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

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). 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°C, 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 BAFF-var 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.