Objectives: In this study, we hypothesized that immune-related miRNAs may be associated with presence/absence of lung involvement in patients with ASSD and help predict disease course.

Methods: A total of 15 ASSD patients were enrolled: 11 with ILD and 4 without ILD. Differentially expressed miRNAs were identified in plasma derived-exosome, using miRNA PCR array (MIHS-111ZG, Qiagen) including 84 miRNAs involved in activation and differentiation of T and B cells.

Results: Among all miRNAs analyzed we found that miR-15b-5p, miR-23a-3p, miR-25-3p, miR-30a-5p and miR29c-3p were up-regulated in ASSD-ILD patients ($p < 0.05$) as compared to patients without lung involvement (Figure 1). To evaluate the effectiveness of the five miRNAs for predicting ILD among ASSD patients, ROC curves were constructed. The AUCs of miR-15b-5p, miR-25-3p, miR-30a-5p and miR29c-3p were 0.83, 0.87, 0.86 and 0.89, respectively ($p = 0.05$ for miR-25-3p and $p < 0.05$ for all other curves). The prediction of the biologic targets and pathways as well as cellular processes by DIANA-mirPath analysis showed that all miRNAs associated with ILD presence are involved in PI3K-Akt signaling pathway.

Conclusion: Our study shows that, in ASSD patients with ILD, miR-15b-5p, miR-23a-3p, miR-25-3p, miR-30a-5p and miR29c-3p were up-regulated compared to patients without evidence of ILD. A clear involvement in immune and inflammatory diseases was documented for the miRNAs identified [2] and, for many of these, studies in the literature indicate a possible role in pulmonary fibrosis [3]. It is notable that these miRNAs were related to PI3K-Akt signaling pathway that regulate cell proliferation, differentiation and apoptosis [4]. It has also been demonstrated that in lung fibroblast the PI3K-Akt signals can be aberrantly activated [5]. The identification of markers could be important in the early identification of the disease and for its treatment.

Figure 1. Comparison of relative levels of five miRNAs among patients with and without lung involvement were expressed as $\log_2$ transformed values. * $p < 0.05$; ** $p < 0.01$

REFERENCES:

- [1] Kalluri M, Oddis CV. Pulmonary manifestations of the idiopathic inflammatory myopathies. *Clinics in chest medicine*. 2010; 31:501–512.
- [2] Prabakar A, Natarajan J. ImmunemiR-a database of prioritized immune miRNA disease associations and its interactome. *MicroRNA*, 2017; 6: 71–78.
- [3] Sessa R, Hata A. Role of microRNAs in lung development and pulmonary diseases. *Pulm Circ*. 2013; 3:315–28.
- [4] Ersahin T, Tuncbag N, Cetin-Altay R. The PI3K/AKT/mTOR interactive pathway. *Mol Biosyst*. 2015; 11:1946–54.
- [5] Zhang XL, Xing RG, Chen L, Liu CR, Miao ZG. PI3K/Akt signaling is involved in the pathogenesis of bleomycin-induced pulmonary fibrosis via regulation of epithelial-mesenchymal transition. *Mol Med Rep*. 2016; 14:5699–5706.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2433

POS0427

CLINICAL CHARACTERISTICS OF PATIENTS WITH SYSTEMIC SCLEROSIS AND GASTRIC ANTRAL VASCULAR ECTASIA (GAVE)

C. Codina¹, A. Guillén-del-Castillo¹, E. Callejas-Moraga², J. Perurena-Prieto³, M. Roca-Herrera², I. Sanz-Pérez¹, A. Gil-Vila¹, A. Selva-O'Callaghan¹, V. Fonollosa-Pla¹, C. P. Simeón-Aznar¹. ¹Hospital Universitari Vall d'Hebron, Systemic Autoimmune Diseases Unit, Internal Medicine Service., Barcelona, Spain; ²Hospital de Sabadell, Systemic Autoimmune Diseases Unit, Internal Medicine Service., Sabadell, Spain; ³Hospital Universitari Vall d'Hebron, Immunology, Barcelona, Spain

Background: Gastric antral vascular ectasia (GAVE) is one of the gastrointestinal (GI) manifestations related to systemic sclerosis (SSc). It can be presented as iron deficiency anemia or even upper gastrointestinal bleeding. GAVE is diagnosed by endoscopy observing an image of confluent vascular ectasias that is oriented longitudinally on the folds of the antrum in the appearance of “watermelon”. The definitive treatment for this manifestation consists in endoscopy guided fulguration when the clinical situation allows it.

Objectives: The objective was to study a cohort of SSc patients at their first endoscopy. The clinical characteristics, laboratory tests and treatments received from SSc patients with GAVE were compared to those without this GI manifestation.

Methods: From the cohort of patients with SSc in Hospital Universitari Vall d'Hebron, a total of 269 patients who had undergone at least one endoscopy during follow-up were selected. Twenty seven were diagnosed with GAVE. We compared the clinical, analytical and treatment characteristics of these patients with the remaining

242 who did not present GAVE. The statistical study was carried out using the SPSS 20.0 package (Chicago, IL), a $p < 0.05$ was considered as statistical significance.

Results: The prevalence of GAVE in SSc patients was 10.0%. Patients with GAVE had a higher median age SSc onset taking into account the first non-Raynaud's phenomenon (RP) symptom attributable to the disease (56.6 vs 48.0 years, $p = 0.001$). The median age at first endoscopy was 56.5 years in GAVE group compared with 61.7 in the group without GAVE.

