Results: Increased frequencies of ILC2 and ILC3 were observed in patients compared to controls, while decreased frequency of ILC1 was found in patients compared with controls ($p=0.008$, $p=0.004$, and $p=0.006$, respectively). We also found the expression of T cell surface markers, CD4 or CD8, on ILCs and their subsets. The results showed that decreased frequencies of CD4⁺CD8⁺ ILCs, CD4⁺CD8⁺ILC1, CD4⁺CD8⁺ ILC2, CD4⁺CD8⁺ ILC2, and CD4⁺CD8⁺CD336⁺ ILC3 were found in patients compared with healthy controls ($p=0.001$, $p=0.017$, $p=0.001$, $p=0.004$, and $p=0.002$, respectively). Furthermore, frequencies of CD4⁺CD8⁺ ILCs and CD4⁺CD8⁺ ILC2 were positively correlated with the SLEDAI-2000 score ($r=-0.548$, $p=0.005$ and $r=-0.613$, $p=0.001$, respectively). Frequencies of CD4⁺CD8⁺ ILCs and CD4⁺CD8⁺ ILC1 were positively related with serum C3 level ($r=0.519$, $p=0.008$ and $r=0.528$, $p=0.007$, respectively), and were positively related with serum C4 level ($r=0.623$, $p=0.001$ and $r=0.643$, $p=0.001$, respectively).

Conclusions: In the present study, we demonstrated that frequencies of circulating ILCs and its subsets were altered in SLE patients and some subpopulations were negatively correlated with SLE disease activity.

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FRI0299 MUCOSAL-ASSOCIATED INVARIANT T CELL DEFICIENCY IN SYSTEMIC LUPUS ERYTHEMATOSUS IS REALTED TO AN INTRINSIC DEFECT IN THE CA2+/CALCINEURIN/NFAT1 SIGNALLINGPATHWAY

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Background: Mucosal-associated invariant T (MAIT) cells contribute to protection against certain microorganism infections and play an important role in mucosal immunity. However, the role of MAIT cells remains enigmatic in autoimmune diseases.

Objectives: Here, we examined the level and function of MAIT cells in patients with rheumatic diseases.

Methods: Patients with systemic lupus erythematosus (SLE; $n=54$), rheumatoid arthritis (RA; $n=66$), Behçet's disease ($n=9$), ankylosing spondylitis ($n=21$), and healthy controls ($n=136$) were enrolled in the study. MAIT cell, cytokine and programmed death-1 (PD-1) levels were measured by flow cytometry.

Results: Circulating MAIT cell levels were significantly reduced in systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) patients. In particular, this MAIT cell deficiency was more prominent in CD8⁺ and double-negative T cell subsets, and significantly correlated with disease activity, such as SLE disease activity index (SLEDAI) and 28-joint disease activity score (DAS28). Interestingly, MAIT cell frequency was significantly correlated with natural killer T (NKT) cell frequency in SLE patients. IFN- γ in MAIT cells was impaired in SLE patients, which was due to an intrinsic defect in the Ca²⁺/calcineurin/NFAT1 signalling pathway. In SLE patients, MAIT cells were poorly activated by α -galactosylceramide-stimulated NKT cells, thereby showing the dysfunction between MAIT cells and NKT cells. Notably, an elevated expression of PD-1 in MAIT cells and NKT cells was associated with SLE. In RA patients, MAIT cell levels were significantly higher in synovial fluid than in peripheral blood.

Conclusions: Our study primarily demonstrates that MAIT cells are numerically and functionally deficient in SLE. In addition, we report a novel finding that this MAIT cell deficiency is associated with NKT cell deficiency and elevated PD-1 expression. These abnormalities possibly contribute to dysregulated mucosal immunity in SLE.

Disclosure of Interest: None declared

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FRI0300

POLYMORPHISM OF 5,10-METHYLENETETRAHYDROFOLATE REDUCTASE (C677T) IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME, ITS ASSOCIATION WITH CARDIOVASCULAR LESIONS

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Background: Many studies have been conducted to determine the role of genetic polymorphism in the occurrence of cardiovascular diseases. The pathogenetic significance of MTHFR polymorphism is the subject of intensive research, especially its connexion with lesions of the cardiovascular system. The frequency of C677T polymorphism in the 5,10-MTHF gene is poorly known in patients with antiphospholipid syndrome (APS), and its relationship with vascular lesions has not been studied yet.

Objectives: The present study aimed to analyse the C677T mutation of the MTHFR gene and its association with endothelial dysfunction and clinical manifestations of cardiovascular lesions in APS.

