327 GENETIC POLYMORPHISM +1444CT IN THE C – REACTIVE PROTEIN IS ASSOCIATED WITH THE SUSCEPTIBILITY FOR SYSTEMIC LUPUS ERYTHEMATOSUS AND DISEASE ACTIVITY

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Background and aims The gene *C-reactive protein* (*CRP*), located at 1q23-24, is a candidate to be investigated as a susceptibility locus for systemic lupus erythematosus (SLE). The aim of the study was to evaluate the association between the +1444CT *CRP* polymorphism with the susceptibility for SLE, disease activity, and CRP serum levels.
Methods The study enrolled 176 SLE patients and 223 healthy controls from Brazilian population. SLE disease activity (SLEDAI), clinical and laboratorial characteristics were evaluated. The +1444CT *CRP* polymorphism was determined using polymerase chain reaction and restriction fragment length polymorphism.
Results The frequency of CC *vs.* TT genotypes and the C *vs.* T allele among the patients differed from the controls (p=0.0201 and p=0.0072, respectively). Patients carrying the T allele presented higher CRP (p=0.017) and showed a trend toward higher IL-6 compared with patients carrying the C allele (p=0.057). The increased CRP was independently of the IL-6 in these subgroups of patients. SLE patients carrying the CC genotype showed positive correlation between CRP and C4 levels (p=0.039), while those with T allele presented a trend toward a negative correlation between CRP and C3 and C4 (p=0.056 and p=0.073, respectively); and a trend toward positive correlation with anti-nucleosome and anti-dsDNA (p=0.052 and p=0.091, respectively).
Conclusions Our data showed that +1444CT *CRP* polymorphism was associated with SLE susceptibility and CRP levels, as well as CRP levels were associated with disease activity, suggesting that this polymorphism may play a role in the pathophysiology of SLE, which may be used as a possible marker of disease activity.

328 CCR5δ32 (RS333) POLYMORPHISM IS ASSOCIATED WITH SUSCEPTIBILITY TO SYSTEMIC LUPUS ERYTHEMATOSUS IN FEMALE BRAZILIAN PATIENTS

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Background and aims The role of *CCR5Δ32*(rs333) polymorphism in the pathogenesis of systemic lupus erythematosus (SLE) has been evaluated worldwide. The aim of this study was to determine the association between *CCR5Δ32*polymorphism with the susceptibility to SLE and the activity of disease in female Southern Brazilian patients.
Methods The study enrolled 169 female SLE patients and 132 unrelated female healthy individuals. Baseline clinical, laboratorial characteristics, and the SLE activity (determined using the SLEDAI) were evaluated according to the *CCR5Δ32*genotypes. The *CCR5Δ32* polymorphism was determined from genomic DNA using a polymerase chain reaction.
Results The frequencies of the genotypes *CCR5*/*CCR5*, *CCR5*/*CCR5Δ32* and *CCR5Δ32*/*CCR5Δ32* were 87.6%, 11.8%, and 0.6%, respectively, among the patients, and 96.2%, 3.8%, and 0.0%, respectively among the controls, [p=0.0116, odds ratio:3.432 (95% confidence interval:1.252–9.40). Patients carrying the *CCR5*/*CCR5Δ32* and *CCR5Δ32*/*CCR5Δ32* genotypes presented earlier age of onset of disease (p=0.0293) and higher levels of anti-dsDNA (p=0.0255), than those carrying the wild type genotype. When the analysis was adjusted for ethnicity, only the age at onset of disease remained associated with the *CCR5Δ32* polymorphism (p<0.05); patients with variant *CCR5Δ32* allele (heterozygous and homozygous), presented lower age at onset of disease than those with the wild type genotype.
Conclusions The results suggest that the *CCR5Δ32* polymorphism might be associated with SLE genetic predisposition among female Brazilian patients and the age at onset of the disease; however, this genetic variant was not associated with the activity of SLE in this population.

329 ELEVATED IFIT3 IN MONOCYTES CONTRIBUTED TO HYPERACTIVE CGAS-STING SIGNALLING PATHWAY IN SLE

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Background and aims IFIT3 is one of the Interferon-stimulated genes showed significantly increase in PBMCs of SLE patients. However, the functions of IFIT3 in dysregulated immune responses of SLE are not fully understood. SLE is featured by over production of nuclear antigens, such as dsDNAs, from debris of numerous dead cells, which give rise to autoantibody production. cGAS-STING signalling pathway has been proposed to play an important role in sensing DNA and producing inflammatory cytokines in SLE. Our study is IFIT3's function in regulating cGAS-STING signalling pathway in SLE.
Methods Monocytes were isolated from SLE patients or healthy controls by Ficoll-paque method and CD14+ magnetic beads. The expression of IFNβ and phosphorylation of IRF3 were measured in either IFIT3 over-expressing or knockout cells upon VACV-70 stimulation by Q-PCR and Western blot. We used Co-IP to identify the interaction between IFIT3 and its interaction proteins.
Results cGAS-STING signalling pathway was over-activated in monocytes from SLE patients compared to healthy controls. The expression of IFIT3 was significantly elevated in SLE patients and was positively correlated with the activity of cGAS-STING signalling pathway. *In vitro*, we revealed that the expression of IFNβ and phosphorylation of IRF3 could be reduced by knocking down IFIT3, while over-expression of