of these known checkpoint inhibitors (PD1, CD152) could be important for SLE immunopathogenesis.

Secondly, the innate lymphoid cell 2 (ILC2) subset (Lin-CD7+CD25+CD127+GFP-) was markedly depressed in SLE (0.11%, 0.1 - 0.25%) versus control (0.41%, 0.25 - 0.55%; p = 0.0293). ILC2s protect epithelial integrity; a reduction suggests impaired protective roles in SLE.

Supervised cell frequencies from bivariate analysis correlate strongly with unsupervised cell frequencies, validating these results (Pearson's correlation coefficient r = 0.9692; p < 0.001 (CD4+CD152+PD1+CD45RO+CD25+FoxP3)); r = 0.8863; p < 0.05 (ILC2)).

Conclusion: With a multi-parametric, unbiased approach comparing SLE subjects to large data of age-matched healthy controls, we identified two immune subsets of potential immunopathogenic importance. With this information, the CyTOF panel can be redesigned to probe more specifically into the SLE immuneome, facilitating disease-specific interrogation.

References:

Disclosure of Interests: none declared
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THU0238
ASSOCIATION OF SYSTEMIC DISEASES OF CONNECTIVE TISSUE (SDCT) AND GERIATRIC PROCESSES
V. Shishkin1,2, G. V. Kudriavtseva3, Y. Malenkova2, V. V. Shishkin2. 1Saint Petersburg State University, Saint-Petersburg, Russian Federation; 2Saint Petersburg State University, Saint-Petersburg, Russian Federation

Background: The approach from the point of view of the evolutionary perspective of finding targets for therapeutic effects among the components of the cellular destruction system is critical both in the treatment of rheumatological diseases and in gerontology.

Objective: To identify relationships between the pathways of cell death in synerial fluid (SF) of people of different age groups with SDCT.

Methods: SF was analyzed in patients of two age groups. Group N 1 of patients: 10 SLE (43±2.3 years), 13 RA (45±1.7 years), 7 SSD (35±1.8 years) and 8 donors (42±2.7 years, postmortem). Group N 2 (age) of patients: 9 SLE (69±1.8 years), 10 RA (65±1.6 years), 5 SSD (65±0.7 years) and 9 donors (66±2.3 years, postmortem).

Conclusion: SF treated with 0.1% Triton-x-100, resuspended in 0.1% citrate buffer (42±2.7 years, postmortem). Group N 2 (age) of patients: 9 SLE (69±1.8 years), 10 RA (65±1.6 years), 5 SSD (65±0.7 years) and 9 donors (66±2.3 years, postmortem).

Disclosure of Interests: none declared
DOI: 10.1136/annrheumdis-2020-eular.2855

THU0239
DYNAMIC TEMPORAL CHANGES IN CLINICAL DISEASE ACTIVITY AND INFILTRATION REPRESENTATION OF A PATHOBIONT LINKED TO LUPUS NEPHRITIS
G. Silverman1, D. Azzouz1, Z. Chen1, J. Deng1, Z. Lü2, D. Fenyo2, A. Alexeyenko3, 1NYU School of Medicine, Department of Medicine, New York, United States of America; 2NYU School of Medicine, Institute for Systems Genetics, New York, United States of America; 3MUSC, Biomedical Informatics Center, Charleston, United States of America

Background: From a cross-sectional cohort, we have identified a candidate gut human anaerobic pathobiont, Ruminococcus gravis (RG) of the family Lachnospiraceae that was linked to active Lupus nephritis (LN)(1). Based on 16S rRNA amplicon analysis, LN patients displayed increased fecal RG abundance, concordant with serum IgG anti-RG antibody responses that appeared interwoven with anti-dsDNA responses implicated in renal pathogenesis. Indeed, monoclonization of germ-free mice is reported to result in generalized inflammation and expansions of Th17 cells. However, RG at low levels are also prevalent in healthy adults, and the temporal dynamics of RG representation within Lupus microbiota ecosystems have not been investigated. Also, genomic sequences of few RG strains have been reported, and these vary greatly in genome structure, gene representation and sequence, which may have broad implications for adaptation to a host with systemic inflammation and/or factors that contribute to immune activation in a susceptible host.

Objective: To investigate the relationships between in vivo RG expansions and disease activity that often wax and wane overtime, we initiated longitudinal studies in Lupus patients and controls. As representation of RG strains alone might alter pathogenic potential, we also sought to characterize RG strains from active LN patients.

Methods: From our cohort, patients were characterized for demographics, clinical disease activity, and serologies including anti-dsDNA, ANA, anti-cardiolipin, antiphospholipid, anti-thrombin, anti-tissue transglutaminase, and anti-bacterial responses of interest. High throughput 16S rRNA amplicon libraries from fecal samples were analyzed using QIIME 2 and DADA2 (1). Also, individual RG colonies were isolated and subjected to whole genome sequencing. Species and strains were then assigned in part based on multi-locus sequence typing and reference guided genomic assemblies.

