

# STRONG CHILDREN'S RESEARCH CENTER

## Summer 2014 Research Scholar

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### ABSTRACT

**Title:**

Whole Exome Sequencing of Developmental Epilepsies

**Background:**

Developmental epilepsies are age-dependent electroclinical syndromes that include Ohtahara syndrome, infantile spasms, early myoclonic encephalopathy, malignant migrating partial seizures of infancy, Lennox-Gastaut syndrome and others. The prevalence of these disorders ranges from 1 in 10,000 to 1 in 100,000 live births<sup>1</sup> and they are associated with autism, intellectual disability, and intractable epilepsy<sup>2</sup>. Mutations in an increasing number of genes have been associated with these disorders.

**Objective:**

Whole exome sequencing (WES) has proved a valuable tool for discovering mutations in genes, allowing for new understanding of disease mechanisms and potential targets for new treatments. Our objective was to sequence the exomes of three proband-parent trios with developmental epilepsy and to reanalyze two previously obtained exomes using new analytical software. Each subject was identified using EEG-based inclusion criteria, review of brain MRI scans, review of clinical data, normal chromosomal microarray, and negative sequencing for most of the known clinically testable genes. WES was performed at the URM C Genomics Research Center, and data were analyzed on the CIRC's BlueHive2 cluster.

**Results:**

Analysis of whole exome data from subject DB13-002, a patient with malignant partial seizures of infancy, confirmed the previously identified *de novo* c.1285C>T / p.R429C mutation in *KCNT1*. Reanalysis of subject DB13-011, another patient with malignant partial seizures of infancy, did not identify compelling variants likely to be causative, confirming our previous findings. Analysis of the three new trios (all with infantile spasms) is pending completion of sequencing.

**Conclusion:**

Identification of mutations in genes for developmental epilepsies leads to improved diagnosis of cause, and as the biological function of more genes is better understood should lead to improved therapies. Improvements and optimization of the data analysis workflow allows the reproducible identification of variants for further biological testing.