Anti-Smith (Sm) antibodies are highly specific for systemic lupus erythematosus (SLE), their associations with some organ involvements were described.

Objectives The aim of our study was to determine clinical, biological and immunological characteristics in SLE patients according to the presence of anti-Sm antibodies.

Methods A retrospective study of a group of Tunisian patients with SLE (fulfilling the ACR revised criteria) was conducted in an internal medicine department. Patients were divided in two groups according to the presence (group 1) or not (group 2) of anti-Sm antibodies. Variables with a p inferior to 0.05 were considered to be statistically significant.

Results Anti-Sm antibodies were screened in 153 among 246 SLE patients and were positive in 64% of patients. Mean age at SLE diagnosis was significantly lower in the group 1 (31.82 years ±12.70 vs 36.16 years ±12.34; p=0.0043). Poor general state was the only clinical feature significantly more frequent in group 1 (54.2% vs 36.5%; p=0.04). Lupus nephritis was more frequent in patients with anti-Sm antibodies without significant difference (47.9% vs 38.2%; p=0.24). Arthritis were more frequent in group 2 (42.6% vs 50%; p=0.38). Central nervous system manifestations (16.7% vs 16.4%, pericarditis (36.1% vs 31.4%) and pleural effusion (23.4% vs 27.8%) were similar in the two groups. Anaemia (77.1% vs 74.5; p=0.7), leucopenia (49% vs 47.2%; p=0.8) and thrombocytopenia (26% vs 15%; p=0.12) were more frequent in patients with anti-Sm antibodies without significant differences. Anti-Sm antibodies were significantly associated with anti-RNP antibodies (78.6% vs 17.6%; p<0.0001). Remission was less frequent is group 1 (70.4% vs 82.9%; p=0.14) and death was more frequent in this group (16% vs 10.3%; p=0.4) without significant differences.

Conclusions In our patients, anti-Sm antibodies prevalence was higher than those reported in other cohorts (5% to 49%). Patients with anti-Sm antibodies seem to develop clinical SLE manifestations earlier than other patients. In our study, anti-Sm antibodies doesn’t influence SLE clinical course and weren’t associated with hematologic disorders, whereas in another series, anti-Sm antibodies were associated with lupus nephritis, serositis, anaemia and leucopenia.

Comparative Tissue Transcriptome Analysis by Next-Generation Sequencing Reveals Novel Pathways That Characterise Genetic Susceptibility and Developmental Biology in Systemic Lupus Erythematosus (SLE)

Purpose Next-generation RNA-sequencing was applied to investigate SLE pathogenesis through a comparative transcriptomic analysis of a peripheral lymphoid organ (spleen) and end-organ tissues (kidneys, brain) of lupus-prone and healthy mice.

Methods NZB/W-F1 lupus-prone mice were sacrificed at the pre-puberty, pre-autoimmunity and nephritic stage of the disease. Age-matched C57 BL6 mice were used as controls. Spleen, kidneys and brain were removed and total RNA was extracted. Paired-end RNA-sequencing was performed with Illumina HiSeq 2000 platform. Relative expression levels of transcripts and differentially expressed genes (DEG) (FC >1.5, p<0.05) were calculated. Functional enrichment analysis was performed with IPA, RNEA and gprofiler.

Results To investigate SLE developmental biology, a comparative analysis between the same organs of the same model at different stages of the disease was performed. In the spleen, brain and kidneys of NZB/W-F1 mice, 277, 6 and 8 DEG at the pre-puberty vs pre-autoimmunity stage; 212, 6 and 8 DEG at the nephritic vs pre-puberty stage; and 15, 6 and 2 DEG at the nephritic vs pre-autoimmunity stage were identified, respectively. In the brain, kidneys and spleen, hierarchical clustering revealed 178, 1012 and 2105 genes respectively that were deregulated in at least 1 of 3 stages. Clusters were subjected to functional enrichment analysis. In the brain, genes were mainly downregulated and enriched for metabolic pathways (glycolysis/TCA cycle/Pentose-Phosphate pathway), whereas overexpressed genes were enriched for Jak/Stat signalling pathway. In kidneys, one of the biggest cluster points towards metabolic pathways, particularly to lipid metabolism. In the spleen, DEG were mainly overexpressed. Of note, early genes were particularly enriched in cell-cycle processes; intermediate genes in membrane-related and extracellular matrix functions; and late genes in inflammatory and immune response pathways. To investigate SLE genetic susceptibility, a comparative analysis of the same organ of lupus-prone vs healthy mice at different stages of the disease was performed. In addition to immune response pathways (interferon signalling/antiogen-presentation), DEG were involved in canonical pathways such as the phagosome, platelet activation, epithelial adherence junction signalling and the extrinsic prothrombin activation pathway.

Conclusions We identified novel stage-specific tissue-dependent pathways involved in immune response, and tissue injury and response in SLE. Validation is in progress.

