Background: A fundamental role of mitochondria in systemic lupus erythematosus (SLE) was recently demonstrated (1). In brief, mitochondrial ROS participate in the formation of neutrophil extracellular traps (NETs) (2), while extrusion of cell-free mitochondria and highly oxidized interferon-mimicking mtDNA causes disease in an animal model of SLE (3-5).

Objectives: The diagnostic and prognostic value of cell-free DNA in SLE is still unknown. The aim of the present study was therefore to examine the clinical utility of cell-free DNA quantification as a non-invasive biomarker in SLE.

Methods: Total DNA was isolated from platelet-free plasma samples of healthy individuals (HC) and consecutive SLE patients. Plasma and clinical data were collected at baseline and follow-up. Copy numbers were quantified by qPCR for mitochondrial (mt) DNA (ATP-6 gene) and nuclear (n) DNA (GAPDH gene).

Results: Fifty-six HC (median age 48.3 ± 13.5, 64% female) and 103 SLE patients (median age 48.8 ± 15.8, 99% female, mean SLEDAI: 3 ± 4) were available for analysis. mtDNA levels were significantly elevated in SLE plasma (1.3x10^6 copies/ml plasma; 95% CI: 7.3x10^5 to 1.7x10^6), compared to HC plasma (8.6x10^5 copies/ml plasma, 95% CI: 6.9x10^5 to 1.0x10^6; p < 0.0001). nDNA levels did not differ between SLE (8.3x10^6 copies/ml plasma, 95% CI: 5.9x10^6 to 1.4x10^7) and HC (1.0x10^7 copies/ml plasma, 95% CI: 2.0x10^6 to 1.5x10^7; p = 0.61).

Receiver operating characteristic curve analysis showed that a cut-off value of 1.9x10^6 mtDNA copy numbers differentiated between SLE and HC with 87.4% sensitivity and 94.6% specificity and an AUC of 0.95 (Figure 1a).

Follow-up data were available for 32 SLE patients (median follow-up 4.0 months, IQR: 4.0), delta mtDNA-levels robustly correlated with changes in SLEDAI-2K (r = 0.51, p = 0.0012, Figure 1b).

Conclusion: The quantification of cell free mtDNA, but not nDNA copy numbers allows a sensitive and specific distinction between healthy individuals and patients with SLE. mtDNA levels correlate cross sectionally with disease activity in SLE patients and within individual SLE patients longitudinally with the SLEDAI. Plasma mtDNA quantification may therefore aid in the diagnosis of SLE and in monitoring SLE activity.

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Declaration of conflict of interest: UW is co- inventor of patents owned by Freiburg University; NV is co- inventor of patents owned by Freiburg University.

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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 psSS 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 psSS could be classified into 3 subtypes, this classification might help for assessing prognosis and guiding precise treatment.

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POS0110 DEVELOPMENT OF DAMAGE AND MORTALITY IN AN INCEPTION COHORT OF SLE PATIENTS

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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: 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). The 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 SLEDAI-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-processed biopsies and was evaluated, after a retrotranscription protocol, using real-time PCR by relative quantification considering the ΔCt (Ci miRNA/Cit housekeeping gene).

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 (ΔCt miR-155: 13.4 ± 10.6 p = 0.08; ΔCt miR-34a: ΔCt 15.1 ± 9.5 p = 0.02) or patients with IgA nephropathy (ΔCt miR-155 p < 0.01 and ΔCt 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 smaller 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 24h-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.

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