GENERATION OF INDUCED PLURIPOTENT STEM CELLS (IPSCS) FOR MODELING CATECHOLAMINERGIC POLYMORPHIC VENTRICULAR TACHYCARDIA (CPVT)

Nazerke Satvaldina[1], Ainur Tolymbekova[1,2], Saule Rakhimova[1], Zhannur Abilova[1], Ainur Akilzhanova[1]

[1]National Laboratory Astana, Nazarbayev University, Astana, 010000, Republic of Kazakhstan;
[2] School of Medicine, Nazarbayev University, Astana, 010000, Republic of Kazakhstan.

Corresponding author: nazerke.satvaldina@nu.edu.kz

Background: Catecholaminergic polymorphic ventricular tachycardia (CPVT) is characterized by ventricular arrhythmias that occur in response to physical or emotional stress. Structural heart disease is typically absent, and this type of arrhythmia is commonly associated with mutations in the RYR2 gene. CPVT is a leading cause of sudden cardiac death in young individuals. In this study, we describe the generation of induced pluripotent stem cells (iPSCs) both from a healthy donor and a patient diagnosed with CPVT.

Materials and methods: A Female individual diagnosed with CPVT (33 y.o.) underwent genetic screening through Sanger sequencing, which identified a de novo RYR2 mutation (c.13892A>T; p.D4631V). Peripheral blood mononuclear cells were collected from both the patient and a healthy donor using density gradient centrifugation. These cells were reprogrammed into induced pluripotent stem cells (iPSCs) using the Sendai virus approach. The iPSCs were cultured in Essential 8™ Flex medium under feeder-free conditions. Verification of pluripotency was conducted by various techniques, including immunocytochemistry and G-banding karyotyping.

Results: Cells exhibited good morphology, forming colonies with clearly defined edges and a rounded appearance, cells within the colonies were tightly packed. Immunostaining verified the presence of the pluripotency marker TRA-1-60. Karyotype analysis confirmed that all derived cell lines retained stable chromosomal integrity.

Conclusion: To serve as a control, iPSCs were successfully generated from a healthy donor. Future perspective includes comparison with patient-derived iPSCs harboring a de novo heterozygous RYR2 mutation (c.13892A>T; p.D4631V). iPSC-based model provides a powerful tool for studying the pathophysiology of CPVT and evaluating potential therapeutic strategies.

Acknowledgement: This study was funded by the Science Committee of the Ministry of Science and Higher Education of the Republic of Kazakhstan: AP19677442 “Modeling of induced pluripotent stem cells (iPSCs) to improve understanding of the mechanisms underlying electrical heart disorders in Kazakhstani patients”; AP23490249 «Functional assessment of novel genetic mutations causing dilated cardiomyopathy using iPSC derived cardiomyocyte modeling in patients of Kazakhstan»; BR24993023 «Improving the diagnostics and therapy of cardiovascular diseases in Kazakhstan by introducing the correction of metabolism with glucagon-like peptide 1 (GLP-1) drugs»; and Nazarbayev University funding CRP grant 211123CRP1608 “Identification and functional characterization of novel genetic mutations causing dilated cardiomyopathy in patients of Kazakhstan”.

Key words: iPSCs, CPVT, cardiac arrhythmia, mutation, personalized medicine