Genetic and Environmental Risk Factors for Systemic Lupus Erythematosus – A Nationwide Population Study

Purpose Environmental- and genetic factors’ influence in the pathogenesis of rheumatic disease including systemic lupus erythematosus (SLE) have individually been extensively researched. Moreover, a synergistic effect of smoking with anti-citrullinated protein has been established for the risk of developing rheumatoid arthritis. In SLE, however, studies on synergistic effect are few and of limited sample size. We aim to investigate if established genetic and environmental risk factors for SLE display additive or synergistic interactions on the risk of SLE.

Methods A case-control designed nationwide epidemiological study of Danish patients with SLE will be conducted. Patient data/
blood samples for genetic analysis will be stored in the DANBIO-database/Danish Reuma Biobank, in which, since 2000/2015 respectively, collection of information regarding e.g. demographics and disease activity-tissue samples from patients with inflammatory- and connective tissue disease has taken place. Patients will be matched (gender/age) against participants in the Danish Blood Donor Study in a 1:10 ratio. Sample size to detect degree of synergy between environmental risk behaviour and minor allele frequency of susceptible genes was calculated. Lifestyle and environmental exposures will be collected by self-report and by pulling data from Danish registries. Genetic analysis will be conducted with Illumina sequencing instruments.

**Results** We identified 966 patients registered in DANBIO with SLE. 20,000 control patients from the Danish Blood Donor Study have completed a self-report questionnaire and genetic sequencing on collected blood samples has been performed. To exemplify the power of this study, we found from the literature risk ratios for developing SLE of about 1.5 for both current smokers and persons with polymorphisms in the signal transducer and activator of transcription 4-gene. By computer modelling we calculated the ability to detect a degree of synergy of 45% with a power of 80%.

**Conclusion** From this study we expect to provide new information on how certain lifestyle and environmental factors may push the development of SLE in genetically predisposed individuals. Hereby point at new candidate sites of intervention in both treatment and prophylaxis.

This project will have the potential to collaborate with similar upcoming projects in Europe allowing analysis of less prevalent genetic aberrations and/or environmental exposures.

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**Abstract PS2:40**

**ASSOCIATION OF PEPTIDYLARGININE DEIMINASE (PADI)-4 POLYMORPHISMS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND LUPUS NEPHRITIS**

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**Purpose** Peptidylarginine deiminase (PAD) 1–4 and PAD6 are responsible for protein citrullination. PAD4 is highly expressed in neutrophils and is essential for NETosis, which has been implicated in the pathogenesis of SLE, especially lupus nephritis (LN).

Single nucleotide polymorphisms (SNPs) in PADI4 are responsible for altered stability of PAD4 transcripts, altered functionality of the enzyme and differential expression in neutrophils. We aimed to investigate the risk of SLE and LN conferred by SNPs in PADI4.

**Methods** 236 SLE patients and 484 healthy controls were genotyped for 9 SNPs in PADI4, to investigate potential associations with occurrence of SLE and LN. Selected SNPs are known to alter functionality and/or expression of the enzyme and/or have previously been associated with other autoimmune diseases, including rheumatoid arthritis. Genotypes were analysed using an in-house multiplex bead-based Luminex assay. All analyses were corrected for age and gender.

**Results** Compared to homozygous carriage of the major allele, heterozygous carriage of the minor allele of rs1748033 as well as both heterozygous and homozygous carriage of the minor allele of rs1635564 were associated with increased occurrence of SLE (p=0.02, OR 1.54, 95% CI: 1.07 to 2.22, and p=0.02, OR 1.55, 95% CI: 1.08 to 2.23 and p=0.03, OR 2.06, 95% CI: 1.07 to 3.94, respectively). Additionally, homozygous minor allele carriage of rs1635564 was associated with an increased occurrence of LN (p=0.03, OR 3.35, 95% CI: 1.2 to 10.97) showing a possible additive effect of the number of minor alleles present (table 1).

Carriages of the minor alleles of five other SNPs (rs11203366, rs11203367, rs874881, rs2240340 and rs11203368) were associated with increased occurrence of LN (table 1).

**Conclusions** Polymorphisms in PADI4 may alter the functionality and/or expression of the enzyme and lead to altered production of NETs, possibly affecting the altered clearance of NETs observed in lupus nephritis, thereby contributing to the pathogenesis of this severe clinical manifestation of SLE. PADI4_rs1635564 could be a potential marker for both SLE and LN.

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**Abstract PS2:41**

**MICRONRNA-155 AND DISEASE ACTIVITY IN SLE PATIENTS**

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**Purpose** The effect of miR-155 on serum levels of 49 inflammatory cytokines and chemokines was studied in 38 SLE patients and 34 healthy controls.

**Materials and Methods** The peripheral blood mononuclear cells (PBMCs) were isolated from fresh blood samples of the patients and healthy controls. The concentration of miR-155 was measured by real-time PCR. The cytokine levels were measured by a multiplex assay using Luminex technology. The expression of miR-155 and cytokines was correlated in SLE patients and healthy controls.

**Results** The concentration of miR-155 was significantly higher in SLE patients compared to healthy controls (p<0.05). A positive correlation was found between the expression of miR-155 and the disease activity score in SLE patients (p<0.05).

**Conclusions** The upregulation of miR-155 in SLE patients may play a role in the pathogenesis of the disease. Further studies are needed to investigate the potential therapeutic role of miR-155 in SLE.