meaningful modules, including yellow, turquoise, grey60 and blue, were identified (Figure 1A,1B). And 183 overlapping gene were screened from the DEGs and the Hub genes in the four modules for further analysis. We final divided pSS patients into three subtypes, of which yellow and turquoise in Sub1, grey60 in Sub2 and blue in Sub3. Sub1 and Sub3 were related to cell metabolism, while Sub2 had connection with virus infection (Figure 1C,1D). Infiltrated immune cells were also different among these three types (Figure 1E,1F).

Conclusion: Patients with pSS could be classified into 3 subtypes, this classification might help for assessing prognosis and guiding precise treatment.

REFERENCES:

- [1] Ramos-Casals M, Brito-Zerón P, Sisó-Almirall A, et al. Primary Sjogren syndrome. *BMJ* (Clinical research ed) 2012;344:e3821. doi: 10.1136/bmj.e3821 [published Online First: 2012/06/16].
- [2] Brito-Zerón P, Baldini C, Bootsma H, et al. Sjogren syndrome. *Nat Rev Dis Primers* 2016;2:16047. doi: 10.1038/nrdp.2016.47 [published Online First: 2016/07/08].
- [3] Segal B, Bowman SJ, Fox PC, et al. Primary Sjogren's Syndrome: health experiences and predictors of health quality among patients in the United States. *Health Qual Life Outcomes* 2009;7:46. doi: 10.1186/1477-7525-7-46 [published Online First: 2009/05/29].

Figure: (A,B) Heatmap of the correlation between module eigengenes and clinical traits of SS. (C,D) Molecular typing of patients with SS based on ferroptosis-related gene expression profiles consensus clustering of GEO samples by NMF, a heatmap displaying the expression pattern of subtypes is shown. (Figure E,F) The scores of 23 immune cells are displayed in boxplots. Adjusted P values were showed as: ns, not significant; *P<0.05; **P<0.01; ***P<0.001.

Acknowledgements: This project was supported by National Science Foundation of China (82001740), Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2402

POS0110 ASSOCIATION OF miR-155 AND miR-34a EXPRESSION IN LUPUS NEPHRITIS RENAL TISSUE WITH DISEASE ONSET AND OUTCOMES

C. Di Mario¹, L. Petricca², M. R. Gigante², S. Costanzi³, G. Vischini⁴, A. Paglionico⁵, V. Varriano¹, L. Bui⁵, G. Tanti⁵, L. Lanzo¹, F. Federico⁵, G. Grandaliano^{3,6}, M. A. D'agostino^{1,2}, S. Alivernini², B. Toluoso², E. Gremese^{1,2}. ¹Division of Rheumatology, Università Cattolica del Sacro Cuore, Rome, Italy; ²Division of Rheumatology, Fondazione Policlinico Universitario A. Gemelli-IRCCS, Rome, Italy; ³Division of Nephrology, Fondazione Policlinico Universitario A. Gemelli-IRCCS, Rome, Italy; ⁴Division of Nephrology, S.Orsola Malpighi Hospital, Bologna, Italy; ⁵Division of Histopathology, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy; ⁶Division of Nephrology, Università Cattolica del Sacro Cuore, Rome, Italy

Background: Epigenetic factors such as non-coding RNA (miRNA) have been shown to be deregulated in Systemic Lupus Erythematosus (SLE). In mouse models, different miRNAs have been associated with lupus nephritis (LN), one of the most severe manifestations of the disease¹.

Objectives: To evaluate the expression of miR-155 and miR-34a in renal tissues as biomarkers of organ involvement and inflammatory tissue activity in patients with LN.

