**Channel name**  
CaV2.2

**Description**  
voltage-gated calcium channel α subunit

**Other names**  
N-type, α1B; 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**  
α₂δ/β₁, β₃, β₄ (ref. 5) possibly γ

**Functional assays**  
voltage clamp, patch clamp, calcium imaging, neurotransmitter release, \(^4\)!Ca uptake into synaptosomes

**Current**  
\(I_{CaN}\)

**Conductance**  
20pS (bullfrog sympathetic neurones)\(^6\); 14.3pS (rabbit BIII cDNA in skeletal muscle myotubes)\(^3\)

**Ion selectivity**  
\(Ba^{2+} > Ca^{2+}\)

**Activation**  
\(V_\alpha = +7.8mV, \tau_\alpha = 3ms \text{ at } +10mV \) (human α₁B/α₂δ/β₁, in HEK 293 cells, 15mM Ba\(^{2+}\) charge carrier)\(^4,5\);  
\(V_\alpha = +9.7mV, \tau_\alpha = 2.8ms \text{ at } +20mV \) (rat α₁B/β₁, in Xenopus oocytes, 40mM Ba\(^{2+}\) charge carrier)\(^2\)

**Inactivation**  
\(V_\text{h} = -61mV, \tau_\text{h} = -200ms \text{ at } +10mV \) (human α₁B/α₂δ/β₁, in HEK 293 cells, 15mM Ba\(^{2+}\) charge carrier)\(^4,5\);  
\(V_\text{h} = -67.5mV, \tau_\text{h} = 112ms \text{ at } +20mV \) (rat α₁B/β₁, in Xenopus oocytes, 40mM Ba\(^{2+}\) charge carrier)\(^2\)

**Activators**  
none

**Gating inhibitors**  
none

**Blockers**  
\(\omega\)-conotoxin GVIA (1–2µM, irreversible block), \(\omega\)-conotoxin MVIIA (SNX-111, ziconotide), \(\omega\)-conotoxin MVIIIC (ref. 8)

**Radioligands**  
\([^\text{[125I]}\]-\(\omega\)-conotoxin GVIA (K\(_d\) = 55pM, human α₁B/α₂δ/β₁, in HEK 293 cells)\(^9\)

**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 CaV2.2 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\(^1,2\); approx. 1/3 of mice lacking a functional CaV2.2 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\(^2\); no point mutations in the native CaV2.2 gene have been reported to date

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**Pharmacological significance**

In rats, intrathecal administration of \(\omega\)-conotoxin GVIA or \(\omega\)-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 \(\omega\)-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\(^{19}\).

**REFERENCES**


