

## QRFP receptor in GtoPdb v.2023.1

Didier Bagnol<sup>1</sup>, Tom I. Bonner<sup>2</sup>, Myrna Carlebur<sup>3</sup>, Anthony P. Davenport<sup>3</sup>, Stephen M. Foord<sup>4</sup>, Shoji Fukusumi<sup>5</sup>, Riccarda Granata<sup>6</sup>, Dan Larhammar<sup>7</sup>, Jérôme Leprince<sup>8</sup>, Janet J. Maguire<sup>3</sup>, Stefany D. Primeaux<sup>9</sup> and Hubert Vaudry<sup>8</sup>

1. Arena Pharmaceuticals, USA
2. National Institute of Mental Health, USA
3. University of Cambridge, UK
4. GlaxoSmithKline, UK
5. University of Tsukuba, Japan
6. University of Torino Medical School, Italy
7. Uppsala University, Sweden
8. Normandy University, France
9. Louisiana State University, USA

### Abstract

The human gene encoding the QRFP receptor (**nomenclature as agreed by the NC-IUPHAR Subcommittee on the QRFP receptor [19]**; QRFP, formerly known as the Peptide P518 receptor), previously designated as an orphan GPCR receptor was identified in 2001 by Lee *et al.* from a hypothalamus cDNA library [17]. However, the reported cDNA (AF411117) is a chimera with bases 1-127 derived from chromosome 1 and bases 155-1368 derived from chromosome 4. When corrected, QRFP (also referred to as SP9155 or AQ27) encodes a 431 amino acid protein that shares sequence similarities in the transmembrane spanning regions with other peptide receptors. These include neuropeptide FF2 (38%), neuropeptide Y<sub>2</sub> (37%) and galanin Gal<sub>1</sub> (35%) receptors. QRFP receptor was identified as a Gs-coupled GPCR [6, 14] that's activated by the endogenous peptides QRFP43 (43RFa) and QRFP26 (26RFa) [6, 14, 11]. However, Gq- and Gi/o-mediated signaling was also reported [11, 25]. Two naturally occurring mutations in the human QRFP receptor lead to distinct and opposite 26RFa-evoked signaling bias [20].

### Contents

This is a citation summary for QRFP receptor 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

