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. Life-style 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.

PS2:40 ASSOCIATION OF PEPTIDYLARGININE DEIMINASE (PADI)-4 POLYMORPHISMS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND LUPUS NEPHRITIS

^{1,2}L Massarenti, ¹C Enevold, ^{1,3}D Damgaard, ²N Ødum, ^{1,3}CH Nielsen, ⁴S Jacobsen. ¹Institute for Inflammation Research, Centre for Rheumatology and Spine Disease, Rigshospitalet, Copenhagen, Denmark; ²Department of Immunology and Microbiology, University of Copenhagen, Denmark; ³Section for Periodontology, Department of Odontology, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark; ⁴Copenhagen Lupus and Vasculitis Clinic, Centre for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen, Denmark

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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.

PS2:41 MICRORNA-155 AND DISEASE ACTIVITY IN SLE PATIENTS

¹R Shumnalieva, ²D Kachakova, ³V Shoumnaieva-Ivanova, ⁴P Miteva, ⁵D Monova, ²R Kaneva, ¹S Monov, ⁶V Popova. ¹Clinic of Rheumatology, Department of Internal Medicine, Medical University Sofia, Bulgaria; ²Molecular Medicine Centre, Department of Medical Chemistry and Biochemistry, Medical University Sofia, Bulgaria; ³University Hospital Alexandrovska, Medical University Sofia, Bulgaria; ⁴University Hospital Prof. Ivan Mitev, Medical University Sofia, Bulgaria; ⁵MVR Institute, Medical University Sofia, Bulgaria; ⁶Department of Rheumatology, Medical Faculty, Medical University – Plovdiv, University Hospital 'Kaspela', Plovdiv, Bulgaria

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Background Recent studies are trying to identify aberrant microRNA levels as a diagnostic signature of SLE as well as

Abstract PS2:40 Table 1 Associations between selected polymorphisms in PADI4 and occurrence of SLE and LN

SLE (n = 236)							Lupus nephritis (n = 136)					
SNPs	P- value	pp vs pq		P- value	pp vs qq		P- value	pp vs pq		P- value	pp vs qq	
		OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI
rs74058715	0.94	1.02	0.58-1.77	NA	NA	NA	0.40	0.69	0.29-1.67	NA	NA	NA
rs11203366	0.33	1.20	0.83-1.76	0.68	1.12	0.66-1.88	0.008	2.23	1.24-4.06	0.78	0.89	0.39-2.01
rs11203367	0.39	1.18	0.81-1.72	0.64	1.13	0.67-1.9	0.009	2.2	1.22-4	0.91	0.96	0.43-2.14
rs874881	0.27	1.24	0.85-1.82	0.89	0.97	0.58-1.6	0.007	2.28	1.26-4.19	0.99	1	0.45-2.21
rs2240340	0.45	1.15	0.79-1.68	0.66	1.12	0.66-1.88	0.005	2.35	1.3-4.28	0.97	0.99	0.44-2.21
rs1748033	0.02	1.54	1.07-2.22	0.58	1.19	0.63-2.19	0.09	1.61	0.92-2.84	0.53	0.73	0.27-1.95
rs11203368	0.86	1.03	0.71-1.5	0.96	1.01	0.6-1.7	0.03	1.95	1.09-3.52	0.81	1.11	0.49-2.49
rs2240335	0.08	1.39	0.96-2.01	0.67	1.13	0.64-1.96	0.29	1.37	0.77-2.45	0.85	0.92	0.38-2.21
rs1635564	0.02	1.55	1.08-2.23	0.03	2.06	1.07-3.94	0.08	1.65	0.94-2.9	0.03	3.35	1.2-10.97
p = major allele, q = minor allele												

p = major allele, q = minor allele