(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.