Background: Systemic lupus erythematosus (SLE) is a systemic inflammatory disease characterized by heterogeneous clinical manifestations (1). Although there are significant developments with its pathogenesis, it is still not fully known. In recent years, pathways such as NéTosis and plasmacytoid dendritic cell (pDC) activation have been emphasized in the pathogenesis of SLE (2, 3).

Objectives: In our study, we aimed to investigate serum LL-37, Galectin-3, and Toll-like receptors-3 (TLR-3) levels, which are thought to be related to pathogenic pathways in SLE patients.

Methods: 17 SLE patients and 33 healthy controls were included in the study. The clinical and laboratory features of the patients were determined. Serum LL-37, Galectin-3, and TLR-3 levels were determined by ELISA (enzyme-linked immunosorbent assay) method using the appropriate commercial kit, and the results were evaluated according to the manufacturer’s instructions.

Results: The clinical and laboratory features of the groups are described in Table 1. In our study, serum LL-37, Galectin-3, and TLR-3 levels were decreased statistically significantly in SLE patients compared to healthy control (p = 0.007, and p = 0.008, respectively).

Table 1. Clinical and laboratory features of the groups in the study

<table>
<thead>
<tr>
<th></th>
<th>Healthy control (n=33)</th>
<th>SLE (n=17)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>34.1 ± 3.7</td>
<td>40 ± 11.4</td>
<td>0.05</td>
</tr>
<tr>
<td>Sex (n: female/male)</td>
<td>33/0</td>
<td>17/0</td>
<td></td>
</tr>
<tr>
<td>LL-37 (ng/ml)</td>
<td>56.0 ± 10.6</td>
<td>14.2 ± 19.3</td>
<td>0.007</td>
</tr>
<tr>
<td>Galectin-3 (ng/ml)</td>
<td>25.5 ± 23.2</td>
<td>6.7 ± 7.6</td>
<td>0.002</td>
</tr>
<tr>
<td>Toll-like receptors-3 (pg/ml)</td>
<td>7893.4 ± 1041.3</td>
<td>916.2 ± 469.7</td>
<td>0.008</td>
</tr>
</tbody>
</table>

Conclusion: It is suggested that LL-37, Galectin-3, and TLR-3 levels have various effects on NéTosis and pDC activation pathways in SLE pathogenesis. In our study, low levels of serum LL-37, Galectin-3, and TLR-3 in SLE patients suggest that they are associated with SLE pathogenesis.

References:

Disclosure of Interests: None declared
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Background: Objectives: It has been established that in cells, in particular in neutrophilic leukocytes of SF, mitochondria form a mitochondrial-reticular dynamic spatial network (MRN). MRN is the epicenter of apoptosis, reflecting structural and functional changes in the immune-complex pathology in SLE and RA.

Methods: SF was analyzed in patients: 10 SLE (43 ± 2.3 years), 13 RA (45 ± 1.6 years) and 8 donors (42 ± 3.7 years, postmortem). Neutrophilic leukocytes from the SF were isolated by standard methods and resuspended in a composition medium: 70 mM NaCl; 140 mM sucrose; 5.6 mM KCl; 10 mM pyruvate; 8 mM MOPS; pH = 7.4. The cell suspension was centrifuged for 5 min at 800g. MRN was isolated by centrifuging the resulting supernatant for 15 min at 12 000g. The resulting MRN fragments were resuspended in citrate-phosphate buffer (pH = 7.4) and used in experiments. The activity of adenosine monophosphate-activated protein kinase (AMPK) was evaluated by Western blotting. Quantitative determination of cytochrome C (Cyt C) was carried out by enzyme immunoassay method using the Human Cytochrome c Platinum ELISA kit (eBioscience, USA). Active forms of oxygen free radicals (AFRF) were registered by EPR. The swelling rate of MRN fragments was determined spectrophotometrically at 540 nm. The electrophoretic mobility (EM) of MRN fragments was determined by the automatic microscope "Parmakon-2t".

Results: MRN of neutrophilic leukocytes of the SF undergoes significant adaptive rearrangements during the development of SLE and RA (tab.1). On average, the results were evaluated according to the manufacturer's instructions.

