EFIS session: Emerging concepts how B cells drive systemic autoimmunity: from bench to clinic

OP0320

CHARACTERISTICS OF PERIPHERAL BLOOD B-CELL SUBSETS IN PATIENTS WITH SJOGREN SYNDROME

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Background: B-cells play a pivotal role in primary Sjogren's syndrome (SS) pathogenesis. Recent studies have shown disturbances in the peripheral B cell populations in primary SS.

Objectives: To examine B-cell subsets in peripheral blood of SS patients (pts) and to analyze the association between B-cell subsets and SS activity.

Methods: Twenty active SS pts (19F/1M): median age 42 years (range) (32-54); disease duration 3 (2-10) years; ESSDAI score ≥ 5 in 6 pts, < 5 in 14 pts), were included. SS was diagnosed based on the ACR-EULAR 2016 criteria. Twenty healthy donors composed the control group. CD19+B cells, memory B-cells (CD19+CD27+), non-switched memory B-cells (CD19+IgD+CD27+), switched memory B-cells (CD19+IgD-CD27+), naïve (CD19+IgD+CD27-), double negative (CD19+IgD-CD27-), transitional (CD19+IgD+CD10+CD38+) B-cells, plasmablasts (CD19+CD38++IgD-CD27+), and plasma cells (CD19+CD38+) were analyzed by multicolor flow cytometry using cytometer Navios (Beckman Coulter, USA).

The nonparametric Mann-Whitney test, the unpaired Student's t test for group comparison, and the Pearson's χ^2 criterion were used for statistical analysis. Data were shown as median (Me) with an interquartile range of 25 - 75 percentile. The differences were considered statistically significant when $p < 0.05$. Statistica 10 for Windows (StatSoft Inc., USA) package was used for statistical data processing.

Results: The percentages/absolute numbers of plasmablasts, plasma cells and transitional B-cells in SS were significantly higher than in healthy donors, $p < 0.01$ for all cases (Table 1).

Table 1. B-cell subsets in patients with SS, SS and MALT lymphoma and healthy donors.

B-cell subsets	SS		HD		Pt 1		FN
	%	Abs. cells/ μ l	%	Abs. cells/ μ l	%	Abs. cells/ μ l	
B lymphocyte	12,8 (7,9 - 19,7)	151 (95-112)	8,5 (7,2-11,0)	200 (100-200)	4,5	31	**
plasma cells	6,9 (4,2-10)	12 (6-22)	0,1 (0,05-0,1)	0,1 (0-0,2)	5,7	13	*
plasmablasts	0,88 (0,37-1,8)	2 (1-3)	0,1 (0,1-0,2)	0,2 (0,1-0,4)	26,6	12	*/**
transitional B-cells	5,7 (0,9-17)	8 (4-32)	0,1 (0-0,1)	0,1 (0-0,3)	0	0	*
switched cells	9,1 (5,9-20,7)	18 (11-29)	12,8 (9,3-17,0)	20 (10-40)	52	16	**
non-switched mem-ory B-cells	4,13 (2,7-5,4)	7 (3-15)	7,4 (3,7-11,1)	10 (5-20)	16	5	**

SS Sjogren's patients; HD healthy donors, Pt 1 patient with SS and MALT lymphoma* SS and HD groups compared, $p < 0.01$ ** Pt 1 and SS group compared

One of the patients (Pt 1) was diagnosed with MALT lymphoma of the parotid salivary gland; she had a distinct B-lymphocyte subpopulations distribution, which was different from the rest of the SS group. She had the lowest percentage / absolute B lymphocyte count of all patients with SS, the highest percentage of switched cells and non-switched memory B-cells, and the highest percentages/ absolute numbers of plasmablasts. For this reason, the patient was excluded from the subsequent analysis (Table 1).

Patients with activity of SS by ESSDAI ≥ 5 had a significantly higher percentage of B cells ($p = 0.007$), and significantly higher absolute B lymphocyte count of naïve cells ($p = 0.04$) and plasmablasts ($p = 0.048$).

