Channel name	$Ca_V2.2$
Description	voltage-gated calcium channel α_1 subunit
Other names	N-type, α_{1B}; rbB-I, rbB-II (in rat)[1,2], BIII (in rabbit)[3]
Molecular information	human: 2339aa, M94172, 2237aa, M94173 (ref. 4), chr. 9q34, *CACN1B* rat: 2336aa, M92905 (ref. 1) mouse: 2329aa, NM007579, NP031605
Associated subunits	$\alpha_2\delta/\beta_1$, β_3, β_4 (ref. 5) possibly γ
Functional assays	voltage clamp, patch clamp, calcium imaging, neurotransmitter release, ^{45}Ca uptake into synaptosomes
Current	$I_{Ca,N}$
Conductance	20pS (bullfrog sympathetic neurones)[6]; 14.3pS (rabbit BIII cDNA in skeletal muscle myotubes)[3]
Ion selectivity	$Ba^{2+} > Ca^{2+}$
Activation	V_a = +7.8mV, τ_a = 3ms at +10mV (human $\alpha_{1B}/\alpha_2\delta/\beta_{1\text{-}3}$ in HEK 293 cells, 15mM Ba^{2+} charge carrier)[4,7]; V_a = +9.7mV, τ_a = 2.8ms at +20mV (rat $\alpha_{1B\text{-}II}/\beta_{1b}$, in *Xenopus* oocytes, 40mM Ba^{2+} charge carrier)[2]
Inactivation	V_h = −61mV, τ_h ~200ms at +10mV (human $\alpha_{1B}/\alpha_2\delta/\beta_{1\text{-}3}$ in HEK 293 cells, 15mM Ba^{2+} charge carrier)[4,7]; V_h = −67.5mV; τ_h = 112ms at +20mV (rat $\alpha_{1B\text{-}II}/\beta_{1b}$ in *Xenopus* oocytes, 40mM Ba^{2+})[2]
Activators	none
Gating inhibitors	none
Blockers	ω-conotoxin GVIA (1–2μM, irreversible block) , ω-conotoxin MVIIA (SNX-111, ziconotide), ω-conotoxin MVIIC (ref. 8)
Radioligands	[^{125}I]-ω-conotoxin GVIA (K_d = 55pM, human $\alpha_{1B}/\alpha_2\delta/\beta_{1\text{-}3}$ in HEK 293 cells)[4]
Channel distribution	neurones (presynaptic terminals, dendrites, cell bodies)[9]
Physiological functions	peptide toxins that selectively inhibit N-type channels block a significant fraction of neurotransmission release in the mammalian peripheral and central nervous systems (ref. 10)
Mutations and pathophysiology	differing reports exist: mice lacking a functional $Ca_V2.2$ gene exhibit a normal life span and no detectable behavioural modifications compared to wild type, but possess an increase in basal mean atrial pressure and other functional alterations to the sympathetic nervous system[11]; approx. 1/3 of mice lacking a functional $Ca_V2.2$ gene did not survive to weaning but surviving animals were normal except for a decrease in anxiety-related behaviour and a suppression of inflammatory and neuropathic pain responses[12]; no point mutations in the native $Ca_V2.2$. gene have been reported to date

Pharmacological significance

in rats, intrathecal administration of ω-conotoxin GVIA or ω-conotoxin MVIIA shows strong effects on inflammatory pain, post-surgical pain, thermal hyperalgesia and mechanical allodynia[13–15]; in humans, intrathecal administration of SNX-111 (ziconotide, synthetic ω-conotoxin MVIIA) to patients unresponsive to intrathecal opiates significantly reduced pain scores and in a number of specific instances resulted in relief after many years of continuous pain[16]

Comments

In case studies, ziconotide has been examined for usefulness in the management of intractable spasticity following spinal cord injury in patients unresponsive to baclofen and morphine[17]. Side effects of intrathecal administration of ziconotide include nystagmus, sedation, confusion, auditory and visual hallucinations, severe agitation and unruly behaviour[18]. Intravenous administration of ziconotide to humans results in significant orthostatic hypotension[19]

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