(1.07–1.50), p=5.0×10–3). Rs1269852 (TNXB-ATF6B, OR 0.80 (0.66–0.98), p=2.7×10–2) and rs1132200 (TMEM39A, OR 0.72 (0.56–0.91), p=6.7×10–3) were negatively associated with SLICC-DI. Using a Kendall Tau correlation model, a positive correlation between the TNXB-ATF6B risk allele and the HLA DRB1*03:01 haplotype was observed (τ=0.91, p<1.0×10–15).

Conclusion In patients with SLE, a high genetic risk score is linked to increased organ damage and a younger age of disease onset. Further, the ATG5 and STAT4 risk alleles were associated with increased organ damage whereas the TNXB-ATF6B and TMEM39A risk alleles were associated with less organ damage. Consequently, genetic profiling of patients with SLE may provide a tool for predicting severity of the disease.

S4A:6 A SIMPLE METHOD TO EVIDENCE SUBCLINICAL ATHEROSCLEROSIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Subclinical atherosclerosis is a major cause of morbidity and mortality in patients with systemic lupus erythematosus.[1,2]

Objective The goal of this study is to assess the subclinical atherosclerosis in patients suffering the above mentioned disease, by measuring the ankle-brachial index.

Method We have studied 97 female patients diagnosed with systemic lupus erythematosus, and a control group of other 64 female patients, not having the disease. For both groups we recorded the demographics, the medical history. We also performed several laboratory tests and the ankle-brachial index measurement.

Results The mean value of ankle-brachial index on patients with systemic lupus erythematosus was statistically lower compared to control group (0,91±0,29 vs 1,14±0,17, p=0,0001). The univariate analysis of specific risk factors, showed that only the length of disease (r=-0,201, p=0,049), and the age of disease diagnosis (r=-0,354, p=0,0001) is statistically correlated with the ankle-brachial index. The multivariate analysis revealed that, among the specific risk factors, only the disease duration (B=-0,647, p=0,001), the age at diagnosis (B=0,326, p=0,002) and the presence of anticardiolipin andibodies (B=-0,338, p=0,003) are statistically correlated with ankle-brachial index.

Conclusions In our study, the determined value of ankle-brachial index on patients with systemic lupus erythematosus, was statistically lower than on the control group, thus revealing the presence of subclinical atherosclerosis.

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S4A:7 INCREASED RISK OF CARDIOVASCULAR DISEASE IN PATIENTS WITH SLE WHO HAVE ASYMPTOMATIC PLAQUE ON VASCULAR ULTRASOUND – A FIVE-YEAR FOLLOW-UP STUDY

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Cardiovascular disease (CVD) causes a quarter of deaths in patients with SLE and imaging studies show that patients with SLE have a higher prevalence of asymptomatic atherosclerotic plaques than age and sex-matched controls. It is not yet clear how strongly presence of these plaques influences the risk of developing CVD subsequently in patients with SLE.

Between 2011–2013, we carried out vascular ultrasound studies of 100 SLE patients, who had no known history of previous CVD. 95% were women and the mean age was 45.2 years. Thirty-six patients had plaque which included 14 with only carotid plaque, 7 with only femoral plaque and 15 with both. This follow-up study describes subsequent onset of CVD in these 100 patients.

The medical records of all 100 scanned patients were reviewed. CVD event were defined as coronary artery disease, peripheral vascular disease and cerebrovascular disease. Where CVD was diagnosed, it was corroborated by relevant blood tests and imaging. We carried out statistical analysis of associations between baseline variables at the time of the scan and risk of developing CVD subsequently.

From the 100 patients scanned, 7 patients were subsequently found to have CVD. Demographic information of these patients is shown in table 1. All the events occurred within a 4 year period from the initial scans. CVD occurred in 6/36 patients with plaque compared to 1/64 without plaque (p=0.002). The average number of plaque sites was 2.4 (CVD patients) compared to 0.7 (p=0.02) in those without CVD. CVD was also significantly associated with age at scan (p=0.02) and mean intima-media thickness (p=0.01). There were no significant associations with gender (p=0.5), ethnicity

Abstract S4A:7 Table 1

Patient	Gender	Age at event	Ethnicity	Event	Smoker	CVS risk factors
1	F	51	Caucasian	Angina	Previous	
2	F	61	Caucasian	NSTEMI	Never	Hypertension
3	F	60	Caucasian	CABG	Never	Hypercholesterolemia, Hypertension
4	F	54	Asian	CABG	Never	PVD
5	F	66	Caucasian	IHD	Never	Hypertension
6	F	53	Caucasian	NSTEMI	Previous	
*7	F	42	Asian	Stroke	Never	Hypercholesterolemia, Hypertension

*Non-plaque patient

(p=0.2), smoking status (p=0.6), high blood pressure (p=0.7), persistent disease activity (p=0.4), HCQ (p=0.6) and prednisolone dose >5 g (p=0.2) at the time of scanning.

