Cav?2 transcription start site variants modulate calcium handling in newborn rat cardiomyocytes

Moreno, Cristian

Hermosilla, Tamara

Morales, Danna

Encina, Matías

Torres-Díaz, Leandro

Díaz, Pablo

Sarmiento, Daniela

Simon, Felipe

Varela, Diego

In the heart, the main pathway for calcium influx is mediated by L-type calcium channels, a multi-subunit complex composed of the pore-forming subunit CaV1.2 and the auxiliary subunits CaV??2?1 and CaV?2. To date, five distinct CaV?2 transcriptional start site (TSS) variants (CaV?2a-e) varying only in the composition and length of the N-terminal domain have been described, each of them granting distinct biophysical properties to the L-type current. However, the physiological role of these variants in Ca2+ handling in the native tissue has not been explored. Our results show that four of these variants are present in neonatal rat cardiomyocytes. The contribution of those CaV?2 TSS variants on endogenous L-type current and Ca2+ handling was explored by adenoviral-mediated overexpression of each CaV?2 variant in cultured newborn rat cardiomyocytes. As expected, all CaV?2 TSS variants increased L-type current density and produced distinctive changes