Methods: Thirty-two SLE patients with LN (age: 32.2 ± 9.2 years) with active renal involvement undergoing ultrasound-guided renal biopsy were enrolled between 2010 and 2019. The nephritic manifestation was present in 13 (41%) patients at disease onset (early-LN SLE), while 19 (59%) patients showed a renal involvement after disease onset (long-LN SLE, mean disease duration at LN onset: 7.3 ± 5.7 years). Twelve age-matched patients with IgA nephropathy were enrolled as control group. Clinical, laboratory and demographic data were collected for each patient. Disease activity was recorded using SLE-DAI-2K and renal activity, using the total SLEDAI-2K fraction including the items related to the renal involvement. MiR-155 and miR-34a expression in renal tissues was carried out by extraction of total RNA from paraffin-preserved biopsies and was evaluated, after a retrotranscription protocol, using real-time PCR by relative quantification considering the ΔCt (Ct miRNA- Ct housekeeping gene)².

Results: MiR-155 and miR-34a expression in renal tissues was higher in LN-SLE patients as compared to IgA nephropathy patients (ΔCt miR-155: 9.4 ± 10.1 vs 21.9 ± 3.6, p<0.01; ΔCt miR-34a: 10.1 ± 9.8 vs 19.2 ± 3.1, p=0.02). MiR-155 and miR-34a expression in LN-SLE patients renal tissues was comparable in the different histological classes. Furthermore, a direct correlation was observed between the expression of miR-155 and miR-34a (r = 0.91, p <0.001). Dividing patients based on nephritic onset, SLE patients with long-LN showed higher expression of miR-155 (ΔCt 6.1 ± 8.7) and miR-34a (ΔCt 7.1 ± 9.0) as compared to patients with early-LN (miR-155: ΔCt 13.4 ± 10.6 p = 0.08; miR-34a: ΔCt 15.1 ± 9.5 p = 0.02) or patients with IgA nephropathy (miR-155 p<0.01 and miR-34a p<0.01). Moreover, in early-LN SLE it was observed an inverse correlation between miR-34a expression and C3 and C4 complement components (r=-0.72; p=0.05 and r=-0.86; p=0.01, respectively) and a direct correlation between miR-155 and 24h-UP (r=0.67; p=0.03). Considering SLE patients with early-LN, the expression of miR-34a was slightly significant in patients who had relapsed (ΔCt 8.2 ± 11.4 vs ΔCt 18.4 ± 7.9 p = 0.08), although no correlation emerged between the expression of miR-155 and miR-34a at the time of the biopsy and with disease activity indices.

Conclusion: MiR-155 and miR-34a may represent tissue biomarkers of inflammatory activation in SLE patients with LN; in particular, the higher expression of these miRNA in long-LN and the correlation between miR-155 expression with p24h-UP in early-LN could indicate a possible role of these biomarkers in renal involvement in patients with SLE with later renal onset. The increased expression of miR-34a could give indications of a disease recurrence suggesting a closer monitoring of patients.

REFERENCES:

- [1] Leiss H et al. *Plosone* 2017.
- [2] Alivernini S et al. *Nat Commun* 2018.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3761

POS0111 DEVELOPMENT OF DAMAGE AND MORTALITY IN AN INCEPTION COHORT OF SLE PATIENTS

C. S. Yee¹, V. Farewell², M. Akil³, P. Lanyon⁴, C. J. Edwards⁵, D. Isenberg⁶, A. Rahman⁶, L. S. Teh⁷, S. Tosounidou⁸, R. Stevens¹, A. Prabu⁹, B. Griffiths¹⁰, N. Mchugh¹¹, I. N. Bruce¹², Y. Ahmad¹³, M. Khamashta¹⁴, C. Gordon⁹ on behalf of British Isles Lupus Assessment Group (BILAG). ¹Doncaster & Bassettlaw Teaching Hospitals NHS Foundation Trust, Department of Rheumatology, Doncaster, United Kingdom; ²University of Cambridge, MRC Biostatistics Unit, Cambridge, United Kingdom; ³Sheffield Teaching Hospitals NHS Foundation Trust, Department of Rheumatology, Sheffield, United Kingdom; ⁴Nottingham University Hospitals NHS Trust, Department of Rheumatology, Nottingham, United Kingdom; ⁵University Hospital Southampton NHS Foundation Trust, Department of Rheumatology, Southampton, United Kingdom; ⁶University College London, Centre for Rheumatology Research, London, United Kingdom; ⁷Royal Blackburn Hospital, Department of Rheumatology, Blackburn, United Kingdom; ⁸Sandwell and West Birmingham Hospitals NHS Trust, Department of Rheumatology, Birmingham, United Kingdom; ⁹University of Birmingham, Rheumatology Research Group, Birmingham, United Kingdom; ¹⁰Newcastle upon Tyne Hospitals NHS Foundation Trust, Department of Rheumatology, Newcastle, United Kingdom; ¹¹Royal National Hospital for Rheumatic Diseases NHS Trust, Department of Rheumatology, Bath, United Kingdom; ¹²The University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom; ¹³Betsi Cadwaldr University Health Board, Department of Rheumatology, Wales, United Kingdom; ¹⁴Guy's and St Thomas' NHS Foundation Trust, Department of Rheumatology, London, United Kingdom