This study shows that the presence of plaque was strongly associated with development of CVD within the next four years in this population of patients. Most CVD events were coronary, so not caused directly by carotid plaque. Vascular ultrasound may be helpful in improving management of CVD risk in patient with SLE.

S4d – Reproduction

S4D:4 VARIANT OF THE TNFSF13B GENE ENCODING FOR B-CELL ACTIVATING FACTOR CONFERS SUSCEPTIBILITY TO SLE, INCREASED SERUM BAFF CYTOKINE AND AUTOANTIBODIES PRODUCTION

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Background Recently, a variant in TNFSF13B, encoding the cytokine and drug target B-cell activating factor (BAFF), has been associated with Systemic Lupus Erythematosus (SLE).[1] The aim of this study was to explore the BAFF-var effect on serologic and clinical features in a cohort of patients affected with SLE.

Methods Overall, 190 Sardinian patients affected with SLE according to the modified 1997 ACR classification criteria and 256 Sardinian healthy controls were enrolled in this study and genotyped for the BAFF-var. In each patient demographic, serologic and clinical characteristics retrospectively collected at the time of SLE diagnosis and pre-therapy were recorded. Sera from 76 SLE patients, collected before starting therapy and stored at −80°, and 79 controls were used to measure soluble BAFF cytokine (ELISA).

Results BAFF-var allelic frequency was higher in SLE patients (0.368) than in healthy controls (0.259) and associated with a higher risk of developing SLE (OR: 1.6; 95% CI: 1.2 to 2.2; p=0.0005). Serum BAFF concentration was significantly increased (p=1.61×10–9) in SLE cases (mean 1530 pg/ml; range 328–9327 pg/ml) versus healthy controls (mean 829 pg/ml; range 527–1410 pg/ml). Notably, when we stratified the data according to BAFF-var, the levels of serum BAFF increased in a genotype dependent way (p=0.001). No association with gender or age at SLE onset and BAFF-var was identified. Stratifying SLE manifestations according to ACR classification criteria, no significant correlation with any of the tested manifestations and the BAFF-var genotype was discovered. However, the quantitative levels of anti-dsDNA autoantibodies increased in a BAFF-var genotype dependent way (p=0.004), being higher in patients with BAFF-var homozygosis (88.5 UI/dl, IQR 4.1–491) than in those with wild-BAFF/BAFF-var heterozygosis (48.5 UI/dl, IQR 9.7–197) and wild BAFF homozygosis (29.0 UI/dl, IQR 3.5–116).

Conclusion BAFF-var is associated with higher risk of SLE in general population and it is associated with increased serum BAFF and anti-dsDNA levels suggesting that it could also impact on SLE phenotype and outcomes.

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S4D:5 TARGETED NEXT-GENERATION SEQUENCING SUGGESTS NOVEL RISK LOCI IN JUVENILE ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Purpose Childhood onset systemic lupus erythematosus (SLE) is associated with a more aggressive disease course and higher mortality risk than adult onset SLE. It has been suggested that juvenile onset SLE cases could have a more genetically determined disease. To identify genetic risk loci in juvenile onset SLE we performed targeted DNA resequencing in a cohort of Swedish SLE patients and control individuals.

Methods Coding and regulatory regions of 1853 genes selected from pathways involved in immunological diseases were resequenced in 958 patients with SLE and in 1030 healthy individuals. All patients fulfilled at least four ACR 1982 classification criteria for SLE. For 117 of the SLE patients the disease onset was at age 18 or younger, 105 of whom were women and 12 men. Capturing of the targeted genes was performed with a Roche NimbleGen custom-made liquid capture library followed by Illumina HiSeq2500 sequencing. 97 264 single nucleotide variants (SNVs) passed quality control and had a minor allele frequency of at least 1%.

Results Single variant case-control association analysis revealed that 40 SNVs were associated with juvenile onset SLE (false-discovery rate <5%). These 40 SNVs were enriched for missense variants (8% vs 1.8% for all SNPs) and were annotated to 15 genes. Two coding SNVs on chromosome 1q25 showed the strongest evidence of association with juvenile onset SLE (p-values<5E-08), one of which results in a predicted deleterious amino acid change. Interestingly, this association exceeded the signal from the human leukocyte antigen region on chromosome 6.

Conclusion Using targeted sequencing we have identified coding SNVs in novel candidate risk loci in juvenile onset SLE. Our finding suggests differences in the genetic risk for childhood and adult onset SLE and provides insight into the genetic aetiology of juvenile onset SLE.