

**A TARGETED SEQUENCING REVEAL OVERLAPPING PATTERN OF GENETIC VARIANTS IN PATIENTS WITH CARDIOMYOPATHY WITH CARDIAC ARRHYTHMIAS IN KAZAKHSTAN**

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**Introduction.** Ventricular tachycardia (VT) is a common symptom in cardiac disorders of different etiology. Abnormalities of ion channels are attributed to mutations in the genes encoding the channel protein and cause altered function of channels, which can predispose to arrhythmias. Due to the high incidence of cardiovascular disorders in Kazakhstan, we enrolled a study cohort of 95 patients of different clinical phenotypes of cardiomyopathies, including DCM, idiopathic VT but also patients with myocardial infarction as a consequence of coronary heart disease. The common denominator among the three main groups was the occurrence of severe episodes of VT in all patients. Using targeted resequencing, we investigated 96 cardiomyopathy associated candidate-genes in this cohort with the aim to detect rare and common variations in these genes associated with VT molecular basis.

**Methods and results:** We have enrolled 95 patients with sporadic (64/95) or familial (26/95) cardiomyopathies (DCM: 37.3%, idiopathic Ventricular Tachycardia (idVT): 38.9%, coronary heart disease with severe episodes of ventricular tachycardia: 24.2%, and others: 3%). Using a customized HaloPlex Target Enrichment System™ (Agilent Technologies Inc., Santa Clara, CA, US) 96 cardiomyopathy associated candidate-genes were sequenced and identified 173 mutations previously associated with cardiomyopathies (disease-associated variants listed in the Human Genome Mutation Database; HGMD). On average, each patient carried >1.6 mutations, irrespective of the initial clinical diagnosis. Furthermore, 215 private (unique) non-synonymous variants were observed in the patient cohort. Prediction scores (f.e. MetaLR) of the private variants indicated high probability of disease association. Including the newly identified high-probability variants, each patient carried on average >4.8 genetic variants. Interestingly, there was no difference in the frequency of genetic variants between the CAD and the DCM subgroup of patients.

**Conclusion:** Our study indicates that CAD patients carry an overlapping pattern of genetic variants as observed for DCM patients or other forms of inheritable cardiac disorders. Multiple genetic mutations and novel variants were observed for most of the patients, independent of initial clinical diagnosis. Because of the wide overlap of the pattern of genetic variants between CAD and DCM patients we have to assume a polygenic effect and a common molecular basis for CAD and DCM or challenge the causal relation of a multitude of genetic mutations.