Background: There had been very limited data on the development of damage and mortality in an inception cohort of SLE patients who were recruited very soon after diagnosis.

Objectives: This study aimed to analyse the development of damage and death in an inception cohort of SLE patients recruited within 1 year of diagnosis with up to 13 years of follow-up.

Methods: This was a prospective multi-centre longitudinal study in the UK of SLE patients recruited within 12 months of achieving 1997 ACR revised criteria for SLE. Data were collected on BILAG-2004, BILAG2004-Pregnancy Index (during pregnancy), SLICC/ACR DI (SDI), cumulative drug exposure and death at every visit. Information on cardiovascular risk factors and antiphospholipid syndrome status were also collected. This study ran from 1st January 2005 to 31st December 2017. Mortality and development of damage were analysed.

Results: There were 273 patients recruited (91.2% female, 59.3% Caucasian, 17.2% African/Caribbean, 17.2% South Asian) with mean age at recruitment of 38.5 years (SD 14.8). 97.8% had no damage at recruitment (2.2% had SDI score of 1). Median follow-up was 73.4 months (range: 1.8, 153.8) with total follow-up of 1767 patient-years.

There were 13 deaths (4.8%): 76.9% female, 84.6% Caucasian, 15.4% South Asian, mean age 62.6 years ($\pm$ SD 15.8) and mean disease duration 3 years ($\pm$ SD 1.8). Causes of death were cancer in 5 (38.5%), infection in 3 (23.1%), ischaemic heart disease in 1 (7.7%) and unknown in 4 (30.8%).

114 new damage items in 83 patients occurred during follow-up. The distribution of damage was musculoskeletal (21, 18.4%), ophthalmic (18, 15.8%), neuropsychiatric (18, 15.8%), renal (14, 12.3%), malignancy (12, 10.5%), cutaneous (7, 6.1%), GIT (7, 6.1%), cardiac (6, 5.3%), pulmonary (4, 3.5%), diabetes mellitus (4, 3.5%) and vascular (3, 2.6%). The rate of development of damage appears to be higher in the first 3 years which subsequently stabilised (Table 1).

Table 1. Incidence rate of development of damage over period of follow-up at 3 yearly intervals

Period of follow-up (year)	Person-years at risk	Number of new items of damage	Incidence rate, per 1000 person-years (95% CI)
0 – 3	753.4	60	79.6 (61.8, 102.6)
3 – 6	534.0	31	58.1 (40.8, 82.6)
6 – 9	321.2	12	37.4 (21.2, 35.8)
9 – 12	152.5	5	32.8 (13.6, 78.7)
> 12	5.9	0	-

Conclusion: Mortality is uncommon during the first 12 years of follow-up for newly diagnosed SLE patients. However, development of damage appears to be higher in the first 3 years before stabilizing to a lower rate subsequently.

