The Ca(v)1.2 L-type Ca2+ channel is the dominant voltage-activated Ca2+ channel in heart and smooth muscle. The functional significance of this channel was studied in intestinal smooth muscle from mice carrying a smooth muscle-specific, conditional inactivation of the Ca(v)1.2 gene (Ca(v)1.2SMACKO mice). Inactivation was complete within 4 wk after tamoxifen treatment and confirmed by RT-PCR, Western blot and functional analysis. Ca(v)1.2SMACKO mice show reduced feces excretion, absence of rhythmic contractions in small and large intestinal muscle and signs of paralytic ileus. Extracellular field stimulation evoked smaller contractions in jejunum muscles from Ca(v)1.2SMACKO than from CTR mice, whereas carbachol-induced contractions of similar magnitude in both muscles. The Ca2+ needed for contraction in jejunum was provided mainly by Ca(v)1.2 channels and by store-operated channels in muscles from CTR and Ca(v)1.2SMACKO mice, respectively. In conclusion, the Ca(v)1.2 channel is essential for electromechanical coupling and important for pharmaco-mechanical coupling in intestinal smooth muscle and cannot be substituted functionally by other Ca2+ entry pathways.
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