5-HT₃ receptors (version 2019.4) in the IUPHAR/BPS Guide to Pharmacology Database

Nicholas M. Barnes¹, Tim G. Hales², Sarah C. R. Lummis³, Beate Niesler⁴ and John A. Peters²

1. University of Birmingham, UK
2. University of Dundee, UK
3. University of Cambridge, UK
4. University of Heidelberg, Germany

Abstract

The 5-HT₃ receptor (nomenclature as agreed by the NC-IUPHAR Subcommittee on 5-Hydroxytryptamine (serotonin) receptors [66]) is a ligand-gated ion channel of the Cys-loop family that includes the zinc-activated channels, nicotinic acetylcholine, GABAₐ and strychnine-sensitive glycine receptors. The receptor exists as a pentamer of 4TM subunits that form an intrinsic cation selective channel [5]. Five human 5-HT₃ receptor subunits have been cloned and homo-oligomeric assemblies of 5-HT₃A and hetero-oligomeric assemblies of 5-HT₃A and 5-HT₃B subunits have been characterised in detail. The 5-HT₃C (HTR3C, Q8WXA8), 5-HT₃D (HTR3D, Q70Z44) and 5-HT₃E (HTR3E, A5X5Y0) subunits [83, 122], like the 5-HT₃B subunit, do not form functional homomers, but are reported to assemble with the 5-HT₃A subunit to influence its functional expression rather than pharmacological profile [124, 63, 157]. 5-HT₃A, -C, -D, and -E subunits also interact with the chaperone RIC-3 which predominantly enhances the surface expression of homomeric 5-HT₃A receptor [157]. The co-expression of 5-HT₃A and 5-HT₃C-E subunits has been demonstrated in human colon [82]. A recombinant hetero-oligomeric 5-HT₃AB receptor has been reported to contain two copies of the 5-HT₃A subunit and three copies of the 5-HT₃B subunit in the order B-B-A-B-A [7], but this is inconsistent with recent reports which show at least one A-A interface [96, 150]. The 5-HT₃B subunit imparts distinctive biophysical properties upon hetero-oligomeric 5-HT₃AB versus homo-oligomeric 5-HT₃A recombinant receptors [32, 41, 56, 85, 139, 129, 79], influences the potency of channel blockers, but generally has only a modest effect upon the apparent affinity of agonists, or the affinity of antagonists ([17], but see [41, 30, 35]) which may be explained by the orthosteric binding site residing at an interface formed between 5-HT₃A subunits [96, 150]. However, 5-HT₃A and 5-HT₃AB receptors differ in their allosteric regulation by some general anaesthetic agents, small alcohols and indoles [138, 135, 71]. The potential diversity of 5-HT₃ receptors is increased by alternative splicing of the genes HTR3A and E [64, 19, 124, 123, 120]. In addition, the use of tissue-specific promoters driving expression from different transcriptional start sites has been reported for the HTR3A, HTR3B, HTR3D and HTR3E genes, which could result in 5-HT₃ subunits harbouring different N-termini [152, 79, 120]. To date, inclusion of the 5-HT₃A subunit appears imperative for 5-HT₃ receptor function.

Contents

This is a citation summary for 5-HT₃ receptors in the Guide to Pharmacology database (GtoPdb). It exists purely
as an adjunct to the database to facilitate the recognition of citations to and from the database by citation analyzers. Readers will almost certainly want to visit the relevant sections of the database which are given here under database links.

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.

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

5-HT\(_3\) receptors
http://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=68

Introduction to 5-HT\(_3\) receptors
http://www.guidetopharmacology.org/GRAC/FamilyIntroductionForward?familyId=68

Channels and Subunits

Complexes
5-HT\(_3\)AB
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=378

5-HT\(_3\)A
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=379

Subunits
5-HT\(_3\)A
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=373

5-HT\(_3\)B
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=374

5-HT\(_3\)C
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=375

5-HT\(_3\)D
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=376

5-HT\(_3\)E
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=377

References


97. Lummis SC, Thompson AJ, Bencherif M and Lester HA. (2011) Varenicline is a potent agonist of the


134. Solt K, Stevens RJ, Davies PA and Raines DE. (2005) General anesthetic-induced channel gating...
enhancement of 5-hydroxytryptamine type 3 receptors depends on receptor subunit composition. J. Pharmacol. Exp. Ther. 315: 771-6 [PMID:16081679]


166. Zhou Q, Verdoorn TA and Lovinger DM. (1998) Alcohols potentiate the function of 5-HT3 receptor-channels on NCB-20 neuroblastoma cells by favouring and stabilizing the open channel state. *J. Physiol. (Lond.)* **507 ( Pt 2)**: 335-52 [PMID:9518697]