Background The circulating free DNA (cfDNA) originating mostly from the abnormal cell apoptosis, necrosis or netosis contains sequences of microorganisms encountered previously by the patients. Therefore, it may be a source of information about past infections and may become a tool to evaluate human microbiome in relation to specific diseases. The aim of the study was to identify bacterial sequences in cfDNA of patients with different types of glomerulopathies.

Methods Blood samples from 9 patients with lupus nephritis (LN), 5 with IgA nephropathy, 4 with membranous nephropathy and 3 healthy controls were collected once. cfDNA was isolated (QI Amp, Qiagen) and quantified (Thermo Fisher Scientific, Waltham). Sequencing libraries were constructed, and quality checked (KAPA-Roche, Basel). Samples were sequenced on NextSeq 550 (Illumina, San Diego), before a multi-step bioanalysis.

Results Bacterial sequences represented 0.031% of the cfDNA. The most frequent bacterial genera in the cfDNA of patients with glomerulopathies included: Esherichia, Streptococcus, Klebsiella, Brevundimonas and Moraxella and they varied between the studied patient groups. The cluster of four LN patients had distinctive bacterial cfDNA pattern which was observed on the species, family, order, class and phylum level.

Conclusions Bacterial sequences in cfDNA of patients with lupus nephritis differ from patients with IgA nephropathy and membranous nephropathy. Validation in a larger patient population is warranted.

Purpose Environmental and genetic factors have individually been extensively researched in the pathogenesis of systemic autoimmune rheumatic diseases (SARDs). Notably, more than half of the associations are shared by at least two autoimmune diseases and SLE exhibits association to almost all. Smoking is an overall risk factor for the development of any SARD. We aim to determine a polygenic risk score for SARD including smoking as a covariate which could advocate for gene-environment interaction.

Methods A case-control study will be conducted to determine a polygenic risk score including smoking.

Data will be retrieved from the UK Biobank, which is a general-population cohort of roughly 0.5 million participants recruited across the UK during 2006–2010. Participants have been genotyped. A genome wide association study (GWAS) will be performed using the Scalable and Accurate Implementation of GEneralized mixed model (SAIGE). Cases are defined to have SARD if having one of the following diagnoses: SLE, rheumatoid arthritis, polymyositis/dermatomyositis, systemic sclerosis or primary Sjögrens syndrome. Controls comprise UK Biobank participants not fulfilling the case definition or having other autoimmune diseases.

Results We have identified 1,048 patients in the UK Biobank with at least one SARD and more than 300,000 matched controls. Results from the initial GWAS calculations are shown in figure 1. Based on a top-100 list of susceptibility SNPs, we will derive a polygenic risk core and determine to which extent smoking, gender and age increase the risk of SARD among subjects which are highly genetically susceptible.
External validity is tested by replication in independent cohorts from the Danish Blood Donor Study and Copenhagen Biobank.

Conclusion Clinical tools based on genetics predictive of SARDs are in wanting but have generally been judged of little to no useful information. In this study, we will provide a validated predictive model of SARD based on multiple genes and interaction with non-genetic factors.

Acknowledgement Supported by the Danish Rheumatism Association

THE DEVELOPMENT AND VALIDATION OF A POLYGENIC RISK SCORE FOR MYOCARDIAL INFARCTION IN SLE

Sarah Reid, Johanna K Sandling, Andrei Alexsson, Pascal Pucholt, Christopher Spjall, Karoline Larang, Andreas Jonsen, Iva Gunnarsson, Anni-Christine Syvaenen, Anne Troldborg, Anders A Bengtsson, Oyvind Molberg, Sven Jacobsson, Elisabet Svennungsson, Lars Rönnblom, Dag Leonard, Uppsala University, Uppsala; Linköping University, Linköping, Sweden; University of Oslo, Oslo, Norway; Lund University, Lund; Karolinska Institutet, Solna, Sweden; Aarhus University, Aarhus; Odense University Hospital, Odense; Copenhagen University Hospital, Copenhagen, Denmark

Background Patients with SLE have increased morbidity and mortality due to cardiovascular disease. Here, we construct and validate a polygenic risk score (PRS) for myocardial infarction (MI) in SLE.

Methods Patients with SLE (European decent, ≥4 ACR-criteria) were genotyped using a 200K Immunochip SNP array (discovery cohort, Sweden, n=776) and custom MassARRAY assays (replication cohort, Norway/Denmark, n=890). In the discovery cohort, 57 SNPs with previously established association with SLE development (p<5.0×10^-8) were investigated for associations with MI using a cox regression model. Significant SNPs were included in a PRS, weighted by their ORs for MI development. The PRS was subsequently validated in the replication cohort.