The IRF5 (rs729302) polymorphism is a genetic risk factor for systemic lupus erythematosus in Algerian patients

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Background Interferon regulatory factor 5 (IRF5) is a transcription factor regulating interferon secretion and was proved to be implicated in the pathogenesis of systemic lupus erythematosus (SLE) in several studies.

The purpose of this case-control study was to investigate whether IRF5 gene polymorphism is involved in the genetic predisposition to SLE in the Algerian population.

Methods IRF5 rs729302 (A/C) polymorphism was analyzed in 120 SLE patients and 98 age and sex matched controls by real time- polymerase chain reaction.

Results Significant association was observed for AA and AC genotypes of IRF5 between patients and healthy subjects (60% vs 73%; 40% vs 27%, p =0.025, respectively).

Patients with SLE had more frequent C allele compared to controls (20% vs 13%, P = 0.041).

However, the allele and genotype frequencies did not show any difference in patients with nephritis in comparison to those without nephritis.

Conclusion The rs729302 C allele and AC genotype can be considered as risk factors for the development of SLE in Algerian patients.

Background A single nucleotide polymorphism in NCF1 (NCF1-339, rs201802880), encoding NADPH oxidase complex 2 subunit p47^linx^, reducing production of reactive oxygen species (ROS) is highly associated with development of systemic lupus erythematosus (SLE). However, the effect of NCF1-339 genotype on SLE regarding pathogenetic processes or comorbidities has not been investigated.

Methods NCF1-339 genotyped SLE subjects from four Swedish university hospitals were investigated regarding neutrophil ROS production (n=31), neutrophil extracellular traps (NETs) (n=31), serum interferon (n=141), autoantibody profiles (n=305) and clinical phenotypes (n=1087).

Results Compared to SLE patients with normal-ROS NCF1-339 genotypes, neutrophils from patients with low-ROS genotypes displayed impaired NET-formation and increased dependence on mitochondrial ROS for canonical NET-release. An increased frequency of low-ROS patients had high serum interferon activity. Patients with low-ROS genotypes had an increased frequency of positivity for antiphospholipid antibodies anti-β2 glycoprotein I and anti-cardiolipin, related to the severe comorbidity antiphospholipid syndrome (APS). No other autoantibodies investigated were associated with NCF1-339 genotype. Clinical characterization revealed a strong association between NCF1-339 low-ROS genotypes and secondary APS.

Conclusions NCF1-339 genotype affects neutrophil functions of ROS production, NET formation and dependence on mitochondrial ROS. SLE subjects with low-ROS NCF1-339 genotypes are associated with high serum interferon, presence of antiphospholipid antibodies and secondary APS.

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