MOLECULAR ANALYSIS OF *GABRA1* AND *EFHC1* GENES IN PATIENTS WITH JUVENILE MYOCLONIC EPILEPSY AND OTHER IDIOPATHIC GENERALIZED EPILEPSIES

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PURPOSE

To identify mutations in the α1-subunit of the $GABA_A$ receptor gene (*GABRA1* - Figure 1), important to neuronal excitability regulation, and EFHC1 protein gene (*EFHC1* Figure 2), involved in the central nervous system development and in cortical and subcortical architecture alterations in patients with juvenile myoclonic epilepsy (JME) and other idiopathic generalized epilepsies (IGEs). In addition, we aimed to establishing possible genotype-phenotype correlations.

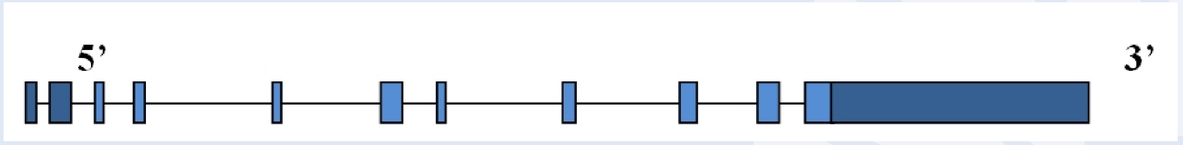

Figure 1- *GABRA1* gene.

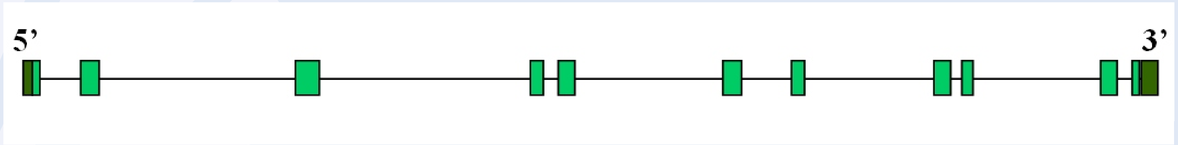

Figure 2- *EFHC1* gene.

METHOD

We screened for *GABRA1*and *EFHC1* mutations in 52 patients with JME and 33 with other IGEs. Algorithms were used for predicting the impact of amino acid exchanges in protein function.

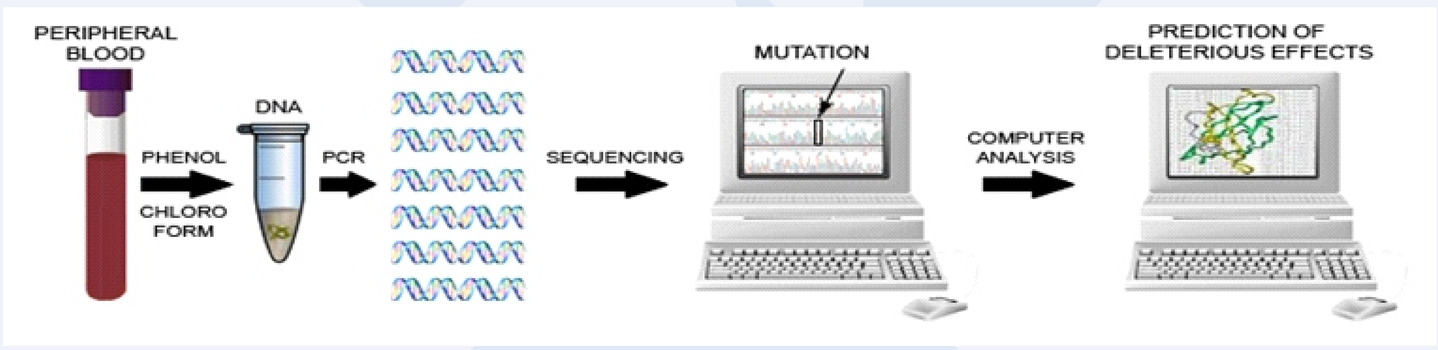

Figure 3. Methods to *GABRA1*and *EFHC1* genes analysis.

RESULTS

In *GABRA1*, we identified three silent mutations (c.96A> G, c.156 T> C and c.1323G> A) and an intronic (IVS1 +9 A> T), all presents in SNPs databases and none potentially deleterious. In EFHC1, we identified two new variants (896A> G and 1766G> A), and six variants already described in SNPs databases (c.475C> T; 545g> A, 685T> C, 1343T> C; 1821A> G and 1855A> C). The predicted pathogenic potential of these variants was controversial.

CONCLUSION

Since deleterious mutations were not found in *GABRA1* in the patients we studied, this gene does not seem to be related to IGE in our cohort.

We found eight sequence alterations in *EFHC1*, seven of those predicted as deleterious by at least one algorithm and affecting only JME patients. However, the deleterious prediction in EFHC1 function did not reach a consensus, revealing the high genetic complexity of JME and related IGEs. In addition, we did not observe preferential location of the mutations along EFHC1.