Conclusion: Immunophenotyping showed disturbed homeostasis of the B-cells subpopulations in our SS cohort. A significant increase in plasmablasts in SS, as well as a positive correlation of the level of plasmablasts with the SS activity and presence of lymphoma could suggest the important role of these cells in the pathogenesis of SS.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.2982

OP0321

DELINEATING THE IMMUNOGENIC DOMAINS OF MDA5 USING PATIENT DERIVED AUTOANTIBODIES

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Background: The presence of myositis specific anti-melanoma differentiation associated protein 5 (MDA5) autoantibodies is associated with mucocutaneous ulcerations, rapidly progressing interstitial lung disease (RPILD), arthritis and mild muscle involvement in patients. RPILD is the major cause of mortality. At present it is unknown which domain of the MDA5 protein is the main elicitor of an immunogenic response.

Objectives: The aim of this study is to delineate the domains in the MDA5 protein that are the target of autoantibodies.

Methods: Anti-MDA5 IgG were isolated from MDA5(+) patient plasma (7 UPMC, 1 KI and 1 KULeuven) by affinity chromatography using an in-house affinity column as described earlier in Ossipova et al, 2014⁽¹⁾. 8 constructs covering different regions of the MDA5 protein were recombinantly produced in *E.coli* (Uniprot ID Q9BYX4, Figure 1). An in-house ELISA was developed to identify the domains with the main epitope(s) by measuring the reactivity of the plasma samples and purified autoantibodies against these MDA5 protein constructs, similar to what was reported by Fernandes-Cerqueira et al, 2018⁽²⁾. The biotinylated MDA5 proteins were immobilized on streptavidin coated plates and subsequently incubated with primary antibodies (purified autoantibodies⁽²⁾ or original plasma) and a HRP-conjugated secondary antibody. The ELISA was developed by the addition of TMB substrate and the optical density (OD) was measured at 450 nm.

Figure 1. Graphical presentation of the constructs representing different (combinations of) domains of the MDA5 protein.

Results: The preliminary data suggest the main reactivity of the plasma samples and the corresponding purified autoantibodies is directed towards the helix-case domains and that there is variability between the patients in the reactivity towards domains located at the end of the protein.

Conclusion: The study aims to resolve the main immunogenic domain of the MDA5 protein, which will lead to more insight in the disease mechanisms. The preliminary results suggest this domain is in the center of the MDA5 protein, but further experiments are necessary. We will use this set up to study differences in reactivity between patients (from different cohorts) and assess if differences in antibody reactivity could be linked to clinical features such as RPILD. Such correlations might be beneficial to predict the disease progression and to apply personal treatment approaches.

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Disclosure of Interests: Eveline Van Gompel: None declared, Catia Cerqueira: None declared, Edvard Wigren: None declared, Susanne Gräslund: None declared, Karine Chemin: None declared, Begum Horuluoglu: None declared, Ellen De Langhe: None declared, Olivier Benveniste: None declared, Ingrid E. Lundberg Consultant of: Consulting fees from Corbus Pharmaceuticals, Inc, Grant/research support from: Research grants from Bristol Myers Squibb and AstraZeneca.

DOI: 10.1136/annrheumdis-2021-eular.4264

[Joint session HPR/ PARE/ ARP] Mastering Self-management: State of art in a New Era

OP0322-HPR

EMPOWERMENT AND ASSOCIATIONS TO DISEASE ACTIVITY AND PAIN IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The WHO describes empowerment as a process in which patients can take control and make informed decisions about their life and health. Empowerment is important for patients with rheumatoid arthritis (RA) since most of the care is provided by the patients themselves.

Objectives: The aim was to study levels of empowerment and associated variables in individuals with RA and to investigate longitudinal clinical data in patients with low and high empowerment.

Methods: This study involved patients with RA from the BARFOT (Better Anti-Rheumatic Pharmacotherapy) cohort, who were recruited between 1992 and 2006 and included in the study at the time for diagnosis (n = 2,837) [1]. The patients were assessed according to a structured protocol at inclusion and after 3, 6, 12, 24, 60, 96, and 180 months. At each follow-up DAS28-3, HAQ and pain were assessed. In 2017, a postal survey was sent to all still living patients (n=1542), with a response rate of 69% (n = 1,065). The questionnaire included disease characteristics, questions about lifestyle habits and the Swedish Rheumatic Disease Empowerment Scale (SWE-RES-23) [2]. The 844 patients who answered the SWE-RES-23 made up the study cohort. Differences in empowerment between groups (lowest third [LE], SWE-RES-23 ≤3.48 vs. highest third [HE], SWE-RES-23 ≥4.04) were analysed with t-tests. Logistic regression analysis was used to study associations with LE vs. all others. Thirdly, differences between LE and HE were studied with longitudinal data (seven time points) of pain, HAQ and disease activity.

