

WHOLE-GENOME SEQUENCING REVEALS GENETIC VARIANTS IN PEDIATRIC EPILEPSY PATIENTS OF KAZAKHSTAN

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Background: Epilepsy is a common neurological disorder with diverse etiologies, among which genetics plays a significant role. Advances in next-generation sequencing (NGS) have enabled the identification of numerous genes and variants associated with epilepsy, improving our understanding of its molecular mechanisms. Determining the genetic basis of epilepsy is crucial for optimizing treatment strategies, particularly in drug-resistant cases where certain variants can influence responsiveness to anti-epileptic drugs (AEDs). This study aimed to explore the genetic landscape of pediatric epilepsy patients in Kazakhstan using whole-genome sequencing (WGS).

Materials and methods: Ten pediatric epilepsy patients of Asian ancestry with epilepsy of unknown etiology were recruited. gDNA was sequenced using the NovaSeq6000 platform. Bioinformatic processing and variant annotation were performed using ANNOVAR and public databases such as ClinVar and Franklin Genoox. Variants were classified according to the American College of Medical Genetics and Genomics (ACMG) guidelines.

Results: We identified 10 pathogenic, 3 likely pathogenic, and 8 VUS variants, several in genes previously linked to epilepsy and neurodevelop-

mental disorders. Notably, a pathogenic variant in KCNT1 (rs397515404) and a likely pathogenic variant in ARX (rs1064794843) were associated with infantile epileptic encephalopathy.

Additionally, a polymorphism in the ABCB1 gene (rs2032582), which encodes P-glycoprotein, was detected in seven patients (five homozygous C/C, two heterozygous A/C). ABCB1 is known to influence AED response and may play a role in drug resistance. However, this variant is currently classified as VUS, and its direct involvement in epilepsy remains uncertain.

Conclusion: This study provides the first comprehensive WGS-based genetic profiling of pediatric epilepsy patients in Kazakhstan, identifying both disease-associated variants and potential pharmacogenomic markers. The discovery of ABCB1 rs2032582 highlights the importance of integrating genetic testing into epilepsy management and underscores the need for larger studies to validate these findings.

Acknowledgement: This research has been funded by the Science Committee of the Ministry of Science and Higher Education of the Republic of Kazakhstan (Program targeted funding No. BR27199879).

Keywords: Epilepsy, NGS, genetic associations