Abstract:

Cardiac CaV1.2 channels play a critical role in cardiac function. It has been proposed that the carboxyl-terminal intracellular tail of the CaV1.2 channel is the target of Ca(2+)-dependent and Ca(2+)-independent regulation of the channel. Recent studies on C-terminal truncated forms of the CaV1.2 channel reported neonatal death, reduced CaV1.2 current, and failure of ?-adrenergic stimulation of these channels in ventricular cardiomyocytes (CMs). Here, we used atrial CMs at embryonic day 18.5 that expressed a C-terminal truncated form of the CaV1.2 channel (Stop/Stop). Surprisingly, the atrial CMs showed robust L-type Ca(2+) currents which could be stimulated by forskolin, an activator of adenylyl cyclase. These currents exhibited a left-ward shift in the voltage-dependent activation curve and a reduced sensitivity to the Ca(2+) channel blocker isradipine as compared to currents in wild-type atrial CMs. RT-PCR analysis revealed normal levels of mRNA for the CaV1.2 channel but a twofold increase in the level of mRNA for the CaV1.3 channel in the Stop/Stop atrium as compared to wild-type atrium. A Western blot analysis indicated an increase of CaV1.3 protein in the Stop/Stop atrium. We suggest that, in contrast to Stop/Stop ventricular CMs, Stop/Stop atrial CMs can compensate the functional loss of the truncated CaV1.2 channel with an upregulation of the CaV1.3 channel.