None declared.

*RA Moura, J. E. Fonseca and L. Graca are joint senior authors.

Disclosure of Interests: None declared.

Table 1. Patient characteristics.

<table>
<thead>
<tr>
<th>Patients</th>
<th>Gender (F/M)</th>
<th>HLA-SE alleles</th>
<th>Joints</th>
<th>Joint swelling prior to biopsy (months)</th>
<th>Stiffness specific joint (median VAS)</th>
<th>Pain specific joint (median VAS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACRA+</td>
<td>n = 12</td>
<td>9/3</td>
<td>0401*, 0404, 0410</td>
<td>1 MTP, 4 MCP, 6 wrists, 1 knee</td>
<td>4 (1-12)*</td>
<td>46 (8-48)</td>
</tr>
<tr>
<td>ACRA-</td>
<td>n = 5</td>
<td>3/2</td>
<td>0401, 0404, 0410</td>
<td>1 MTP, 2 wrists, 1 ankle</td>
<td>5 (0.25-7)</td>
<td>59 (15-73)</td>
</tr>
<tr>
<td>SKW3</td>
<td>n = 4</td>
<td>4/0</td>
<td>0401, 0404, 0407</td>
<td>1 MCP, 3 wrists</td>
<td>2 (1-6)</td>
<td>50.5 (42-84)</td>
</tr>
<tr>
<td>lines</td>
<td>patients</td>
<td>n = 2</td>
<td>0401 n=2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Data not available for one patient. One patient with prior RA-diagnosis, but after 9 months of treatment remission lasting for 20 years.

Artificial T cell lines were generated from the expanded clones of HLA-DRB1*0401 RA subjects. Our in vitro stimulation protocol identified virus specific CD4 T cells in all samples. So far, no citrulline reactivity has been found. HCMV followed by HHV were the most commonly found viral reactivities, whereas others were found only in one donor (e.g. JCV, EBV). The majority of clones are thus "orphans," to which we are still seeking the driving antigen.

Conclusion: Clonally expanded T cell lines are found in the synovium of early RA patients and include virus-specific CD4+ T cells. Our data show that the local T cell repertoire is broad already at the time of RA diagnosis.

Disclosure of Interests: Sara Turcino: None declared, Erik at Klint Paid instructor for: Abbvie (courses and lectures), An De Bondt Employee of: Janssen, Muhammad Sohel Mia: None declared, Ana Catrina: None declared, Frederik Steweit: Employee of: Janssen, Vivianne Malmström Grant/research support from: VM has had research grants from Janssen Pharmaceutical

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AB0045  ULTRASOUND GUIDED BIOPSY OF JR A JOINTS AT TIME OF CLINICAL DIAGNOSIS CONTAIN PROFOUND T CELL CLONALITIES

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Background: Rheumatoid arthritis (RA) is a disease characterized by synovial joint inflammation, mainly affecting small joints. Histological findings in synovial biopsies ranges from inflammatory infiltration including ectopic lymphoid structures, to a cell sparse fibroblast phenotype. T cells in affected joints are non-naive and have by flow cytometry approaches been shown to have a wide TCR-beta clonal repertoire. To assess the capacity of circulating T cells to produce lineage cytokines, PBMCs were cultured for 4 hours in the presence of 50 ng/mL PMA, 16 μg/mL calcium ionophore and 10 μg/mL BFA. Cells were then intracellularly stained for IFNγ (Th1 cells), IL-17 (Th17 cells) and IL-4 (Th2) by flow cytometry.

Table 1. Individual T cell clones were isolated from: VM has had research grants from Janssen Pharmaceutical

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AB0046  NO EVIDENCE FOR DISTURBED TH1 AND TH17 FREQUENCIES IN GCA AND PMR PATIENTS - A STUDY IN THE GRONINGEN GPS COHORT

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Background: Giant cell arteritis (GCA) is an aging-associated inflammatory disease of the large-sized arteries. GCA clinically and pathogenically overlaps with polymyalgia rheumatica (PMR), which affects the shoulders and hips. In the inflamed tissues, infiltrated CD4+ T-cells display a disturbed Th cell distribution, that may contribute to the development of the diseases. GCA arthritis contain pro-inflammatory Th1 helper 1 (Th1) and Th17 cells, but almost no Th2 cells or regulatory T-cells. In addition to CD4+ T-cells, macrophages are dominant in GCA and PMR tissue infiltrates. We previously found an altered distribution of monocyte subsets, the precursors of macrophages, in the blood of GCA and PMR patients. Others reported changes in the distribution of Th cells in the blood of treatment-naive GCA and PMR patients as well.

Objectives: We sought to replicate previous studies showing a disturbed Th cell distribution in the blood of GCA and PMR patients. Next, we aimed to link the disturbed Th cell distribution to the altered monocyte subset counts.

Methods: To assess the capacity of circulating T cells to produce lineage cytokines, PBMCs were cultured for 4 hours in the presence of 50 ng/mL PMA, 16 μg/mL calcium ionophore and 10 μg/mL BFA. Cells were then intracellularly stained for IFNγ (Th1 cells), IL-17 (Th17 cells) and IL-4 (Th2) by flow cytometry.

References:

Disclosure of Interests: None declared.

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*RA Moura, JE Fonseca and L Graca are joint senior authors.

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Disclosure of Interests: None declared.

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