Table 1. EXPRESSION OF INDUCTORS OF AUTOAPOTOSIS, APOPTOSIS, NECROSIS AND ELECTROPHORETIC MOBILITY OF MRN FRAGMENTS OF NEUTROPHILIC LEUKOCYTES OF SF IN SLE AND RA

<table>
<thead>
<tr>
<th>Experience</th>
<th>Terms</th>
<th>AMPK, cond unity/ml protein</th>
<th>Cyt C, ng/ml</th>
<th>AFRF, unit/ml protein</th>
<th>Swelling rate of MRN, min. -  mV · sec</th>
<th>EM, mV · sec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor (6)</td>
<td></td>
<td>0.51±0.05</td>
<td>23.7±5.4</td>
<td>3.72±2.4</td>
<td>0.177±0.004</td>
<td>1.58±0.07</td>
</tr>
<tr>
<td>SLE (10)</td>
<td></td>
<td>1.73±0.04**</td>
<td>49.3±6.5</td>
<td>21.3±5.1*</td>
<td>0.435±0.005***</td>
<td>0.35±0.05***</td>
</tr>
<tr>
<td>RA (13)</td>
<td></td>
<td>1.25±0.07**</td>
<td>47.8±4.8</td>
<td>15.7±4.3*</td>
<td>0.41±0.007***</td>
<td>0.41±0.07***</td>
</tr>
</tbody>
</table>

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

Conclusion: Endoplasmic stress occurs in SF cells during the development of SLE and RA, blocking of autophagy and apoptosis leads to a breakdown of neutrophilic leukocyte MRN, accumulation of high molecular products of tissue decay - phlogogens in the intercellular space, among which the expression in the context is characterized by proteins - chaperones Hsp 60-100. These processes are accompanied by a shift in the bioelectrohomeostasis of MRN neutrophilic leukocytes, an increase in their swelling rate and a significant decrease in their electrokinetic potential. The described MRN reactions of neutrophilic leukocytes of the SF should be taken into account when developing pharmacologically induced apoptosis as a new approach in the treatment of autoimmune diseases.

References:

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Background: Objectives: 1. This study, developed within the Innovative Medicines Initiative Joint Undertaking project PRECISESADS framework, aimed to identify specific molecular profiles involved in the enhanced CV-risk present in SLE patients and to analyze the relevance of the sustained positivity for anti-dsDNA on the establishment of their atherothrombotic status.

Methods: One hundred and twenty-four SLE consecutive patients (not including patients with associated antiphospholipid syndrome), belonging to the PRECIS-ESADS project, were evaluated for the presence of CVD and its association with positivity for anti-dsDNA antibodies. A second cohort of 62 SLE patients was included, of which endothelial dysfunction, lipid profile, the presence of atheroma plaques (identified by a pathologic increase in the carotid intima media thickness -CIMT-), and the frequencies of anti-dsDNA positivity for 7 years, were evaluated. Serum inflammatory and oxidative stress biomolecules, and
NETosis-derived bioproducts were further evaluated by multiplex assay and specific commercial kits, respectively. Besides, miRNomes were identified using next-generation sequencing. Clinical significance of the biomolecules analyzed was explored by correlation/association studies with immunological and CV-risk features.

**Results:** A significant relationship among the incidence of CVD (i.e. thrombosis or cardiac involvement) and the positivity for anti-dsDNA antibodies was recognized in the first SLE cohort. Accordingly, in the second SLE cohort, significantly impaired micro-vascular endothelial function (identified by evaluation of hyperemia post-occlusion area), increased atherosclerotic index and pathologic increase in the CIMT were assessed in patients positive for anti-dsDNA in relation to anti-dsDNA negative patients. Around a 65% of SLE patients displayed a sustained positivity for anti-dsDNA antibodies for more than 7 years. These patients showed a distinctive and specific molecular profile compared with patients that had remained negative for anti-dsDNA, including increased inflammatory profile (IL1B, IL2, IL6, IL17, EOTAXIN, FGF, GMCSF, IFNγ, IP10, RANTES, TNF), enhanced oxidative status (lipperoxides), and higher NETosis (nucleosomes, elastase). Levels of those microbiomes were closely interconnected and associated to their regulatory miRNAs, which accordingly exhibited differential expression in SLE anti-dsDNA(+) vs anti-dsDNA(-) patients. Finally, the frequency for positivity of anti-dsDNA significantly correlated both with markers of endothelial dysfunction and with the presence of atheroma plaques in SLE patients, pointing at the direct involvement of anti-dsDNA-Abs in the development of these processes.