Results: Responders were mean 65 (SD13) years old, disease duration 15.6 (3.9) years, and 74% were women. The LE group (n=282) were older and were more often women, and reported worse overall health compared with the HE group (n=270), Table 1.

Table 1. Descriptives at questionnaire 2017, including all participants and comparisons between highest and lowest third of SWE-RES-23

	All	Low SWERES*	High SWERES*	p-value
	Mean (sd)	Mean (sd)	Mean (sd)	
N	844	282	270	
Sex, women, %	74	78	69	0.015
Age	65 (13)	66 (13)	63 (12)	0.002
Disease duration, year	15.6 (3.9)	15.7 (4.1)	15.6 (3.8)	0.917
TJC28 (0-28)	5 (6)	6 (8)	4 (5)	<0.001
SJC28 (0-28)	3 (5)	3 (4)	3 (4)	0.334
PatGA (0-10)	3 (2)	4 (3)	2 (2)	<0.001
Pain (0-10)	3 (2)	4 (3)	3 (2)	<0.001
Fatigue (0-10)	4 (3)	5 (3)	3 (3)	<0.001
HAQ (0-3)	0.62 (0.61)	0.81 (0.69)	0.42 (0.51)	<0.001
EQ5D (0-1)	0.70 (0.25)	0.62 (0.29)	0.79 (0.19)	<0.001
SWERES	3.8 (0.7)	3.1 (0.3)	4.6 (0.3)	<0.001

*tricotomized data, lowest third vs. highest third

Figure 1. Panel showing mean DAS28-3 (A), ESR (B), VAS pain (C) and HAQ (D) over 15 years in the different groups.

Regarding lifestyle habits, there were no differences between the groups in smoking habits, diets, or drinking habits. Moderate physical activity for ≥150 min/week was reported by 27% in the LE group vs. 41% in the HE group, $p < 0.001$. Vigorous physical activity ≥60 min/week was reported by 22% vs. 37% in the LE and the HE group respectively, $p < 0.001$.

In the logistic regression analysis (n=844), several factors were associated with LE: being a woman (OR 1.40, 95% CI 1.00-1.97), pain-related factors as higher tender joint count (OR 1.04, 95% CI 1.01-1.06), worse patient global assessment (OR 1.19, 95% CI 1.12-1.27), pain (OR 1.14, 95% CI 1.08-1.21), fatigue (OR 1.14, 95% CI 1.09-1.21), HAQ (OR 2.08, 95% CI 1.64-2.64) and EQ-5D (OR 0.16, 95% CI 0.09-0.28). There were also associations between moderate physical activity (<150 min/week) (OR 1.60, 95% CI 1.16-2.19) and vigorous (< 60 min/week) (OR 1.50, 95% CI 1.07-2.10) and LE.

Analysing longitudinal data, the LE group reported worse pain and HAQ at all timepoints, a worse DAS28-3 at year 2 and 8, and a worse ESR at 15 years follow-up compared with the HE group ($p < 0.05$).

Conclusion: In patients with RA, low empowerment is associated with worse all over health. Interventions aimed to improve empowerment may include mastering of pain, physical function, and improved physical activity.

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Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.455

Members and Volunteers – Unknown beings? How to explore their interests, establish contacts and support

OP0323-PARE

“CELEBRATING THE 50TH ANNIVERSARY OF OUR ORGANISATION IN TIMES OF PANDEMIC: HOW WE USED DIGITAL TOOLS TO OVERCOME CHALLENGES AND DIFFICULTIES AND CAME INTO CONTACT WITH MORE PARTICIPANTS AND VIEWERS THAN EVER ENVISAGED!”

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Background: The German League against Arthritis (DRL) with about 300.000 members wanted to celebrate its 50th anniversary in 2020. The original idea to perform a large jubilee gala was crossed by the limitation of contact and the precaution for members our organisation in times of pandemic.

Objectives: It was a big challenge to transfer the celebration into a digital form in the pandemic. Our goal was to reach as many people (with RMDs, their family, colleagues, politicians) as possible, not only members of our organisation. We wanted to generate even more awareness for people with RMDs, their needs and difficulties nationwide.

Methods: We decided to focus on digital formats and produced video clips and podcasts that were presented online. Some of the topics of the videos: Voluntary work,