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Título	The single nucleotide variant n.60 G > C in the microRNA-146a associated with susceptibility to drug-resistant epilepsy
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Resumo	Objective: The aim of this study was to evaluate single nucleotide variants (SNVs) n.-411A > G (rs57095329) and n.60 G > C (rs2910164) in microRNA (miR)-146a, related to suppressing of TRAF6 with risk for epilepsy, as well as miR-146a and TRAF6 levels. Methods: DNAs were extracted from epileptogenic tissues and blood leukocytes from drug-resistant epilepsy patients and healthy-individuals, respectively. Genotypes were identified by real-time PCR. Hardy-Weinberg equilibrium (HWE) and Fisher or X2 tests evaluated the difference between groups. The disease risk was assessed by odds ratio (OR) with 95 % confidence interval (95 %CI). The prognostic impact on probability seizure-free survival (PSF) was evaluated by Kaplan-Meier and log-rank tests. Results: For rs57095329 both control and patient samples were not in HWE ($p < 0.05$) and the genotypes prevalence was similar in patients and controls ($p>0.05$). For rs2910164, control samples were in HWE ($p = 0.61$), contrasting with patients ($p = 0.03$), and similar frequencies of wild-type homozygous (GG) (43.4 % vs. 34.4 %, $p = 0.2$) and variant (CC) genotypes (8.0 % vs. 6.6 %, $p = 0.6$) were observed in patients and controls, respectively. However, increased frequency of heterozygous (GC) was observed in patients compared to controls (59.0 % vs. 42.7 %, $p = 0.04$) with 1.98 (95 %CI=1.09-3.57) risk for epilepsy. The miR-146a expression level in the epileptogenic tissues was lower in the GC ($p = 0.02$) and CC ($p = 0.09$) compared to GG genotype. TRAF6 expression level was higher in CC than in GG genotype ($p = 0.09$). Interestingly, there was an increased frequency of patients

	harboring GC genotype and less time until surgery compared to patients harboring GG or CC (36.06 % vs. 11.5 %, p = 0.01), confirmed by PSF (p = 0.04). Conclusions: The GC genotype for SNV rs2910164 appears associated with susceptibility to drug-resistant epilepsy due to the decreased MIR146a expression, favoring NF-kB pathway through TRAF6.
Fomento	