

## Thyrotropin-releasing hormone receptors in GtoPdb v.2023.1

Anthony P. Davenport<sup>1</sup>, Marvin Gershengorn<sup>2</sup> and Rebecca Hills<sup>3</sup>

1. University of Cambridge, UK
2. National Institutes of Health, USA
3. University of Edinburgh, UK

### Abstract

Thyrotropin-releasing hormone (TRH) receptors (**provisional nomenclature as recommended by NC-IUPHAR [14]**) are activated by the endogenous tripeptide TRH (pGlu-His-ProNH<sub>2</sub>). TRH and TRH analogues fail to distinguish TRH<sub>1</sub> and TRH<sub>2</sub> receptors [29]. [<sup>3</sup>H]TRH (human, mouse, rat) is able to label both TRH<sub>1</sub> and TRH<sub>2</sub> receptors with K<sub>d</sub> values of 13 and 9 nM respectively. Synthesis and biology of ring-modified L-Histidine containing TRH analogues has been reported [23].

### Contents

This is a citation summary for Thyrotropin-releasing hormone 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. For further details see [4].

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

[Thyrotropin-releasing hormone receptors](#)

<https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=63>

[Introduction to Thyrotropin-releasing hormone receptors](#)

<https://www.guidetopharmacology.org/GRAC/FamilyIntroductionForward?familyId=63>

Receptors

[TRH<sub>1</sub> receptor](#)

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=363>

[TRH<sub>2</sub> receptor](#)