Results: 16S rRNA analysis of 34 samples, at 2-4 timepoints from 14 SLE patients, documented highly conserved patterns of gut community representation over time in 10/14 patients, based in part on unsupervised hierarchical cluster analysis. Notably, independent of vaccinations in clinical disease activity of up to 8 SLEDAI points, conserved microbiome phylotypic abundance/composition was documented at a family level, and the level of amplicon sequence variants that approximate identification of individual species. In pilot studies, from two active lupus nephritis patients hundreds of fecal bacterial colonies were detected even in patients with dramatic changes in disease activity, which was linked to active Lupus nephritis (LN)(1). Based on 16S rRNA sequence analysis, these Lupus-patient fecal colonies were found to distribute into only four distinct RG strains, which differed from reported strains.

Conclusion: Our findings suggest that many Lupus patients have little or no detectable perturbations in representation of the Lachnospiraceae family or abundance of RG species overtime. Moreover, this seeming microbiota stability was documented even in patients with dramatic changes in disease activity. However, these approaches are inadequate to detect shifts between RG strains. In pilot studies we have isolated and characterized the genomes of four unique RG strains from active LN patients, which include variations in gene content and sequence that may have implications for the host-commensal relationship and immune activation. Broadening of these studies to larger number of SLE patients and healthy subjects, with metagenomic surveys of strain representation in genomic shotgun libraries are currently in progress, in coordination with increases and also the acid-base balance shifts, the number of active forms of oxygen radicals increases, ox-red changes, the compartments of cellular destruction are activated, the activity of the cytokine system of the organism is disturbed (cytokines - regulators of apoptosis, the expression of chaperones decreases and immuno-oxygenase homeostasis shifts. Inhibition of the genetically determined process of cell death, apoptosis, underlies the development of autoimmune diseases, immunepro-litterary pathology (carcinogenesis) and geriatalogical changes.


Disclosure of Interests: none declared
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TAB.1 SOME MARKERS OF AUTOAPHOTX, APOTOPSIS AND NECROSIS IN SF OF DONORS AND PATIENTS WITH SDCT (Msm): AMPK (cond.unit/mg protein), ATP-ase (nM Pi/mg/mg protein), AFRF (unit/mg protein); Cyt c, p S3, 8-Oh-DG - (ng/ml)

<table>
<thead>
<tr>
<th>Group</th>
<th>AMPK</th>
<th>ATP-ase</th>
<th>AFRF</th>
<th>Cyt c</th>
<th>p S3</th>
<th>8-Oh-DG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor</td>
<td>1.8±0.9</td>
<td>3.7±0.3</td>
<td>9.7±2.3</td>
<td>10.4±0.3</td>
<td>0.7±0.1</td>
<td>9.5±0.8</td>
</tr>
<tr>
<td>SLE (10)</td>
<td>4.9±0.3*</td>
<td>10.3±0.9</td>
<td>43.4±0.7</td>
<td>40.1±2.8</td>
<td>1.7±0.1</td>
<td>28.3±1.4*</td>
</tr>
<tr>
<td>RA (13)</td>
<td>7.3±0.2***</td>
<td>9.7±0.5</td>
<td>32.8±4.6</td>
<td>29.3±3.7</td>
<td>1.5±0.06</td>
<td>23.8±0.9</td>
</tr>
<tr>
<td>SSD (7)</td>
<td>4.3±0.3</td>
<td>5.9±0.4</td>
<td>13.4±3.2</td>
<td>18.0±3.7</td>
<td>0.9±0.1</td>
<td>23.7±0.8*</td>
</tr>
<tr>
<td>Group N2</td>
<td>AMPK</td>
<td>ATP-ase</td>
<td>AFRF</td>
<td>Cyt c</td>
<td>p S3</td>
<td>8-Oh-DG</td>
</tr>
<tr>
<td>Donor</td>
<td>1.9±0.4</td>
<td>0.9±0.2</td>
<td>24.8±5.1</td>
<td>15.2±3.4</td>
<td>1.3±0.2</td>
<td>18.3±0.2</td>
</tr>
<tr>
<td>SLE (9)</td>
<td>18.2±0.2***</td>
<td>4.2±0.3</td>
<td>64.6±3.1</td>
<td>52.8±3.9</td>
<td>3.4±0.1</td>
<td>44.8±0.7</td>
</tr>
<tr>
<td>RA (10)</td>
<td>17.0±0.4***</td>
<td>4.0±0.2</td>
<td>54.6±1.6</td>
<td>44.3±3.3</td>
<td>3.2±0.3</td>
<td>42.2±0.4*</td>
</tr>
<tr>
<td>SSD (5)</td>
<td>9.8±0.3*</td>
<td>2.8±0.2</td>
<td>38.8±4.4</td>
<td>38.6±2.9</td>
<td>2.9±0.1</td>
<td>30.7±0.3*</td>
</tr>
</tbody>
</table>

Notes: difference with the control norm: * - p<0.05; ** - p<0.01; *** - p<0.001

Autophagy (especially in the case of SLE, as well as RA) is directly involved in the formation of the immune response and the inflammatory process. During aging, as well as during SDCT, there is a sharp increase in the activity of AMPK (intracellular energy sensor), expression of apoptosis inducers of oxygen radicals increases, ox-red changes, the compartments of cellular