Calcium (voltage-gated)

Overview: Calcium (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 Ertel *et al.* (2000) and approved by the NC-IUPHAR subcommittee on Ca^{2+} channels (Catterall *et al.*, 2005). Ca^{2+} channels form hetero-oligomeric complexes. The α1 subunit is pore-forming and provides the extracellular binding site(s) for practically all agonists and antagonists. The 10 cloned α subunits can be grouped into three families: (i) the high voltage-activated dihydropyridine-sensitive (L-type, $Ca_V1.x$) channels; (ii) the high voltage-activated dihydropyridine-insensitive ($Ca_V2.x$) channels; and (iii) 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 and a pore-forming region between transmembrane domains S5 and S6. Gating is thought to be associated with the membrane-spanning S4 segment, which contains highly conserved positive charges. Many 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. The γ subunits have not been proven to associate with channels other than α1s. The α2–δ1 and α2–δ2 subunits bind gabapentin and pregabalin.

Nomenclature	$Ca_V1.1$	$Ca_V1.2$	$Ca_V1.3$	$Ca_V1.4$	$Ca_V2.1$
Alternative names	L-type, α_{1S}, skeletal muscle L	L-type, α_{1C}, cardiac or smooth muscle L	L-type, α_{1D}	L-type, α_{1F}	P-type, Q-type, α_{1a}
Ensembl ID	ENSG00000081248	ENSG00000151067	ENSG00000157388	ENSG00000102001	ENSG00000141837
Activators	(-)-(*S*)-BayK8644 SZ(+)-(*S*)-202-791 FPL64176	(-)-(*S*)-BayK8644 SZ(+)-(*S*)-202-791 FPL64176	(-)-(*S*)-BayK8644	(-)-(*S*)-BayK8644	
Blockers	Dihydropyridine antagonists, for example nifedipine, diltiazem, verapamil, calciseptine	Dihydropyridine antagonists, for example nifedipine, diltiazem, verapamil, calciseptine	Less sensitive to dihydropyridine antagonists verapamil	Less sensitive to dihydropyridine antagonists	ω-Agatoxin IVA (P: IC_{50} ~ 1 nM) (Q: IC_{50} ~ 90 nM) ω-Agatoxin IVB, ω-Conotoxin, MVIIC
Functional characteristics	High voltage-activated, slow inactivation	High voltage-activated, slow inactivation (Ca^{2+}-dependent)	Low–moderate voltage-activated, slow inactivation (Ca^{2+}-dependent)	Moderate voltage-activated, slow inactivation (Ca^{2+}-independent)	Moderate voltage-activated, moderate inactivation

Nomenclature	$Ca_V2.2$	$Ca_V2.3$	$Ca_V3.1$	$Ca_V3.2$	$Ca_V3.3$
Alternative names	N-type, α_{1B}	R-type, α_{1E}	T-type, α_{1G}	T-type, α_{1H}	T-type, α_{1I}
Ensembl ID	ENSG00000148408	ENSG00000198216	ENSG00000006283	ENSG00000196557	ENSG00000100346
Blockers	ω-Conotoxin GVIA, ω-Conotoxin MVIIC	SNX482 (may not be completely specific), high Ni^{2+}	Mibefradil, low sensitivity to Ni^{2+}, kurtoxin, SB-209712	Mibefradil, high sensitivity to Ni^{2+}, kurtoxin, SB-209712	Mibefradil, low sensitivity to Ni^{2+}, kurtoxin, SB-209712
Functional characteristics	High voltage-activated, moderate inactivation	Moderate voltage-activated, fast inactivation	Low voltage-activated, fast inactivation	Low voltage-activated, fast inactivation	Low voltage-activated, moderate inactivation

In many cell types, P and Q current components cannot be adequately separated, and many researchers in the field have adopted the terminology 'P/Q-type' current when referring to either component. Ziconotide (a synthetic peptide equivalent to ω-conotoxin) has been approved for the treatment of chronic pain (Williams *et al.*, 2008).

Abbreviations: **(-)-(*S*)-SNX482**, 41 amino acid peptide-(GVDKAGCRYMFGGCSVNDDCCPRLGCHSLFSYCAWDLTFSD); **(-)-(*S*)-BAYK8664**, methyl-1,4-dihydro-2,6-dimethyl-3-nitro-4-(2-trifluromethylphenyl)-pyridine-5-carboxylate; **FPL64176**, 2,5-dimethyl-4-[2(phenylmethyl) benzoyl]-H-pyrrole-3-carboxylate; **SB-209712**, (1,6,bis{1-[4-(3-phenylpropyl)piperidinyl]}hexane); **SZ(+)-(*S*)-202-791**, isopropyl 4-(2,1,3-benzoxadiazol-4-yl)-1,4-dihydro-2,6-dimethyl-5-nitro-3-pyridinecarboxylate

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