Methods: We studied 82 patients with APS, including 34 (41.6%) with primary antiphospholipid syndrome (PAPS) and 48 (58.4%) with secondary antiphospholipid syndrome (SAPS). The analysis of the MTHFR C677T mutation was performed by PCR followed by digestion according to Frosst et al. All patients were assessed for the endothelium-dependent vasodilatation of brachial artery (EDVD), the thickness of the intima-media of the common carotid artery (IMT), the presence of atherosclerotic plaque (AP) and clinical manifestations of cardiovascular lesions

Results: There were 10.8% of homozygotes (677-TT), 37.8% of heterozygotes (677-CT) and 51.4% of homozygotes (677-CC) in the control group, and the frequency of T-alleles amounted to 29.7%. The incidence of T-alleles was higher among the patients with APS than in the control group and was 35.4%. The prevalence of homozygotes (677-TT), heterozygotes (677-CT) and homozygotes (677-CC) was not significantly different between the PAPS and SAPS groups (44.1%, 38.2%, 17.7% and 45.8%, 39.6%, 14.6% respectively $p<0.05$). The frequency of T-alleles was higher in PAPS group than in SAPS group (36.8% against 34.4%, respectively $p<0.05$). The analysis of structural and functional vascular lesions in homozygotes (677-CC), homozygotes (677-TT) and heterozygotes (677-CT) did not reveal significant differences in both mean values and the proportion of individuals with IMT thickness (0.86 ± 0.03 mm, 0.88 ± 0.05 mm, 0.90 ± 0.03 and 35.3%, 38.5%, 51.7% respectively $p<0.05$) with decrease of EDVD (7.09 ± 0.49 , 6.32 ± 1.0 , 6.92 ± 0.58 and 47.0%, 53.8%, 48.3% respectively $p<0.05$) and the presence of AP (26.5%, 23.1%, 48.3% respectively $p<0.05$). Although there was a tendency of IMT thickness increase and EDVD decrease for T-carriers. The proportion of persons with IMT thickness (>0.90 mm) and the decrease of EDVD BA ($\leq 8.0\%$) among the homozygote 677-TT was 3%–6.5% higher than that of the 677-CC homozygote. The frequency of clinical manifestations of cardiovascular lesions (myocardial infarction, stroke, TIA) was in 1.2–1.8 times more often among the homozygotes 677-TT than 677-CC homozygote.

Conclusions: The mutation of the C677T of the MTHFR gene is not a risk factor for the development of atherosclerotic vascular damage in patients with APS, due to the lack of associative interrelationships between the decrease of EDVD, increase of IMT, clinical manifestations on the one hand, and the MTHFR polymorphism on the other

Disclosure of Interest: None declared

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FRI0301

SERUM EXOSOMES INVOLVED IN THE PROGRESSION OF LUPUS NEPHRITIS

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Background: Systemic lupus erythematosus (SLE is a chronic autoimmune disease that systemically affects several important organs).¹ Lupus nephritis (LN is one of the most severe complications of SLE).² Exosomes are important mediators of biological information and play a part in the occurrence and development of various diseases including LN.³

Objectives: The aim of study was to find whether exosomes participate in the pathogenesis of lupus nephritis.

Methods: We studied 10 patients with SLE but no LN, 10 patients with LN and 10 healthy people which are in line with the SLE classification criteria of American College of Rheumatology diagnostic (ACR) in 1997 and the LN pathological classification of ISN and RPS in 2003. Exosomes were isolated from the serum by ultracentrifugation and confirmed by transmission electron microscope and western blot. The internalisation of exosomes was detected by immunofluorescence. Then exosomes were injected into MRL/lpr mouse via the tail vein and co-cultured with mesangial cells. Flow cytometry was used to detect the alteration of cell cycle. The cell proliferation was determined by CCK-8 assay. The inflammatory cytokines (TNF- α , IL-6) and collagen I level in medium supernatant by ELISA, signal pathway by immunoblotting. Additionally, High-throughput sequencing was used to detect the expression of miRNAs in exosomes.

Results: The proteinuria and the percent of kidney crescent formation index of LN group was significantly high than other three groups. Exosomes can be absorbed by mesangial cells quickly. The secretion of inflammatory cytokines and collagen I of LN group were higher than NLN and control group ($p < 0.05$). PI3K/AKT pathway are involved. But there was no significant difference between NLN group and control group. High-throughput sequencing revealed 11 up-regulated miRNA in SLE relative LN, 3 up-regulated miRNA in LN relative healthy people.

Conclusions: LN exosomes can enhance the proliferation and secretion of mesangial cells in which PI3K/AKT pathway is activated. This tip us exosomes may involve in the pathogenesis of LN.

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SLE, Sjögren's and APS – clinical aspects (other than treatment)

FRIO302 SYSTEMIC LUPUS ERYTHEMATOSUS-ASSOCIATED THROMBOTIC MICROANGIOPATHIES IN 60 PATIENTS: CLINICAL FEATURES, PROGNOSIS AND TREATMENT IN A FRENCH MULTICENTRIC COHORT

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Background: The occurrence of a TMA during SLE is a rare event that complicates 1% to 4% of lupus. The full spectrum of TMA can be encountered in the course of SLE: acquired thrombotic thrombocytopenic purpura (TTP), TMA associated with glomerulonephritis (TMA GN), atypical hemolytic uremic syndrome (aHUS), microangiopathic antiphospholipid syndrome (MAPS; defined or probable catastrophic antiphospholipid syndrome) or HELLP syndrome during pregnancy.