Acknowledgements: Versus Arthritis, Vifor Pharma

Disclosure of Interests: Chee-Seng Yee Consultant of: Bristol Myer Squibb, ImmuPharma, Grant/research support from: Vifor Pharma, Vernon Farewell: None declared, Mohammed Akil: None declared, Peter Lanyon: None declared, Christopher John Edwards Consultant of: Glaxo Smith Kline, Roche, Grant/research support from: Glaxo Smith Kline, Roche, David Isenberg: None declared, Anisur Rahman: None declared, Lee-Suan Teh: None declared, Sofia Tosounidou: None declared, Robert Stevens: None declared, Ahtiveer Prabu: None declared, Bridget Griffiths: None declared, Neil McHugh: None declared, Ian N. Bruce: None declared, Yasmeen Ahmad: None declared, Munther Khamashta: None declared, Caroline Gordon Speakers bureau: UCB, Consultant of: Center for Disease Control, Astra-Zeneca, MGP, Sanofi and UCB

DOI: 10.1136/annrheumdis-2021-eular.8

Translating vasculitis

POS0112 CD8+ T-CELL INFILTRATION IS ASSOCIATED WITH LESIONAL GM-CSF OVEREXPRESSION IN GCA

W. F. Jiemy¹, B. Reitsem², A. Kwant², W. Abdulahad^{1,2}, A. Boots², P. Heeringa¹, E. Brouwer². ¹University of Groningen, University Medical Center Groningen, Department of Pathology and Medical Biology, Groningen, Netherlands;

²University of Groningen, University Medical Center Groningen, Department of Rheumatology and Clinical Immunology, Groningen, Netherlands

Background: Giant cell arteritis (GCA) is a large-vessel vasculitis characterized by granulomatous T cell- and macrophage infiltration. Granulocyte-macrophage colony stimulating factor (GM-CSF) is present in GCA-affected vessels where it may be involved in skewing of tissue destructive macrophages (1). Furthermore, a recent phase 2 clinical trial demonstrated that GM-CSF receptor blockade was superior to placebo at 26 weeks in GCA. However, the cellular source of GM-CSF in GCA is still unclear.

Objectives: As T cells have been identified as a major source of GM-CSF in other immune-mediated diseases such as multiple sclerosis, we investigated whether T cells are GM-CSF producers in GCA patients, both systemically and locally.

Methods: GM-CSF production capacity by PMA-stimulated PBMCs from newly diagnosed, untreated GCA patients and HCs (N=10 each) was assessed using flow cytometry. Temporal artery biopsies (TABs, N=5) were immunohistochemically stained for CD3, CD8 and GM-CSF. Colocalization of these markers was assessed with immunofluorescence.

Results: Proportions of CD4+ (median GCA=3.1%; HCs=2.76%) and CD8+ (median GCA=5.8%; HCs=5.8%) T cells produced GM-CSF after *in vitro* stimulation, but no significant differences were found between the groups. Immunofluorescence staining confirmed that CD3+ T cells (both CD8+ and CD8-) were positive for GM-CSF in TABs. Interestingly, GM-CSF positivity in TABs correlated strongly with the extent of CD8+ T-cell infiltration ($r=0.74$, $p<0.01$), but not with CD3+ T-cell infiltration ($r=0.38$, $p=0.16$).

Conclusion: Our data imply that T cells are an important source of GM-CSF in GCA lesions. The correlation of the extent of CD8+ T-cell infiltration with GM-CSF positivity suggests that CD8+ T cells are the major source of local GM-CSF overexpression in tissue.

REFERENCES:

- [1] W.F. Jiemy, Y. Sleen, K.S. Geest, H.A. Berge, W.H. Abdulahad, M. Sandoz, A.M. Boots, P. Heeringa, E. Brouwer, Distinct macrophage phenotypes skewed by local granulocyte macrophage colony stimulating factor (GM-CSF) and macrophage colony stimulating factor (M-CSF) are associated with tissue destruction and intimal hyperplasia in giant cell arteritis, Clin. Transl. Immunol. 9 (2020).

