SF) stimulation was analysed by ELISA. FAO was inhibited by etomoxir or enhanced with exogenous carnitine supplements. Transcriptomics of RA blood monocytes and RA-SF macrophages was carried out by microarray.

Results We report that hypoxia exacerbates CCL20 and IL-1 β release in response to LPS and increases glycolytic intermediates at the expense of carnitines. Modulation of carnitine identified a novel role for FAO in the production of CCL20 in response to LPS. Transcriptomics of RA blood monocytes and RA-SF macrophages revealed that fatty acid metabolism was altered and CCL20 was increased when monocytes enter the RA milieu. *In vitro* analysis of monocytes showed that RA-SF increases carnitine abundance and CCL20 production in hypoxia, which was exacerbated by exogenous carnitine.

Conclusions This work has revealed a novel inflammatory mechanism in RA which links FAO to CCL20 production in human monocytes. This may contribute to RA disease pathogenesis by promoting the recruitment of Th17 cells and osteoclastogenesis.^{2, 3}

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Disclosure of Interest None declared.

P109

EXPRESSION LEVELS OF MIR-21 AND MIR-29 IN THE SERUM OF SYSTEMIC SCLEROSIS PATIENTS

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Introduction Recent studies reveal the important role of microRNAs (miRNAs) in the pathogenesis of systemic sclerosis (SSc). miRNAs are involved in key biological pathways that regulate the fibrotic process in SSc.¹ Deregulated expression of miRNAs has been found in the serum, in skin tissues, in skin fibroblasts as well as in endothelial cells of patients with SSc.²

Objectives The aim of our study was to evaluate the expression levels of miR-21 and miR-29 in the serum of SSc patients and to determine their correlation with clinical and immunological parameters.

Methods 34 patients fulfilling the ACR/EULAR 2013 classification criteria for SSc were included in the study. miR-21 and miR-29 expression levels in the serum were determined by PCR (SYBR Green technology). 2^{- $\Delta\Delta C_t$} method was used for analysis. 14 healthy donors were used as controls.

Results Expression levels of miR-21 were upregulated in the serum of 17 (50.0%) of the patients. The expression of miR-29 was downregulated in 15 (44.12%) of the patients. Receiver operating characteristic (ROC) curve analysis was conducted in order to evaluate the diagnostic accuracy of the expression levels of the studied miRNA in the serum. Area

under the curve (AUC) for miR-21 was 0.634 (95% CI=0.479–0.790), p=0.147 with 64.7% sensitivity and 64.3% specificity. AUC for miR-29 was 0.605 (95% CI=0.420–0.790), with 64.3% sensitivity and 52.9% specificity but without statistical significance (p=0.257). The multimarker analysis of the ROC curves for both miRNAs showed AUC=0.714 (95% CI=0.569–0.860), p=0.021 with 79.4% sensitivity and 42.9% specificity. Levels of miR-29 correlated with the levels of miR-21 in the serum (with Spearman correlation coefficient 0.517, p=0.00017) and with the presence of anti-Scl70 antibodies in the serum (with Spearman correlation coefficient 0.438, p=0.010).

Conclusions Our data showed a deregulation of miR-21 and miR-29 in the serum of patients with SSc which could suggests their potential role in the disease pathogenesis. Further analysis with higher number of patients is needed to confirm if these miRNAs could be used in the clinical practice as diagnostic biomarkers as well as biomarkers for both disease activity and progression.

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P110/O18

EPIGENETIC CHANGES BY INHIBITION OF DOT1L AFFECT WNT SIGNALING, PROLIFERATION AND CELL CYCLE IN DERMAL FIBROBLASTS, WITH NO OVERALL EFFECT ON COLLAGEN DEPOSITION IN MODELS OF FIBROSIS

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Career situation of first and presenting author Student for a master or a PhD.

Introduction The role of epigenetic factors in the pathophysiology of fibrosis, a hallmark of Systemic Sclerosis, is increasingly explored. DOT1L, the unique H3K79-methyltransferase, methylates histone 3 at the Lysine residue at position 79, thereby regulating gene expression programs. In cartilage and bone, DOT1L has cell-type specific effects on Wnt signaling, a pathway suggested to play an important role in fibrosis.

Objectives To study the role of DOT1L in fibrosis.

Methods Primary human dermal fibroblasts were treated with DOT1L-inhibitor EPZ-5676 or vehicle and stimulated with TGF- β . Expression of smooth muscle alpha 2 actin (ACTA2) and Wnt target genes was measured by RT-qPCR. Western Blot was done for dimethylated H3K79 and β -catenin. Picrosirius Red staining measured collagen deposition. 5-Bromo-2'-deoxy-uridine (BrdU) labeling for proliferation and flow cytometry with Propidium Iodide for cell cycle analysis was done. Col1a2;Cre-ERT²;DOT1L^{fl/fl} mice, injected