

Ligand-gated ion channels in GtoPdb v.2025.3

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11. Salk Institute, USA
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Abstract

Ligand-gated ion channels (LGICs) are integral membrane proteins that contain a pore which allows the regulated flow of selected ions across the plasma membrane. Ion flux is passive and driven by the electrochemical gradient for the permeant ions. These channels are open, or gated, by the binding of

a neurotransmitter to an orthosteric site(s) that triggers a conformational change that results in the conducting state. Modulation of gating can occur by the binding of endogenous, or exogenous, modulators to allosteric sites. LGICs mediate fast synaptic transmission, on a millisecond time scale, in the nervous system and at the somatic neuromuscular junction. Such transmission involves the release of a neurotransmitter from a pre-synaptic neurone and the subsequent activation of post-synaptically located receptors that mediate a rapid, phasic, electrical signal (the excitatory, or inhibitory, post-synaptic potential). However, in addition to their traditional role in phasic neurotransmission, it is now established that some LGICs mediate a tonic form of neuronal regulation that results from the activation of extra-synaptic receptors by ambient levels of neurotransmitter. The expression of some LGICs by non-excitabile cells is suggestive of additional functions.

By convention, the LGICs comprise the excitatory, cation-selective, nicotinic acetylcholine [959, 210], 5-HT₃ [68, 1441], ionotropic glutamate [856, 1375] and P2X receptors [659, 1330] and the inhibitory, anion-selective, GABA_A [1066, 83] and glycine receptors [878, 1539]. The nicotinic acetylcholine, 5-HT₃, GABA_A and glycine receptors (and an additional zinc-activated channel) are pentameric structures and are frequently referred to as the Cys-loop receptors due to the presence of a defining loop of residues formed by a disulphide bond in the extracellular domain of their constituent subunits [966, 1357]. However, the prokaryotic ancestors of these receptors contain no such loop and the term pentameric ligand-gated ion channel (pLGIC) is gaining acceptance in the literature [573]. The ionotropic glutamate and P2X receptors are tetrameric and trimeric structures, respectively. Multiple genes encode the subunits of LGICs and the majority of these receptors are heteromultimers. Such combinational diversity results, within each class of LGIC, in a wide range of receptors with differing pharmacological and biophysical properties and varying patterns of expression within the nervous system and other tissues. The LGICs thus present attractive targets for new therapeutic agents with improved discrimination between receptor isoforms and a reduced propensity for off-target effects. The development of novel, faster screening techniques for compounds acting on LGICs [359] will greatly aid in the development of such agents.

Contents

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[GtoPdb](#) is an expert-driven guide to pharmacological targets and the substances that act on them. GtoPdb is a reference work which is most usefully represented as an on-line database. As in any publication this work should be appropriately cited, and the papers it cites should also be recognized. This document provides a citation for the relevant parts of the database, and also provides a reference list for the research cited by those parts. For further details see [175].

Please note that the database version for the citations given in GtoPdb are to the most recent preceding version in which the family or its subfamilies and targets were substantially changed. The links below are to the current version. If you need to consult the cited version, rather than the most recent version, please contact the GtoPdb curators.

Database links

Ligand-gated ion channels

<https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=697>

5-HT₃ receptors

<https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=68>

Introduction to 5-HT₃ receptors

<https://www.guidetopharmacology.org/GRAC/FamilyIntroductionForward?familyId=68>

Channels and Subunits

Complexes

5-HT₃AB

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=378>

5-HT₃A

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=379>

Subunits

5-HT₃A

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=373>

5-HT₃B

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=374>

5-HT₃C

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=375>

5-HT₃D

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=376>

5-HT₃E

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=377>

Acid-sensing (proton-gated) ion channels (ASICs)

<https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=118>

Channels and Subunits

ASIC1

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=684>

ASIC2

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=685>

ASIC3

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=686>

Epithelial sodium channel (ENaC)

<https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=122>

Introduction to Epithelial sodium channel (ENaC)

<https://www.guidetopharmacology.org/GRAC/FamilyIntroductionForward?familyId=122>

