



Association study between a single nucleotide polymorphism localized in the microRNA-binding site of *NEUROG2* and focal cortical dysplasia .

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Abstract

Focal cortical dysplasia (FCD) is a cortical malformation associated with severe drug-resistant epilepsy. Our group previously identified a microRNA (miRNA) hsa-miR-34a, which regulates expression of *NEUROG2* gene as possibly related to the mechanisms underlying this type of cortical malformation. Computational predictions identified that a single nucleotide polymorphism (SNP) in *NEUROG2* (rs57336627) that can change hsa-miR-34a affinity for this gene. Therefore, we aim to evaluate if there is any association between SNP rs57336627 and FCD in a case-control study. We accessed 11 patients with FCD and 315 controls and performed quantitative PCR (qPCR) to identify SNP rs57336627. We did not observe any significant difference in allele frequency of rs57336627 when comparing patients and control, although the frequency of allele A of rs57336627 was higher in patients.

Key words:

SNP, MicroRNA, Association.

Introduction

Focal cortical dysplasia (FCD) is a malformation of the cerebral cortex usually associated with cell abnormalities, giant/dysmorphic neurons and balloon cells and severe drug-resistant epilepsy. The mechanisms involved in the pathogenesis of type II FCD are not completely understood. Our group previously identified abnormal expression of hsa-miR-34a and its target gene *NEUROG2* in abnormal brain tissue of patients with FCD. This gene plays a central role in cell fate specification and neuronal differentiation in many regions of the central nervous system¹. Computational predictions² indicate the presence of a single nucleotide polymorphism (SNP), rs57336627 (G>A), within hsa-miR-34a binding site and showed that hsa-miR-34a had a higher binding affinity for the G genotype rather than for the A genotype. Our hypothesis is that abnormal expression of *NEUROG2* could be caused by the presence of this SNP in the 5'UTR region. This would lead to instability on the miRNA binding site or the miRNA inability to bind to *NEUROG2*, causing a less efficient suppression of this gene. In this study, we evaluated whether SNP rs57336627 localized in the miRNA-binding site of *NEUROG2* could be associated with FCD.

Results and Discussion

We genotyped a total of 315 controls and 11 patients with FCD type II using qPCR. Our results indicate that Hardy-Weinberg equilibrium was maintained between case and controls, $p = 0.4801$. Furthermore, we found that allelic distribution of rs57336627 was different among cases and controls. Frequency in patients was 13.6% for allele A and 86.7% for G; whereas in controls, allele A is 8.8% and G is 91.2%. However, this difference is not statistically significant, Fisher's Exact Test, $p = 0.4345$. Although we did not observe statistical association between SNP rs57336627 and FCD, most likely due to our relative small sample size, we found that frequency of allele A was 1.5 fold higher in patients than in controls². Functional studies are in progress to help better understand this issue.

Conclusions

Although we did not observe statistical difference in allele frequency of rs57336627 between FCD patients and controls, we found a higher frequency of allele A in patients when compared to controls.

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¹Guillemot, F. et al. *European Journal of Neuroscience*, Vol. 23, pp. 857–868, 2006

²Krüger J et al, *Nucleic Acids Res.* Jul;34(Web Server issue):W451-4, 2006