### QRFP receptor

<https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=54>

### Introduction to QRFP receptor

<https://www.guidetopharmacology.org/GRAC/FamilyIntroductionForward?familyId=54>

### Receptors

#### QRFP receptor

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=333>

## References

1. Alim K, Lefranc B, Sopkova-de Oliveira Santos J, Dubessy C, Picot M, Boutin JA, Vaudry H, Chartrel N, Vaudry D and Chuquet J *et al.* (2018) Design, Synthesis, Molecular Dynamics Simulation, and Functional Evaluation of a Novel Series of 26RFa Peptide Analogues Containing a Mono- or Polyalkyl Guanidino Arginine Derivative. *J Med Chem* **61**: 10185-10197 [PMID:30358997]
2. Baribault H, Danao J, Gupte J, Yang L, Sun B, Richards W and Tian H. (2006) The G-protein-coupled receptor GPR103 regulates bone formation. *Mol Cell Biol* **26**: 709-17 [PMID:16382160]
3. Bruzzone F, Lectez B, Alexandre D, Jégou S, Mounien L, Tollemmer H, Chatenet D, Leprince J, Vallarino M and Vaudry H *et al.* (2007) Distribution of 26RFa binding sites and GPR103 mRNA in the central nervous system of the rat. *J Comp Neurol* **503**: 573-91 [PMID:17534937]
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. Chartrel N, Bruzzone F, Dujardin C, Leprince J, Tollemmer H, Anouar Y, Vallarino M, Costentin J and Vaudry H. (2005) Identification of 26RFa from frog brain: a novel hypothalamic neuropeptide with orexigenic activity in mammals. *Ann N Y Acad Sci* **1040**: 80-3 [PMID:15891009]
6. Chartrel N, Dujardin C, Anouar Y, Leprince J, Decker A, Clerens S, Do-Régo JC, Vandesande F, Llorens-Cortes C and Costentin J *et al.* (2003) Identification of 26RFa, a hypothalamic neuropeptide of the RFamide peptide family with orexigenic activity. *Proc Natl Acad Sci USA* **100**: 15247-52 [PMID:14657341]
7. Davies J, Chen J, Pink R, Carter D, Saunders N, Sotiriadis G, Bai B, Pan Y, Howlett D and Payne A *et al.* (2015) Orexin receptors exert a neuroprotective effect in Alzheimer's disease (AD) via heterodimerization with GPR103. *Sci Rep* **5**: 12584 [PMID:26223541]
8. do Rego JC, Leprince J, Chartrel N, Vaudry H and Costentin J. (2006) Behavioral effects of 26RFamide and related peptides. *Peptides* **27**: 2715-21 [PMID:16730856]
9. Egido EM, Hernández R, Leprince J, Chartrel N, Vaudry H, Marco J and Silvestre RA. (2007) 26RFa, a novel orexigenic neuropeptide, inhibits insulin secretion in the rat pancreas. *Peptides* **28**: 725-30 [PMID:16777265]
10. Fukusumi S, Fujii R and Hinuma S. (2006) Recent advances in mammalian RFamide peptides: the discovery and functional analyses of PrRP, RFRPs and QRFP. *Peptides* **27**: 1073-86 [PMID:16500002]
11. Fukusumi S, Yoshida H, Fujii R, Maruyama M, Komatsu H, Habata Y, Shintani Y, Hinuma S and Fujino M. (2003) A new peptidic ligand and its receptor regulating adrenal function in rats. *J Biol Chem* **278**: 46387-95 [PMID:12960173]
12. Georgsson J, Bergström F, Nordqvist A, Watson MJ, Blundell CD, Johansson MJ, Petersson AU, Yuan ZQ, Zhou Y and Kristensson L *et al.* (2014) GPR103 antagonists demonstrating anorexigenic activity in vivo: design and development of pyrrolo[2,3-c]pyridines that mimic the C-terminal Arg-Phe motif of QRFP26. *J Med Chem* **57**: 5935-48 [PMID:24937104]
13. Georgsson J, Bergström F, Nordqvist A, Watson MJ, Blundell CD, Johansson MJ, Petersson AU, Yuan ZQ, Zhou Y and Kristensson L *et al.* (2015) Correction to GPR103 Antagonists Demonstrating Anorexigenic Activity in Vivo: Design and Development of Pyrrolo[2,3-c]pyridines That Mimic the C-Terminal Arg-Phe Motif of QRFP26. *J Med Chem* **58**: 4086 [PMID:25875054]
14. Jiang Y, Luo L, Gustafson EL, Yadav D, Laverty M, Murgolo N, Vassileva G, Zeng M, Laz TM and Behan J *et al.* (2003) Identification and characterization of a novel RF-amide peptide ligand for orphan G-protein-coupled receptor SP9155. *J Biol Chem* **278**: 27652-7 [PMID:12714592]
15. Kampe J, Wiedmer P, Pfluger PT, Castaneda TR, Burget L, Mondala H, Kerr J, Liaw C, Oldfield BJ and Tschöp MH *et al.* (2006) Effect of central administration of QRFP(26) peptide on energy balance and

