Univariation and multiple linear regression analyses for 23 single nucleotide polymorphisms in 14 chronic glomerular disease’s predisposing genes and systemic lupus erythematosus in Han Chinese

Sir,

Systemic lupus erythematosus (SLE) is a prototypical autoimmune rheumatic disease principally affecting women during childbearing years. It is the most heterogeneous autoimmune disease that affects multiple organs.[1] However, the exact pathogenesis of SLE remains uncertain, and might be involving numerous genes which leads to inconsistent findings in genetic studies. One possibility of failure to replicate some single-locus results is that the underlying genetics of SLE is based on multiple genes with minor effects.

In our present preliminary study, the relationship between 23 single nucleotide polymorphisms (SNPs) in 14 chronic Glomerular disease’s predisposing genes and SLE of Han Chinese had been explored, and interesting results had been found. We included 18 unrelated individuals of Han as case group (male 2, female 16, aged between 14 and 60, average 37.4) with a firm diagnosis of SLE based on American Rheumatism Association criteria, and included 37 unrelated males of Han as control group (aged between 34 and 54, average 44.32) recruited from a company-based health screening program in medical examination center of the 181st Hospital of Chinese People’s Liberation Army. Genotyping of 23 SNPs in 14 genes was carried out by the BaiO gene array for chronic glomerular disease’s predisposing genes. The procedures of deoxyribonucleic acid (DNA) extraction, polymerase chain reaction (PCR) amplification, hybridization, gene array detection and analysis were strictly according to the manuals of BaiO genotype detecting gene array kit.

The results of genotype distribution in two groups showed that two SNPs sites rs12720270 and rs7574865 had significant differences in genotype frequency between SLE and the matched controls for all of the 22 SNPs ($P = 0.038$ and 0.011, separately, analyzed by using $\chi^2$ test). In addition, the results of allele analysis showed that two SNPs sites rs7574865 and rs12720270 had significant differences in allele frequency between SLE and the matched controls for all of the 22 SNPs ($P = 0.025$ and 0.043, separately, analyzed by using Fisher’s exact test).

In our current study, we found that two genes STAT4 (rs7574865) and tyrosine kinase 2 (TYK2, rs12720270) were associated with the significant risk of SLE in the Han Chinese. Previous evidences suggested that the variant form of STAT4 (rs7574865) may play a putative key role in the development of a variety of autoimmune diseases.[2-4] Previous studies found a significant association of the STAT4 polymorphism with susceptibility to both Rheumatoid arthritis and SLE by using Fisher’s exact test.[5,6] These findings indicated that STAT4 is a common genetic risk factor for autoimmune diseases, with similar strength across major racial groups. In our study, STAT4 had significant differences in allele frequency and genotype frequency between SLE and the matched controls, this result was consistent with previous researches. Recently, Some investigations showed association to SLE from individual SNPs and haplotypes in TYK2.[7-9] However, we found no association with susceptibility either rs2304256 or rs280519, only rs12720270 showed association with increased risk of SLE in our study, these results confirm previous findings and provide additional resolution regarding the causal polymorphisms in this gene.

Altogether, our findings revealed that STAT4 (rs7574865) and TYK2 (rs12720270) might play key roles in the pathogenesis of SLE in the Han Chinese, and regulation of the expression of these two genes might become a new target in the treatment of SLE. Further replications in larger independent samples is warranted.

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