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Post-transcriptional modification modulates Ca_V channel function

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Alternative splicing is an exquisite posttranscriptional mechanism that can be employed to fine-tune Ca^{2+}-depedent regulation of voltage-gated (Ca_V) calcium channels. Here, we show that the generation of splice isoforms via alternative splicing could selectively diversify channel function in subcellular compartments of the neuron.

Alternative splicing of the EF-hand, encoded by exon 37a/b, of the $Ca_V2.1$ P/Q-type channels determines Ca^{2+}/Calmodulin dependent facilitation (CDF). The expression of the mutually exclusive exon 37a/b is developmentally regulated and exhibits selective sub-cellular localization in neurons. The over-expression of transiently transfected $Ca_V2.1_{EFa}$ clones in hippocampal neuron results in pair-pulsed depression while expression of $Ca_V2.1_{EFb}$ clones produced pair-pulsed facilitation.

Post-transcriptional modifications of the C-terminal IQ-domain, encoded by exon 41, of the $Ca_V1.3$ L-type channels however regulate Ca^{2+}-dependent inhibition (CDI). The $Ca_V1.3$ gene is alternatively spliced extensively in particular in the I-II loop regiuons and the C-terminus. The lack of CDI in the $Ca_V1.3$ channels may play an important role in cochlear amplification and activity-dependent transcription in the hair cells or in the pacemaker activity of the suprachiasmatic neurons.