L-type CaV1.2 calcium channels: from in vitro findings to in vivo function.

The L-type Cav1.2 calcium channel is present throughout the animal kingdom and is essential for some aspects of CNS function, cardiac and smooth muscle contractility, neuroendocrine regulation, and multiple other processes. The L-type CaV1.2 channel is built by up to four subunits; all subunits exist in various splice variants that potentially affect the biophysical and biological functions of the channel. Many of the CaV1.2 channel properties have been analyzed in heterologous expression systems including regulation of the L-type CaV1.2 channel by Ca(2+) itself and protein kinases. However, targeted mutations of the calcium channel genes confirmed only some of these in vitro findings. Substitution of the respective serines by alanine showed that ?-adrenergic upregulation of the cardiac CaV1.2 channel did not depend on the phosphorylation of the in vitro specified amino acids. Moreover, well-established in vitro phosphorylation sites of the CaV?2 subunit of the cardiac L-type CaV1.2 channel were found to be irrelevant for the in vivo regulation of the channel. However, the molecular basis of some kinetic properties, such as Ca(2+)-dependent inactivation and facilitation, has been approved by in vivo mutagenesis of the CaV1.2?1 gene. This article summarizes recent findings on the in vivo relevance of well-established in vitro results.