

to understand the role of specific microRNAs as biomarkers for disease activity (DA) and progression. Our aim was to evaluate the peripheral blood (PB) expression of miR-155 in SLE patients and to determine its correlation with the DA in the clinical practice.

**Materials and methods** We studied 40 SLE patients and 32 healthy controls. miR-155 expression levels in whole PB samples were determined by PCR (SYBR Green technology). 2- $\delta\delta$  Ct method was used for analysis. The DA was assessed by SLE DA index (SLEDAI).

Results miR-155 was upregulated in 50.0% of the patients and without difference in its expression levels in 17 (42.5%) of the patients. ROC curve analysis was conducted in order to evaluate the diagnostic accuracy of the PB expression levels of the studied miRNA. AUC for miR-155 was 0.691 (95% CI: 0.566 to 0.817),  $p=0.005$  with 77.5% sensitivity and 50.0% specificity when the RQ cut value was 1.03. Levels of miR-155 correlated with the diagnosis ( $r_s$  0,330,  $p=0,005$ ), with patient's age ( $r_s$  0,366,  $p=0,002$ ) as well as with the presence of secondary Raynaud phenomenon ( $r_s$  0,250,  $p=0,035$ ). There was no correlations with SLEDAI ( $p=0$ , 894) nor with the immunological activity according to ANA titer ( $p=0.399$ ), a-dsDNA ( $p=0.817$ ), a-Sm ( $p=0.285$ ), a-b2GPI ( $p=0.903$ ), a-CL antibodies ( $p=0.857$ ) and C3 and C4 complement levels ( $p=0.062$  and  $p=0.550$ , respectively).

**Conclusions** We found a dysregulation of miR-155 in SLE which could suggest its role in the disease pathogenesis. There was no correlation between PB levels of miR-155 and DA as a whole as well as with the immunological activity which might reflect the variants of SLE DA in the studied patients, the difference in their genetic background or in the used medications but larger study is needed to confirm these results in the clinical practice.

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PS2:42

#### UNMETHYLATED CPG-RICH DNA FRAGMENTS ARE ASSOCIATED WITH THE PRESENCE OF LUPUS NEPHRITIS AND INFLUENCE TLR9-MEDIATED RENAL RESPONSE

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**Purpose** In systemic lupus erythematosus (SLE), lupus nephritis (LN) represents one of the most severe organ complications. LN is associated with persistent inflammation and perpetuated fibroblast activation, both determined by epigenetic mechanisms involving aberrant CpG DNA promoter methylation. During SLE progression, global methylation patterns are commonly lost. CpG DNA promoter methylation patterns are not limited to the kidney, circulating CpG-rich DNA is also detectable in the blood. However, little is known about its specific contribution to determining disease progression. In the kidney, CpG-rich DNA activates TLR9 signalling mechanisms involved in inflammation and fibrogenesis. Based on these observations, we hypothesised that CpG-rich DNA promoter fragments potentially accelerate renal inflammation and fibrogenesis in SLE-associated LN.

**Methods** First, CPG-rich DNA from blood samples of SLE patients with and without LN were collected. Then, we tested

how these DNA promoter fragments influenced the LN phenotype in a TMPD ('pristane')-induced mouse model. The renal response to the administration of either human or synthetic methylated/unmethylated CpG-rich DNA oligonucleotides (ODN) was observed. Downstream effects of the administration of circulating CpG-rich DNA fragments on TLR9-signalling were analysed in endothelial cell cultures.

**Results** Circulating CpG-rich DNA promoter fragments are detectable in SLE patients' blood. LN was associated with accumulation of unmethylated CpG-rich DNA promoter fragments, implicating a mechanistic link. In a rodent model of pristane-induced lupus, administration of CpG-rich DNA (isolated from LN patients or synthetic unmethylated CpG-rich DNA ODN) worsened the renal phenotype. TLR9-mediated intrarenal inflammation can be therapeutically targeted by administration of synthetic methylated CpG-rich DNA oligonucleotides, ultimately associated with suppression of TLR9-mediated signalling responses and renal injury in experimental LN.

**Conclusions** Our results implicate accumulation of unmethylated CpG-rich promoter DNA fragments in LN. Furthermore, these unmethylated CpG-rich promoter DNA fragments causally contribute to TLR9-mediated inflammation and renal fibrogenesis and administration of methylated CpG-rich ODN attenuated intrarenal TLR9-mediated inflammatory signalling responses. Therefore, biomonitoring of CpG-rich promoter DNA fragments and modulation of intrarenal TLR9 signalling might be a promising therapeutic target in LN.

PS2:43

#### IS LUPUS MORE PREVALENT IN WORLD'S MOST STRESSED COUNTRIES?

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**Background** A number of studies have implicated psychological stress as a trigger for autoimmune diseases. In a questionnaire study involving 120 lupus patients emotional stress was selected in over 75% cases as a trigger for their disease.<sup>1</sup> The role of stress as a trigger in lupus however is controversial. Here we study whether there is an association between the prevalence of lupus in various countries and their reported stress measures.

**Methods** We undertook a literature review of the reported prevalence of lupus in various countries across the world. We then recorded the reported stress index in those countries from Bloomberg's study,<sup>2</sup> which utilised seven equally weighted variables: homicide rates, GDP per capita income inequality, corruption perception, unemployment, urban air pollution and life expectancy to rank 74 countries according to stress levels. Pearson's correlation was used to measure association between national stress indices and lupus prevalence

**Results** Results are presented in graph 1. Prevalence data was only available in the literature for limited countries. Of the countries studied no correlation was found between national stress indices and lupus prevalence ( $r=-0.028$ ,  $p$ -value 0.449).

**Conclusion** We found no association between a country's prevalence of lupus and the measured stressfulness of its living environment.