Glycine receptors in GtoPdb v.2021.3

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Abstract

The inhibitory glycine receptor (nomenclature as agreed by the NC-IUPHAR Subcommittee on Glycine Receptors) is a member of the Cys-loop superfamily of transmitter-gated ion channels that includes the zinc activated channels, GABA_A, nicotinic acetylcholine and 5-HT_3 receptors and Zn²⁺-activated channels. The receptor is expressed either as a homo-pentamer of α subunits, or a complex now thought to harbour 2α and 3ß subunits [33, 7], that contain an intrinsic anion channel. Four differentially expressed isoforms of the α-subunit (α1-α4) and one variant of the β-subunit (β1, GLRB, P48167) have been identified by genomic and cDNA cloning. Further diversity originates from alternative splicing of the primary gene transcripts for α1 (α1INS and α1del), α2 (α2A and α2B), α3 (α3S and α3L) and β (βΔ7) subunits and by mRNA editing of the α2 and α3 subunit [83, 93, 21]. Both α2 splicing and α3 mRNA editing can produce subunits (i.e., α2B and α3P185L) with enhanced agonist sensitivity. Predominantly, the adult form of the receptor contains α1 (or α3) and β subunits whereas the immature form is mostly composed of only α2 subunits. The α4 subunit is a pseudogene in humans. High resolution molecular structures are available for the a1 and a3 homomeric receptors [50, 20]. As in other Cys-loop receptors, the orthosteric binding site for agonists and the competitive antagonist strychnine is formed at the interfaces between the subunits’ extracellular domains. Inclusion of the β-subunit in the pentameric glycine receptor contributes to agonist binding, reduces single channel conductance and alters pharmacology. The β-subunit also anchors the receptor, via an amphipathic sequence within the large intracellular loop region, to gephyrin. This a cytoskeletal attachment protein that binds to a number of subsynaptic proteins involved in cytoskeletal structure and thus clusters and anchors hetero-oligomeric receptors to the synapse [56, 54, 88]. G protein βγ subunits enhance the open state probability of native and recombinant glycine receptors by association with domains within the large intracellular loop [124, 123]. Intracellular chloride concentration modulates the kinetics of native and recombinant glycine receptors [96]. Intracellular Ca²⁺ appears to increase native and recombinant glycine receptor affinity, prolonging channel open events, by a mechanism that does not involve phosphorylation [27]. Extracellular Zn²⁺ potentiates GlyR function at nanomolar concentrations [86], and causes inhibition at higher micromolar concentrations (17).

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Database links

Glycine receptors
https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=73
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https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=426
glycine receptor β subunit
https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=427

References


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