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=754>

## References

1. Aragay AM, Katz A and Simon MI. (1992) The G alpha q and G alpha 11 proteins couple the thyrotropin-releasing hormone receptor to phospholipase C in GH3 rat pituitary cells. *J Biol Chem* **267**: 24983-8 [PMID:1334076]
2. Boler J, Enzmann F, Folkers K, Bowers CY and Schally AV. (1969) The identity of chemical and hormonal properties of the thyrotropin releasing hormone and pyroglutamyl-histidyl-proline amide. *Biochem Biophys Res Commun* **37**: 705-10 [PMID:4982117]
3. Bonomi M, Busnelli M, Beck-Peccoz P, Costanzo D, Antonica F, Dolci C, Pilotta A, Buzi F and Persani L. (2009) A family with complete resistance to thyrotropin-releasing hormone. *N Engl J Med* **360**: 731-4 [PMID:19213692]
4. Buneman P, Christie G, Davies JA, Dimitrellou R, Harding SD, Pawson AJ, Sharman JL and Wu Y. (2020) Why data citation isn't working, and what to do about it *Database* **2020** [PMID:32367113]
5. Burgus R, Dunn TF, Desiderio D, Ward DN, Vale W and Guillemin R. (1970) Characterization of ovine hypothalamic hypophysiotropic TSH-releasing factor. *Nature* **226**: 321-5 [PMID:4985794]
6. Calzá L, Giardino L, Ceccatelli S, Zanni M, Elde R and Hökfelt T. (1992) Distribution of thyrotropin-releasing hormone receptor messenger RNA in the rat brain: an in situ hybridization study. *Neuroscience* **51**: 891-909 [PMID:1488129]
7. Cao J, O'Donnell D, Vu H, Payza K, Pou C, Godbout C, Jakob A, Pelletier M, Lembo P and Ahmad S *et al.* (1998) Cloning and characterization of a cDNA encoding a novel subtype of rat thyrotropin-releasing hormone receptor. *J Biol Chem* **273**: 32281-7 [PMID:9822707]
8. Collu R, Tang J, Castagné J, Lagacé G, Masson N, Huot C, Deal C, Delvin E, Faccenda E and Eidne KA *et al.* (1997) A novel mechanism for isolated central hypothyroidism: inactivating mutations in the thyrotropin-releasing hormone receptor gene. *J Clin Endocrinol Metab* **82**: 1561-5 [PMID:9141550]
9. de la Peña P, Delgado LM, del Camino D and Barros F. (1992) Cloning and expression of the thyrotropin-releasing hormone receptor from GH3 rat anterior pituitary cells. *Biochem J* **284 ( Pt 3)**: 891-9 [PMID:1377915]
10. Drummond AH, Hughes PJ, Ruiz-Larrea F and Joels LA. (1989) Use of receptor antagonist in elucidating the mechanism of action of TRH in GH3 cells. *Ann N Y Acad Sci* **553**: 197-204 [PMID:2566295]
11. Duthie SM, Taylor PL, Anderson L, Cook J and Eidne KA. (1993) Cloning and functional characterisation of the human TRH receptor. *Mol Cell Endocrinol* **95**: R11-5 [PMID:8243797]
12. Engel S, Neumann S, Kaur N, Monga V, Jain R, Northup J and Gershengorn MC. (2006) Low affinity analogs of thyrotropin-releasing hormone are super-agonists. *J Biol Chem* **281**: 13103-9 [PMID:16551618]
13. Engel S, Skoumbourdis AP, Childress J, Neumann S, Deschamps JR, Thomas CJ, Colson AO, Costanzi S and Gershengorn MC. (2008) A virtual screen for diverse ligands: discovery of selective G protein-coupled receptor antagonists. *J Am Chem Soc* **130**: 5115-23 [PMID:18357984]
14. Foord SM, Bonner TI, Neubig RR, Rosser EM, Pin JP, Davenport AP, Spedding M and Harmar AJ. (2005) International Union of Pharmacology. XLVI. G protein-coupled receptor list. *Pharmacol Rev* **57**: 279-88 [PMID:15914470]
15. Geras-Raaka E and Gershengorn MC. (1987) Measurement of changes in cellular calcium metabolism in response to thyrotropin-releasing hormone. *Meth Enzymol* **141**: 36-53 [PMID:3110553]
16. Gershengorn MC and Osman R. (1996) Molecular and cellular biology of thyrotropin-releasing hormone receptors. *Physiol Rev* **76**: 175-91 [PMID:8592728]
17. Harder S, Lu X, Wang W, Buck F, Gershengorn MC and Bruhn TO. (2001) Regulator of G protein signaling 4 suppresses basal and thyrotropin releasing-hormone (TRH)-stimulated signaling by two mouse TRH receptors, TRH-R(1) and TRH-R(2). *Endocrinology* **142**: 1188-94 [PMID:11181534]
18. Hollenberg AN. (2008) The role of the thyrotropin-releasing hormone (TRH) neuron as a metabolic sensor. *Thyroid* **18**: 131-9 [PMID:18279013]
19. Hsieh KP and Martin TF. (1992) Thyrotropin-releasing hormone and gonadotropin-releasing hormone receptors activate phospholipase C by coupling to the guanosine triphosphate-binding proteins Gq and G11. *Mol Endocrinol* **6**: 1673-81 [PMID:1333052]
20. Imai A and Gershengorn MC. (1987) Measurement of lipid turnover in response to thyrotropin-releasing hormone. *Meth Enzymol* **141**: 100-1 [PMID:3037241]
21. Itadani H, Nakamura T, Itoh J, Iwaasa H, Kanatani A, Borkowski J, Ihara M and Ohta M. (1998) Cloning