Compared with SSc patients without GAVE, patients with GAVE had a higher prevalence of Barrett's esophagus (14.8% vs. 3.7%, $p = 0.011$), intestinal involvement (37% vs. 18.6%, $p = 0.024$) and a trend towards a lower prevalence of interstitial lung disease (25.9% vs 45.0%, $p = 0.057$).

No difference was identified in the prevalence of scleroderma renal crisis. Patients with GAVE presented a higher frequency of early or active Cutolo capillaroscopy pattern with a predominance of enlarged capillaries or megacapillaries (84.6% vs 62.4%, $p = 0.025$), greater frequency of anti-centromere antibodies (63.0% vs. 42.1%, $p = 0.039$) and a trend towards a lower proportion of anti-topoisomerase I (3.7% vs. 18.6%, $p = 0.052$). No difference was found in prevalence of anti-RNA polymerase III antibodies between groups. Patients with GAVE were treated less frequently with non-glucocorticoid immunosuppressants prior to diagnostic endoscopy (0% vs 20.2%, $p = 0.010$). The 33.3% of patients with GAVE were treated with endoscopic fulguration, and 66.7% of them received supplementary treatment with oral iron.

Conclusion: SSc patients with GAVE had higher age at SSc onset, more frequency of Barrett's esophagus and intestinal involvement, prevalence of anti-centromere antibodies, early or active Cutolo scleroderma pattern and lower prior non-glucocorticoids treatment.

REFERENCES:

- [1] Ghrénassia E, Avouac J, Khanna D, T.Derk C, Distler O, Suliman Y, et al. Prevalence, Correlates and Outcomes of Gastric Antral Vascular Ectasia in Systemic Sclerosis: A EUSTAR Case-control Study. *The Journal of Rheumatology*. 2014; 41:1.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2847

POS0428

REGULATION OF IFN SIGNATURE BY HDAC CLASS IIa-CD52 AXIS IN SYSTEMIC SCLEROSIS

M. Rudnik¹, A. Hukara¹, P. Blyszczuk¹, O. Distler¹, G. Kania¹. ¹University Hospital Zurich, University of Zurich, Department of Rheumatology, Center of Experimental Rheumatology, Zurich, Switzerland

Background: Systemic sclerosis (SSc) is associated with an interferon (IFN) signature, which is defined by a higher expression of IFN-stimulated genes (mainly in response to IFN α). Histone deacetylases (HDACs) are a family of epigenetic modifiers mediating immune function. HDACs function via diverse molecular mechanisms, including direct inhibition of gene transcription or indirectly through modulation of nuclear transcription factors such as NF- κ B and STATs. CD52 protein regulates T cell receptor and NF- κ B signalling. Previously, we showed downregulation of CD52 in SSc monocytes, however, the influence of CD52 on IFN signalling has not been studied yet.

Objectives: We investigated the role of CD52 in the regulation of IFN response in monocytes. Moreover, we explored the regulatory mechanisms of CD52 expression to identify the involvement of HDACs in that process.

Methods: RNAseq of CD14⁺ monocytes isolated from peripheral blood of lcSSc (n=5, age=54.4 $\pm$ 6.7), dcSSc patients (n=5, age=51.8 $\pm$ 7.2) and age- and sex-matched healthy controls (HC) (n=5, age=50.8 $\pm$ 9.7) was performed using Illumina HiSeq 4000 platform. Differentially expressed genes were computed using DESeq2 algorithm. Gene ontology and pathway analysis were performed using Metacore software and ShinyApp. CD52 activity in monocytes was blocked by monoclonal antibody Alemtuzumab [10ug/ml] and IFN signature genes expression was assessed upon IFN α stimulation [1ng/ml] by qPCR and ELISA. HDAC-dependent regulation of CD52 expression in CD14⁺ monocytes from HC was analysed on mRNA and protein levels after treatment with pan-HDAC inhibitor valproic acid and HDAC class IIa inhibitor TMP269 [both 2.5 μ M].

Results: Pathway analysis revealed significant alterations in interferon signalling in SSc monocytes. Monocytes treated with Alemtuzumab and IFN α showed induced expression of *STAT1* ($p=0.023$, N=4), *CXCL9* ($p=0.062$, N=4) and *CXCL10* ($p=0.005$, N=4). RNAseq revealed a specific HDAC expression pattern in SSc monocytes with induced expression of HDAC4, 6, 10, 11 ($p < 0.05$) and reduced HDAC1, 3 and 8 ($p < 0.05$). CD52 mRNA was significantly decreased after IFN α stimulation ($p=0.001$, N=3). Treatment with valproic acid and HDAC class IIa inhibitor TMP269 resulted in decreased phosphorylation of STAT1 ($p < 0.01$, N=4) followed by a declined level of *CXCL10* ($p < 0.01$, N=4) and restored level of *CD52* mRNA ($p < 0.001$, N=4).

Conclusion: Our findings demonstrated a new aspect of pro-inflammatory type I IFN signalling in SSc. We described a novel regulation feedback loop in monocytes, in which CD52 suppresses IFN signature, while its expression is inhibited by IFN-induced HDAC activity (mainly HDAC class IIa). Therefore, targeting the CD52-IFN-HDAC axis might serve as a novel therapeutic strategy in SSc.