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## TARGETED NEXT GENERATION SEQUENCING REVEALS NEW INSIGHTS INTO THE GENETIC BASIS OF INHERITED ARRHYTHMIA IN KAZAKHSTANI PATIENTS

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**Introduction:** Ventricular arrhythmias are caused by mutations of ion channels and their interacting proteins. Most arrhythmia syndromes are inherited in an autosomal dominant manner, such that first-degree family members have a 50% chance of inheriting the disease. Identification of the mutation allows for predictive genetic testing in other living family members. Variable penetrance is common in all arrhythmia syndromes, the same mutation in the same family causing wide variation in phenotype. This suggests that other factors such as genetic modifiers and environmental factors may influence the phenotype.

Recent advances in genetic sequencing techniques and the potential of therapeutic intervention in patients with inherited cardiac arrhythmias have garnered this group of disorders much attention in the scientific community. The purpose of the study was to identify the mutational spectrum of ventricular tachycardia (VT) in Kazakhstani patients.

**Material and Methods:** using predeveloped a targeted panel of 96 known cardiac disease genes, associated with cardiomyopathy and arrhythmia we screened 92 patients, diagnosed with VT and dilated cardiomyopathy (VT DCM) or idiopathic VT (iVT).

**Results.** Targeted sequencing and stepwise filtering of the annotated variants identified a total of 307 unique variants in 74 genes totaling up in 456 variants for the overall study group. Variants included one in/del variant, four splice-site variants and 451 single-nucleotide variants (SNV) within the coding exonic regions. Seven (0.15%) of the SNVs were unique stop-gain variants, three of those residing in the TTN gene. 168 HGMD mutations (61 unique) were observed in 37 genes. According to ACMG variants were classified as 9 pathogenic (KCNJ2R218Q and TTN R5338X in iVT patients, KCNQ1c.477+1G>A, LMNA Q353X, MYH7 F244L, TTN L17465X and W21011X, DSG2c.2334+1G>A, GAA W746C in VT DCM patients), 11 likely pathogenic, 97 variants with uncertain significance and rest as benign were observed.

**Conclusions:** Individuals presenting with VT either secondary to DCM or of idiopathic etiology carry multiple rare mutations and potentially pathogenic sequence variants in cardiac risk genes in a similar pattern and at a comparable frequency. Further studies are needed to identify more mutations causing VT in a larger cohort of patients.

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