**Conclusion:** 1. Positivity for anti-dsDNA antibodies confers a specific molecular profile linked to an enhanced CV-risk in SLE patients. 2. Moreover, the sustained positivity for anti-dsDNA antibodies fosters the establishment of an atherothrombotic status in these autoimmune patients.

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**AB0137 DIVERSITY ANALYSIS OF INTESTINAL FLORA IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

Z. Mingxing1, X. F. Yin1. The Second Hospital of Shanxi Medical University, Taiyuan, China

**Background:** Systemic lupus erythematosus (SLE) is a multiple systemic autoimmune disease and its pathogenesis is still not fully understanding. In recent years, there has been reports on the relationship between SLE and intestinal flora.

**Objectives:** To study the diversity and the intestinal microbes in patients with SLE and further provide new ideas for clinical treatment.

**Methods:** The stool samples of 28 patients with SLE and 125 normal healthy adults were collected. The 16S rRNA in the specimen was sequenced using the Roche/454 high-throughput sequencing platform, and the differences between the two groups were compared at the level of the phylum and genus.

**Results:** In SLE patients, as the picture show, the levels of fusobacteria, proteobacteria and TM7 were significantly higher (P<0.05) and the number of Firmicutes was significantly decreased (P<0.05) than that of healthy controls at the genus level. Additionally, the number of lachnospira, roseburia, gemmiger, devosia, desulfovibrio were significantly higher (P<0.05) and the number of fir obstac and TM7 were significantly higher (P<0.05) and the number of fir obstac and TM7 were significantly higher (P<0.05) and the number of fir obstac and TM7 were significantly higher (P<0.05) and the number of fir obstac and TM7 were significantly higher (P<0.05) and the number of fir obstac and TM7 were significantly higher (P<0.05)

**Conclusion:** The diversity of intestinal flora in patients with SLE altered from that of normal population. The differences are likely to be one of the pathogenesis of lupus, which might provide theoretical foundation for the regulation of intestinal flora to treat autoimmune diseases such as lupus.

**Disclosure of Interests:** None declared DOI: 10.1136/annrheumdis-2020-eular.5943

**AB0138 INCREASED CD38 EXPRESSION LEVELS ON IMMUNE CELL SUBSETS IN SYSTEMIC LUPUS ERYTHEMATOSUS**

L. Ostendorf1,2, P. Enghard1,2, P. Durek1,2, F. Heinrich1, M. F. Mashreghi1, G. R. Burmester1, A. Radbruch1, F. Hiepe1,2, T. Alexander1,2, Charité – Universitätsmedizin Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany; 2Deutsches Rheuma-Forschungszentrum (DRFZ), Berlin, Germany; 3Charité – Universitätsmedizin Berlin, Department of Nephrology, Berlin, Germany

**Background:** Plasma Cells (PCs) are implicated in the pathogenesis of Systemic Lupus erythematosus (SLE) and their targeting proved a promising treatment modality. As there is a monoclonal therapeutic antibody targeting CD38 licensed for clinical use in multiple myeloma, plasma cell depletion via CD38 seems to represent a promising path in SLE treatment. While CD38 is highly expressed on plasmacells, it is present on the surface of subsets of T and B lymphocytes as well as myeloid cells.

**Objectives:** Here we aim to identify the differential expression of CD38 on peripheral blood leukocytes in SLE compared to healthy controls (HC) investigate the function of CD38+ T lymphocytes

**Methods:** We performed flow cytometry to investigate the expression of CD38 on peripheral blood mononuclear cells of SLE patients (n=36) and HCs (n=20). We additionally analyzed the expression of T lymphocytes within the urine of patients with lupus nephritis as well as the skin of SLE patients. We investigated the

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**Disclosure of Interests:** None declared DOI: 10.1136/annrheumdis-2020-eular.5943

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