- and characterization of a new subtype of thyrotropin-releasing hormone receptors. *Biochem Biophys Res Commun* **250**: 68-71 [PMID:9735333]
22. Matre V, Karlsten HE, Wright MS, Lundell I, Fjeldheim AK, Gabrielsen OS, Larhammar D and Gautvik KM. (1993) Molecular cloning of a functional human thyrotropin-releasing hormone receptor. *Biochem Biophys Res Commun* **195**: 179-85 [PMID:8395824]
  23. Meena CL, Thakur A, Nandekar PP, Sharma SS, Sangamwar AT and Jain R. (2016) Synthesis and biology of ring-modified l-Histidine containing thyrotropin-releasing hormone (TRH) analogues. *Eur J Med Chem* **111**: 72-83 [PMID:26854379]
  24. O'Dowd BF, Lee DK, Huang W, Nguyen T, Cheng R, Liu Y, Wang B, Gershengorn MC and George SR. (2000) TRH-R2 exhibits similar binding and acute signaling but distinct regulation and anatomic distribution compared with TRH-R1. *Mol Endocrinol* **14**: 183-93 [PMID:10628757]
  25. Perret G, Valensi P, Hugues JN, Vassy R and Uzzan B. (1988) Use of a pharmacokinetic model to characterize the thyrotropin (TSH) and prolactin (PRL) response to thyrotropin-releasing hormone (THR) in man. *Methods Find Exp Clin Pharmacol* **10**: 387-91 [PMID:3137402]
  26. Rabeler R, Mittag J, Geffers L, R  ther U, Leitges M, Parlow AF, Visser TJ and Bauer K. (2004) Generation of thyrotropin-releasing hormone receptor 1-deficient mice as an animal model of central hypothyroidism. *Mol Endocrinol* **18**: 1450-60 [PMID:14988432]
  27. Regard JB, Sato IT and Coughlin SR. (2008) Anatomical profiling of G protein-coupled receptor expression. *Cell* **135**: 561-71 [PMID:18984166]
  28. Straub RE, Frech GC, Joho RH and Gershengorn MC. (1990) Expression cloning of a cDNA encoding the mouse pituitary thyrotropin-releasing hormone receptor. *Proc Natl Acad Sci USA* **87**: 9514-8 [PMID:2175902]
  29. Sun Y, Lu X and Gershengorn MC. (2003) Thyrotropin-releasing hormone receptors -- similarities and differences. *J Mol Endocrinol* **30**: 87-97 [PMID:12683933]
  30. Sun Y, Zupan B, Raaka BM, Toth M and Gershengorn MC. (2009) TRH-receptor-type-2-deficient mice are euthyroid and exhibit increased depression and reduced anxiety phenotypes. *Neuropsychopharmacology* **34**: 1601-8 [PMID:19078951]
  31. Taylor RL and Burt DR. (1981) Preparation of 3H-[3-M3-His2]TRH as an improved ligand for TRH receptors. *Neuroendocrinology* **32**: 310-6 [PMID:6264336]
  32. Thirunarayanan N, Nir EA, Raaka BM and Gershengorn MC. (2013) Thyrotropin-releasing hormone receptor type 1 (TRH-R1), not TRH-R2, primarily mediates taltirelin actions in the CNS of mice. *Neuropsychopharmacology* **38**: 950-6 [PMID:23303050]
  33. Thirunarayanan N, Raaka BM and Gershengorn MC. (2012) Taltirelin is a superagonist at the human thyrotropin-releasing hormone receptor. *Front Endocrinol (Lausanne)* **3**: 120 [PMID:23087672]
  34. Vale W, Rivier J and Burgus R. (1971) Synthetic TRF (thyrotropin releasing factor) analogues. II. pGlu-N3imMe-His-Pro-NH2: a synthetic analogue with specific activity greater than that of TRF2. *Endocrinology* **89**: 1485-8 [PMID:5001013]
  35. Wang W and Gershengorn MC. (1999) Rat TRH receptor type 2 exhibits higher basal signaling activity than TRH receptor type 1. *Endocrinology* **140**: 4916-9 [PMID:10499553]
  36. Zabavnik J, Arbuthnott G and Eidne KA. (1993) Distribution of thyrotrophin-releasing hormone receptor messenger RNA in rat pituitary and brain. *Neuroscience* **53**: 877-87 [PMID:8387653]
  37. Zeng H, Schimpf BA, Rohde AD, Pavlova MN, Gragerov A and Bergmann JE. (2007) Thyrotropin-releasing hormone receptor 1-deficient mice display increased depression and anxiety-like behavior. *Mol Endocrinol* **21**: 2795-804 [PMID:17666589]
  38. Zhao D, Yang J, Jones KE, Gerald C, Suzuki Y, Hogan PG, Chin WW and Tashjian Jr AH. (1992) Molecular cloning of a complementary deoxyribonucleic acid encoding the thyrotropin-releasing hormone receptor and regulation of its messenger ribonucleic acid in rat GH cells. *Endocrinology* **130**: 3529-36 [PMID:1317787]