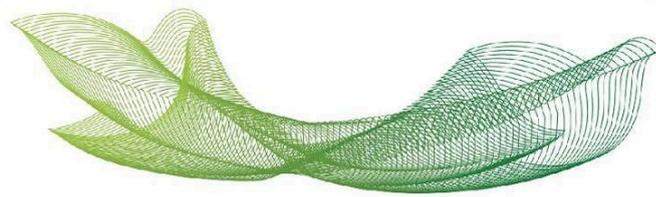




Tipo	Periódico
Título	Single-Base Gene Variants in MIR-146A and SCN1A Genes Related to the Epileptogenic Process in Drug-Responsive and Drug-Resistant Temporal Lobe Epilepsy-A Preliminary Study in a Brazilian Cohort Sample
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Resumo	<p>The drug-resistant temporal lobe epilepsy (TLE) has recently been associated with single nucleotide variants (SNVs) in microRNA(miR)-146a (MIR-146A) (rs2910164) and Sodium Voltage-Gated Channel Alpha Subunit 1 (SCN1A) (rs2298771 and rs3812718) genes. Moreover, no studies have shown an association between these SNVs and susceptibility to drug-resistant and drug-responsive TLE in Brazil. Thus, deoxyribonucleic acid (DNA) samples from 120 patients with TLE (55 drug-responsive and 65 drug-resistant) were evaluated by real-time polymerase chain reaction (RT-PCR). A total of 1171 healthy blood donor individuals from the Online Archive of Brazilian Mutations (ABraOM, from Portuguese Arquivo Brasileiro On-line de Mutações), a repository containing genomic variants of the Brazilian population, were added as a control population for the studied SNVs. MIR-146A and SCN1A relative expression was performed by quantitative RT-PCR (qRT-PCR). The statistical analysis protocol was performed using an alpha error of 0.05. TLE patient samples and ABraOM control samples were in Hardy-Weinberg equilibrium for all studied SNVs. For rs2910164, the frequencies of the homozygous genotype (CC) (15.00% vs. 9.65%) and C allele (37.80% vs. 29.97%) were superior in patients with TLE compared to controls with a higher risk for TLE disease [odds ratio (OR) = 1.89 (95% confidence interval (95%CI) = 1.06-3.37); OR = 1.38 (95%CI = 1.04-1.82), respectively]. Drug-responsive patients also presented higher frequencies of the CC genotype [21.81% vs. 9.65%; OR = 2.58 (95%CI = 1.25-5.30)] and C allele [39.09% vs. 29.97%; OR = 1.50 (95%CI = 1.01-2.22)] compared to controls. For rs2298771, the frequency of the heterozygous genotype (AG) (51.67% vs. 40.40%) was superior in patients with TLE compared to controls with a higher risk for TLE disease [OR = 2.42 (95%CI = 1.08-5.41)].</p>



Drug-resistant patients presented a higher AG frequency [56.92% vs. 40.40%; OR = 3.36 (95%CI = 1.04-17.30)] compared to the control group. For rs3812718, the prevalence of genotypes and alleles were similar in both studied groups. The MIR-146A relative expression level was lower in drug-resistant compared to drug-responsive patients for GC (1.6 vs. 0.1, p-value = 0.049) and CC (1.8 vs. 0.6, p-value = 0.039). Also, the SCN1A relative expression levels in samples from TLE patients were significantly higher in AG [2.09 vs. 1.10, p-value = 0.038] and GG (3.19 vs. 1.10, p-value < 0.001) compared to the AA genotype. In conclusion, the rs2910164-CC and rs2298771-AG genotypes are exerting significant risk influence, respectively, on responsive disease and resistant disease, probably due to an upregulated nuclear factor kappa B (NF-kB) and SCN1A loss of function.

Fomento

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