Disclosure of Interests: William Febry Jiemy: None declared, Rosanne Reitsem: None declared, Ayla Kwant: None declared, Wayel Abdulahad: None declared, Annemieke Boots Consultant of: Grünenthal GmbH until 2017, Peter Heeringa: None declared, Elisabeth Brouwer Speakers bureau: Roche, paid to the UMCG

DOI: 10.1136/annrheumdis-2021-eular.1899

POS0113 BAFF-APRIL-BAFFR PATHWAY ON THE PATHOGENESIS OF IMMUNOGLOBULIN-A VASCULITIS

D. Prieto-Peña¹, S. Remuzgo Martinez¹, F. Genre¹, V. Pulito-Cueto¹, B. Atienza-Mateo^{1,2}, B. Sevilla³, J. Llorca⁴, N. Ortego⁵, L. Lera-Gómez¹, M. Leonardo⁶, A. Peñalba⁶, J. Narváez⁷, L. Martín-Penagos⁸, J. A. Miranda-Filloy⁹, L. Caminal Montero¹⁰, P. Collado¹¹, J. Sanchez Perez¹², D. De Argila¹², E. Rubio-Romero¹³, M. Leon Luque¹³, J. M. Blanco-Madruga¹⁴, E. Galindez¹⁴, J. Martín Ibáñez¹⁵, S. Castañeda¹⁶, R. Blanco¹, M. A. González-Gay^{1,17,18}, R. López-Mejías¹.

¹Research Group on Genetic Epidemiology and Atherosclerosis in Systemic Diseases and in Metabolic Bone Diseases of the Musculoskeletal System, Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain; ²López Albo Post-Residency Programme, Hospital Universitario Marqués de Valdecilla, Santander, Spain; ³Hospital Universitario San Cecilio, Division of Pediatrics, Granada, Spain; ⁴Department of Epidemiology and Computational Biology, School of Medicine, University of Cantabria, and CIBER Epidemiología y Salud Pública (CIBERESP), IDIVAL, Santander, Spain; ⁵Hospital Universitario San Cecilio, Systemic Autoimmune Diseases Unit, Granada, Spain; ⁶Hospital Universitario Marqués de Valdecilla, Division of Pediatrics, Santander, Spain; ⁷Hospital Universitario de Bellvitge, Division of Rheumatology, Barcelona, Spain; ⁸Hospital Universitario Marqués de Valdecilla, Division of Nephrology, Santander, Spain; ⁹Hospital Universitario Lucus Augusti, Division of Rheumatology, Lugo, Spain; ¹⁰Hospital Universitario Central de Asturias, Division of Rheumatology, Oviedo, Spain; ¹¹Hospital Universitario Severo Ochoa, Division of Rheumatology, Madrid, Spain; ¹²Hospital Universitario de La Princesa, Dermatology Department, Madrid, Spain; ¹³Hospital Universitario Virgen del Rocío, Division of Rheumatology, Sevilla, Spain; ¹⁴Hospital Universitario de Basurto, Division of Rheumatology, Bilbao, Spain; ¹⁵Instituto de Parasitología y Biomedicina 'López-Neyra', CSIC, PTS Granada, Granada, Spain; ¹⁶Hospital Universitario la Princesa, IIS-IP, Division of Rheumatology, Madrid, Spain; ¹⁷University of Cantabria, School of Medicine, Santander, Spain; ¹⁸University of the Witwatersrand, Cardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, Faculty of Health Sciences, Johannesburg, South Africa

Background: BAFF, APRIL and BAFFR are genes that encode cytokines with a key role in the development and survival of B-lymphocytes [1-4]. The B cell-activating factor (BAFF, also known as BlyS), a proliferation-inducing ligand (APRIL) and BAFF receptor (BAFFR), respectively. Previous genetic studies have revealed that the BAFF-APRIL-BAFFR pathway is implicated in the genetic predisposition to several immune-mediated diseases [5].

Objectives: To determine whether the BAFF-APRIL-BAFFR pathway represents a novel genetic risk factor for the pathogenesis of Immunoglobulin-A vasculitis (IgAV), an inflammatory disease in which IgA deposits and B-lymphocytes are crucial [6, 7].

Methods: A functional BAFF polymorphism (rs374039502) and two tag variants within APRIL (rs11552708 and rs6608) and BAFFR (rs7290134 and rs77874543)