GENETIC SPECTRUM OF CHANNELOPATHIES IN KAZAKHSTANI PATIENTS REVEALED BY TARGETED NGS PANEL

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Background: Channelopathies are among the major causes of sudden cardiac death (SCD). Mutations in ion channel genes have been associated with life-threatening arrhythmias. This study aimed to characterize genetic spectrum of Kazakhstani patients with channelopathies using targeted next-generation sequencing (NGS), which may facilitate personalized therapeutic strategies.

Material and methods: Genomic DNA was extracted from whole blood samples of patients with clinically diagnosed channelopathies. Targeted NGS was performed on the NovaSeq 6000 platform (Illumina) using the TruSight Cardio panel, which covers 174 genes associated with inherited cardiovascular disorders. Bioinformatic analysis was performed using standard pipelines, and variants were classified according to the American College of Medical Genetics and Genomics (ACMG) guidelines. International databases (ClinVar, MutationTaster, gnomAD, Polyphen-2) were additionally used for variant interpretation.

Results: Genetic screening revealed 23 rare variants. We found five disease-causing pathogenic (P) and likely pathogenic (LP) variants in our study. Namely, disease-causing mutations are detected in SCN5A, KCNQ2, CACNB2, KCNQ1. In addition, 11 variants of unknown significance (VUS) with suggestive evidence of pathogenicity were identified in patients. Moreover, several variants were located in genes previously implicated in arrhythmia susceptibility, warranting further investigation. The results of genetic screening were reported to clinicians to support further clinical decision-making and patient management.

Conclusion: Our study demonstrated genetic profiles of patients with channelopathies by using the TruSight Cardio panel. Genetic screening revealed clinically significant variants within ion channel genes.

Acknowledgement: The study was funded by grants from the Committee of the Ministry of Science and Higher Education, Republic of Kazakhstan (AP23490249, BR24993023) and Nazarbayev University CRP - 211123CRP1608.

Keywords: channelopathies, mutations, targeted sequencing