

Investigating a stop-gain variant associate with cell differentiation and synaptic machinery in focal cortical dysplasia

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Abstract

C-terminal binding protein 2 (CTBP2) gene can be related with mechanisms involved in the pathogenesis of type II Focal cortical dysplasia (FCD). The main goal of this work is to investigate the frequency of a single nucleotide variant (SNV) identified in CTBP2, rs76555439, in a cohort of patients with FCD and compare it with healthy control individuals.

Key words:

CTBP2 gene, Sanger sequencing, FCD

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. We have previously identified a rare stop-gain variant, rs76555439, located in the C-terminal binding protein 2 (*CTBP2*) gene in a few patients with FCD¹. This variant is absent in our in-house control database of 29 samples as well as in 2 independent control databases: Exome Variant Server and Exome Aggregation Consortium (ExAC). Furthermore, *CTBP2* gene has been related to: i) transcriptional corepressors that associate with DNA-binding transcription factors and have been linked to the regulation of the transition of neural precursor cells to a differentiated state and ii) specialized synapses known as synaptic ribbons². In this context, the goal of this work is to investigate the frequency of the *CTBP2* variant (rs76555439) in additional patients with FCD as well as healthy control individuals in order to assess a possible genetic association.

Results and Discussion

We assessed a total of 17 patients with type II FCD as well as 315 control individuals. We are using Sanger sequencing to identify the candidate variant in all samples

Results of Sanger sequencing is shown in figure 1.

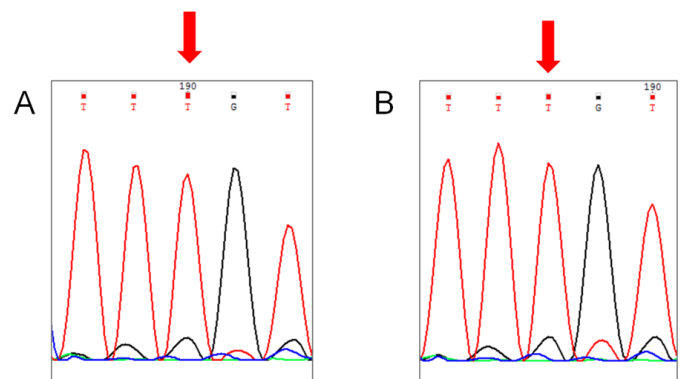


Figure 1. Sequence electropherograms showing the *CTBP2* variant, rs76555439 (T>A). The arrow indicates the homozygous T/T in (A) FCD and (B) control individual.

Conclusions

To date, we have completed sequencing in only a few patients and controls and an homozygous T/T genotype was identified in all patients with FCD (n=9) and in all eight control individuals studied.

Acknowledgement

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¹ Kim, T. Ctpb2 Modulates NuRD-Mediated Deacetylation of H3K27 and Facilitates PRC2-Mediated H3K27me3 in Active Embryonic Stem Cell Genes During Exit from Pluripotency. *Stem Cells*. **2015**, 33, 2442-2455.

²Rutherford, M. Resolving the structure of inner ear ribbon synapses with STED microscopy. *Synapse*. **2015**, 69, 242-55.