Abstract: Voltage-gated calcium (Ca2+) channels play a key role in the control of heart contraction and are essential for normal heart development. The Cav1.2 L-type calcium channel is the predominant isoform in cardiomyocytes and is essential for excitation-contraction coupling. Although the inactivation of the Cav1.2 gene caused embryonic lethality before embryonic day E14.5, hearts were contracting before E14 depending on a dihydropyridine-sensitive calcium influx. We analyzed the consequences of the deletion of the Cav1.2 channel on the expression level of other voltage-gated calcium channels in the embryonic mouse heart and isolated cardiomyocytes. A strong compensatory up-regulation of the Cav1.3 calcium channel was observed on the mRNA as well as on the protein level. Reverse transcriptase PCR indicated that the recently identified new Cav1.3(1b) isoform was strongly up-regulated, whereas a more moderate increase was found for the Cav1.3(1a) variant. Heterologous expression of Cav1.3(1b) in HEK293 cells induced Ba2+ currents with properties similar to those found in Cav1.2 (-/-) cardiomyocytes, suggesting that this isoform constitutes a major component of the residual L-type calcium current in Cav1.2 (-/-) cardiomyocytes. In summary, our results imply that calcium channel expression is dynamically regulated during heart development.
development and that the Cav1.3 channel may substitute for Cav1.2 during early embryogenesis.