Objectives: To describe the clinical phenotype of TMA in lupus, to specify the prognosis and to identify factors allowing early classification and management of the different subtypes.

Methods: We performed a French multicentric retrospective study from January 1987 to December 2017 in units of internal medicine, nephrology and ICU. Inclusion criteria associated SLE defined by the ACR and/or SLICC criteria and a TMA defined either by the presence of microangiopathic anaemia and peripheral thrombocytopenia, either by histological signs of TMA.

Results: 68 events of TMA occurred in 60 SLE patients; median age was 24 years; 56 women (F/M ratio: 14). Diagnosis of SLE was assessed at a paediatric age in 24 (35.8%) patients. Clinical manifestations of SLE were: acute cutaneous lupus (n=48, 71%), arthritis (n=36, 53%), pleuritis (n=13, 19%), pericarditis (n=25, 37%), renal involvement (n=39, 57% including 20 class IV glomerulonephritis) and auto-immune cytopenia (n=22, 32%). Triggering factors of TMA were: lupus flare (n=38), infections (n=12), pregnancy and peripartum (n=3), or therapeutic rupture (n=4). Clinical and biological features at diagnosis of each subtypes of TMA are presented in table 1. A platelet count lower than 28 000/mm³ was predictive of TTP diagnosis (Se=90,5%, Sp=88,5%), likewise a creatinine plasma level greater than 100 µmol/L was predictive of TMA GN (Se=88,5%, Sp=85%). The treatment of TMA included (alone or in combination): corticosteroids in all cases, plasma exchange (n=52), cyclophosphamide (n=28), Rituximab (n=15), Eculizumab (n=2), antiplatelet agent (n=36), and/or effective anticoagulation (n=26). The median duration of follow-up was 150 months. Among TMA GN patients, the final median GFR was 58 mL/min (range: 0–120) with 5 individuals on chronic dialysis and 1 kidney transplant. Among TTP patients, one died from TMA, whereas the final median GFR of survivors (n=59) was 97 mL/min (range: 64–150), without any patient requiring dialysis.

Table 1 Comparisons of clinical and laboratory data in different subtypes of TMA in SLE

	TTP	TMA GN	MAPS	HELLP syndrome	Anti-factor II autoantibody
Number of events	28	28	12	5	1
Gender (female/male)	18/10	13/15	11/1	3/2	1/0
Age at diagnosis of SLE (median [range], years)	24.3 [7-46]	24.7 [14-51]	27 [14-44]	24 [24-30]	30
Age at diagnosis of TMA (median [range], years)	24 [9-52]	27.5 [18-56]	41 [28-59]	29 [24-34]	30
Number with neurological disorder (%)	12 (43)	15 (54)	2 (17)	2 (40)	1
Number with acute renal failure (%)	12 (43)	26 (100)	12 (100)	2 (40)	0
Hb (median ± SE, g/L)	7.2 ± 2.3	7.5 ± 1.8	6.7 ± 1.3	6.3 ± 2.3	6.4
Haematocrit (median [range], %)	18.7 [10-35]	19.5 [10-43]	16.2 [10-41]	16.1 [10-31]	41
Creatinine levels (median ± SE, µmol/L)	80 ± 36.4*	309 ± 206*	128 ± 280	187 ± 142	36
CS (median ± SE)	0.00 ± 0.24*	0.3 ± 0.22*	0.79 ± 0.25	1.1 ± 0.4	1.19
Anti-ONA (median ± SE, ELISA R.U.)	200 ± 241	232 ± 220	300 ± 160	100 ± 140	31
ADAMTS13 activity (median ± SE, %)	9 ± 2*	48 ± 24*	42 ± 10	Not available	65
Urine protein (median ± SE, g/24h)	0.3 ± 1.3*	4 ± 2.3*	2 ± 1.3	9 ± 1.7	0.1
Hematuria (number of patients, %)	9 (34)	17 (64)	5 (42)	0	0
aCL positivity (number of patients, %)	9 (34)	4 (15)	11 (92)	0	0
Anti-beta2GPI (number of patients, %)	1 (3)	1 (3)	1 (8)	1 (20)	0

Abbreviations: SLE = systemic lupus erythematosus, TMA = thrombotic microangiopathy, Hb = hemoglobin, aCL = anticardiolipin, TMA GN = thrombotic microangiopathy associated with glomerulonephritis, MAPS = microangiopathic antiphospholipid syndrome, HELLP = hemolysis, elevated liver enzymes, low platelets.

* p < 0,05 in comparison between patient suffering from TTP or TMA GN with the rest of the cohort.

Conclusions: SLE-associated TMA is a heterogeneous syndrome. TTP with a decreased ADAMTS13 activity and a low platelets level (<28000/mm³) have a good renal prognosis, whereas TMA GN with a high creatinine level (>100 µmol/L)