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Voltage-gated calcium channels (Ca_V) in GtoPdb v.2025.3

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Abstract

Ca^{2+} channels are voltage-gated ion channels present in the membrane of most excitable cells. The nomenclature for Ca^{2+}channels was proposed by [136] and **approved by the NC-IUPHAR Subcommittee on Ca^{2+} channels [75]**. Most Ca^{2+} channels form hetero-oligomeric complexes. The α1 subunit is pore-forming and provides the binding site(s) for practically all agonists and antagonists. The 10 cloned α1-subunits can be grouped into three families: (1) the high-voltage activated dihydropyridine-sensitive (L-type, $Ca_V1.x$) channels; (2) the high- to moderate-voltage activated dihydropyridine-insensitive ($Ca_V2.x$) channels and (3) the low-voltage-activated (T-type, $Ca_V3.x$) channels. Each α1 subunit has four homologous repeats (I-IV), each repeat having six transmembrane domains (S1-S6) forming a voltage-sensing domain (VSD, S1-S4) coupled to a pore-forming module (S5, S6 and their connecting linker that contains the selectivity filter. Voltage-dependent gating is driven by voltage-induced transmembrane movements of the S4-helix enabled by conserved positive charges interacting with negative counter-charges within the VSD [74]. All of the α1-subunit genes give rise to alternatively spliced products. At least for high-voltage activated channels, it is likely that native channels comprise co-assemblies of α1, β and α2-δ subunits. CACHD1 is an α2δ-like protein that modulates Ca_v3 channel activity [100]. The γ subunits have not been proven to associate with channels other than the α1s skeletal muscle $Ca_v1.1$ channel. The α2-δ1 and α2-δ2 subunits bind gabapentin and pregabalin [92].

Contents

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