Cyclic nucleotide-regulated channels (CNG) in GtoPdb v.2023.1

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Abstract

Cyclic nucleotide-gated (CNG) channels are responsible for signalling in the primary sensory cells of the vertebrate visual and olfactory systems. CNG channels are voltage-independent cation channels formed as tetramers. Each subunit has 6TM, with the pore-forming domain between TM5 and TM6. CNG channels were first found in rod photoreceptors [83, 120], where light signals through rhodopsin and transducin to stimulate phosphodiesterase and reduce intracellular cyclic GMP level. This results in a closure of CNG channels and a reduced ‘dark current’. Similar channels were found in the cilia of olfactory neurons [181] and the pineal gland [71]. The cyclic nucleotides bind to a domain in the C terminus of the subunit protein: other channels directly binding cyclic nucleotides include hyperpolarisation-activated, cyclic nucleotide-gated channels (HCN), ether-a-go-go and certain plant potassium channels.

The HCN channels are cation channels that are activated by hyperpolarisation at voltages negative to ~50 mV. The cyclic nucleotides cyclic AMP and cyclic GMP directly bind to the cyclic nucleotide-binding domain of HCN channels and shift their activation curves to more positive voltages, thereby enhancing channel activity. HCN channels underlie pacemaker currents found in many excitable cells including cardiac cells and neurons [65, 192]. In native cells, these currents have a variety of names, such as $I_h$, $I_q$ and $I_f$. The four known HCN channels have six transmembrane domains and form tetramers. It is believed that the channels can form heteromers with each other, as has been shown for HCN1 and HCN4 [2]. High resolution structural studies of CNG and HCN channels has provided insight into the the gating processes of these channels [139, 146, 140]. A standardised nomenclature for CNG and HCN channels has been proposed by the NC-IUPHAR Subcommittee on voltage-gated ion channels [108].

Contents

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**Database links**

**Cyclic nucleotide-regulated channels (CNG)**
https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=71

**Introduction to Cyclic nucleotide-regulated channels (CNG)**
https://www.guidetopharmacology.org/GRAC/FamilyIntroductionForward?familyId=71

**Channels and Subunits**
- **CNGA1**
  https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=394
- **CNGA2**
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- **CNGA3**
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- **HCN4**
  https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=403

**References**


51. Chen TY, Illing M, Molday LL, Hsu YT, Yau KW and Molday RS. (1994) Subunit 2 (or beta) of retinal rod cGMP-gated cation channel is a component of the 240-kDa channel-associated protein and mediates
cGMP-gated cation channel is a component of the 240-kDa channel-associated protein and mediates
Ca(2+)-calmodulin modulation. *Proc Natl Acad Sci USA* **91**: 11757-61 [PMID:7526403]


pacemaker channel HCN1 with filamin A. J Biol Chem 279: 43847-53 [PMID:15292205]
115. Jenkins PM, Zhang L, Thomas G and Martens JR. (2009) PACS-1 mediates phosphorylation-dependent


147. Liman ER and Buck LB. (1994) A second subunit of the olfactory cyclic nucleotide-gated channel confers high sensitivity to cAMP. Neuron 13: 611-21 [PMID:7522482]


Role of subunit heteromerization and N-linked glycosylation in the formation of functional neuronal tissues.


gated channels. Neuron 42: 401-10 [PMID:15134637]


214. Santoro B, Grant SG, Bartsch D and Kandel ER. (1997) Interactive cloning with the SH3 domain of N-src identifies a new brain specific ion channel protein, with homology to eag and cyclic nucleotide-gated channels. Proc Natl Acad Sci USA 94: 14815-20 [PMID:9405696]


216. Santoro B, Lee JY, Englot DJ, Gildersleeve S, Piskorowski RA, Siegelbaum SA, Winawer MR and...


Selvakumar D, Drescher MJ and Drescher DG. (2013) Cyclic nucleotide-gated channel α-3 (CNGA3) interacts with stereocilia tip-link cadherin 23 + exon 68 or alternatively with myosin VIIa, two proteins required for hair cell mechanotransduction. *J Biol Chem* **288**: 7215-29 [PMID:23329832]


256. Wei JY, Cohen ED and Barnstable CJ. (1997) Direct blockade of both cloned rat rod photoreceptor cyclic

nucleotide-gated non-selective cation (CNG) channel alpha-subunit and native CNG channels from Xenopus rod outer segments by H-8, a non-specific cyclic nucleotide-dependent protein kinase inhibitor. *Neurosci Lett* **233**: 37-40 [PMID:9324234]


275. Zagotta WN, Olivier NB, Black KD, Young EC, Olson R and Gouaux E. (2003) Structural basis for