Channels and Subunits

Complexes

ENaC $\alpha\beta\gamma$

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=742>

Subunits

ENaC α

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=738>

ENaC β

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=739>

ENaC γ

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=741>

ENaC δ

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=740>

GABA_A receptors

<https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=72>

Introduction to GABA_A receptors

<https://www.guidetopharmacology.org/GRAC/FamilyIntroductionForward?familyId=72>

Channels and Subunits

GABA_A receptor $\alpha 1$ subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=404>

GABA_A receptor $\alpha 2$ subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=405>

GABA_A receptor $\alpha 3$ subunit

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GABA_A receptor $\alpha 4$ subunit

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GABA_A receptor $\alpha 5$ subunit

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GABA_A receptor $\alpha 6$ subunit

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GABA_A receptor $\beta 1$ subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=410>

GABA_A receptor $\beta 2$ subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=411>

GABA_A receptor $\beta 3$ subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=412>

GABA_A receptor $\gamma 1$ subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=413>

GABA_A receptor $\gamma 2$ subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=414>

GABA_A receptor $\gamma 3$ subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=415>

GABA_A receptor δ subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=416>

GABA_A receptor ε subunit

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GABA_A receptor θ subunit

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GABA_A receptor π subunit

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GABA_A receptor ρ1 subunit

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GABA_A receptor ρ2 subunit

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GABA_A receptor ρ3 subunit

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Glycine receptors

<https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=73>

Introduction to Glycine receptors

<https://www.guidetopharmacology.org/GRAC/FamilyIntroductionForward?familyId=73>

Channels and Subunits

Complexes

Glycine Receptor (All subtypes)

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=428>

Subunits

glycine receptor α1 subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=423>

glycine receptor α2 subunit

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glycine receptor α3 subunit

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glycine receptor α4 subunit (*pseudogene in humans*)

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=426>

glycine receptor β subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=427>

Ionotropic glutamate receptors

<https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=75>

Channels and Subunits

GluA1

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=444>

GluA2

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=445>

GluA3

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=446>

GluA4

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=447>

GluD1

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=448>

GluD2

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=449>

GluK1

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=450>

GluK2

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=451>

GluK3

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=452>

GluK4

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=453>

GluK5

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GluN1

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=455>

GluN2A

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=456>

GluN2B

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GluN2C

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=458>

GluN2D

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GluN3A

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GluN3B

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IP₃ receptors

<https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=123>

Channels and Subunits

IP₃R1

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=743>

IP₃R2

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=744>

IP₃R3

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=745>

Nicotinic acetylcholine receptors (nACh)

<https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=76>

Introduction to Nicotinic acetylcholine receptors (nACh)

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Channels and Subunits

nicotinic acetylcholine receptor α 1 subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=462>

nicotinic acetylcholine receptor α 2 subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=463>

nicotinic acetylcholine receptor α 3 subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=464>

nicotinic acetylcholine receptor α 4 subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=465>

nicotinic acetylcholine receptor α 5 subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=466>

nicotinic acetylcholine receptor α 6 subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=467>

nicotinic acetylcholine receptor α 7 subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=468>

nicotinic acetylcholine receptor α 8 subunit (avian)

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=752>

nicotinic acetylcholine receptor α 9 subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=469>

nicotinic acetylcholine receptor α 10 subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=470>

nicotinic acetylcholine receptor β 1 subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=471>

nicotinic acetylcholine receptor β 2 subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=472>

nicotinic acetylcholine receptor β 3 subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=473>

nicotinic acetylcholine receptor β 4 subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=474>

nicotinic acetylcholine receptor γ subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=475>

nicotinic acetylcholine receptor δ subunit

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=476>

nicotinic acetylcholine receptor ϵ subunit

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P2X receptors

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Introduction to P2X receptors

<https://www.guidetopharmacology.org/GRAC/FamilyIntroductionForward?familyId=77>

Channels and Subunits

P2X1

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=478>

P2X2

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P2X3

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P2X4

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P2X5

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P2X6

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P2X7

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ZAC

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Introduction to ZAC

<https://www.guidetopharmacology.org/GRAC/FamilyIntroductionForward?familyId=83>

Channels and Subunits

ZAC

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=587>

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