

Multiple sclerosis susceptibility in a Brazilian sample, HLA and *CIITA* genes

Estudo de associação entre a susceptibilidade à esclerose múltipla e fatores relacionados ao HLA

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ABSTRACT

Introduction: The multiple sclerosis (MS) is a chronic disease of the central nervous system that affects mainly young adults. This disease is characterized by the spread of demyelinating lesions in time and space. This condition may be influenced by genetic factors as heterogeneity, incomplete penetrance, polygenic inheritance and epigenetic factors, which makes this complex disease a challenge for geneticists. **Objectives:** The aim of this study was to investigate the association between HLA alleles from *DQA1*, *DQB1* and *DRB1* loci (6p21.3), genetic polymorphisms -168A/G (rs3087456) and +1614 G/C (rs4774) in the *CIITA* gene (16p13) and susceptibility to MS in a miscegenated sample from Rio de Janeiro state, RJ, Brazil. **Method:** DNA samples from 52 patients with relapsing remitting multiple sclerosis (MSRR) [21 males (40.38%) and 31 females (59.62%)] and 116 healthy controls [46 males (39.65%) and 70 females (60.35%)] matched by race, sex and age were analyzed by techniques of PCR, SSP-PCR, electrophoresis and DNA sequencing. **Results:** A significant association between MS and *HLA-DRB1*15:01* allele was observed [p value=.002; Odds Ratio (OR)=3.2], especially in women (p=.001; OR=4.9), which remained statistically significant after Bonferroni correction. Furthermore, it was observed that the polymorphism +1614 G/C, "C/C" profile, in association with the allele *DRB1*15:01* influences the increased susceptibility to MS in women (p=.029; OR=5.6). In addition, it was observed that the "G/G" profile in *CIITA* polymorphism +1614G/C may be associated with the resistance to MS (p=.02; OR=0.23), as well as *HLA-DRB1*11:02* (p=.02, OR=0.5). The *HLA-DQB1*06:02* allele also has been implicated as a possible susceptibility factor for MS (p=.02; OR=1.8, data not confirmed after Bonferroni's correction). **Conclusion:** Together, these results reinforce the polygenic nature of MS, and proposed that the *CIITA* gene, which is the regulator of the expression of HLA-D, is an additive factor to *DRB1*15:01* allele, previously described as a genetic susceptibility factor to MS in Brazilians.

Keywords: *CIITA* gene, HLA, rs4774*C, *HLA-DRB1*15:01*, multiple sclerosis.