- characterization of a second QRFP receptor in rat. *Brain Res* **1119**: 133-49 [PMID:16996040]
16. Kuc RE, Mitchell JD and Davenport AD. (2006) The novel ligand [125I]-QRFP43 reveals a remarkably discrete distribution of the orphan receptor GPR103 in human adrenal. *Proceedings of the British Pharmacological Society* **4**: abst186
  17. Lee DK, Nguyen T, Lynch KR, Cheng R, Vanti WB, Arkhitko O, Lewis T, Evans JF, George SR and O'Dowd BF. (2001) Discovery and mapping of ten novel G protein-coupled receptor genes. *Gene* **275**: 83-91 [PMID:11574155]
  18. Lefranc B, Alim K, Neveu C, Le Marec O, Dubessy C, Boutin JA, Chuquet J, Vaudry D, Prévost G and Picot M *et al.*. (2021) Point-Substitution of Phenylalanine Residues of 26RFa Neuropeptide: A Structure-Activity Relationship Study. *Molecules* **26** [PMID:34299587]
  19. Leprince J, Bagnol D, Bureau R, Fukusumi S, Granata R, Hinuma S, Larhammar D, Primeaux S, Sopkova-de Oliveiras Santos J and Tsutsui K *et al.*. (2017) The Arg-Phe-amide peptide 26RFa/glutamine RF-amide peptide and its receptor: IUPHAR Review 24. *Br J Pharmacol* **174**: 3573-3607 [PMID:28613414]
  20. Ma Q, Cao Z, Li H, Wang W, Tian Y, Yan L, Liao Y, Chen X, Chen Y and Shi Y *et al.*. (2021) Two naturally occurring mutations of human GPR103 define distinct G protein selection bias. *Biochim Biophys Acta Mol Cell Res* **1868**: 119046 [PMID:33872671]
  21. Moriya R, Sano H, Umeda T, Ito M, Takahashi Y, Matsuda M, Ishihara A, Kanatani A and Iwaasa H. (2006) RFamide peptide QRFP43 causes obesity with hyperphagia and reduced thermogenesis in mice. *Endocrinology* **147**: 2916-22 [PMID:16543370]
  22. Navarro VM, Fernández-Fernández R, Nogueiras R, Vigo E, Tovar S, Chartrel N, Le Marec O, Leprince J, Aguilar E and Pinilla L *et al.*. (2006) Novel role of 26RFa, a hypothalamic RFamide orexigenic peptide, as putative regulator of the gonadotropic axis. *J Physiol (Lond.)* **573**: 237-49 [PMID:16543265]
  23. Neveu C, Lefranc B, Tasseau O, Do-Rego JC, Bourmaud A, Chan P, Bauchat P, Le Marec O, Chuquet J and Guilhaudis L *et al.*. (2012) Rational design of a low molecular weight, stable, potent, and long-lasting GPR103 aza- $\beta$ -pseudopeptide agonist. *J Med Chem* **55**: 7516-24 [PMID:22800498]
  24. Patel SR, Murphy KG, Thompson EL, Patterson M, Curtis AE, Ghatei MA and Bloom SR. (2008) Pyroglutamylated RFamide peptide 43 stimulates the hypothalamic-pituitary-gonadal axis via gonadotropin-releasing hormone in rats. *Endocrinology* **149**: 4747-54 [PMID:18535111]
  25. Ramanjaneya M, Karteris E, Chen J, Rucinski M, Ziolkowska A, Ahmed N, Kagerer S, Jöhren O, Lehnert H and Malendowicz LK *et al.*. (2013) QRFP induces aldosterone production via PKC and T-type calcium channel-mediated pathways in human adrenocortical cells: evidence for a novel role of GPR103. *Am J Physiol Endocrinol Metab* **305**: E1049-58 [PMID:23964068]
  26. Southern C, Cook JM, Neetoo-Isseljee Z, Taylor DL, Kettleborough CA, Merritt A, Bassoni DL, Raab WJ, Quinn E and Wehrman TS *et al.*. (2013) Screening  $\beta$ -Arrestin Recruitment for the Identification of Natural Ligands for Orphan G-Protein-Coupled Receptors. *J Biomol Screen* **18**: 599-609 [PMID:23396314]
  27. Takayasu S, Sakurai T, Iwasaki S, Teranishi H, Yamanaka A, Williams SC, Iguchi H, Kawasaki YI, Ikeda Y and Sakakibara I *et al.*. (2006) A neuropeptide ligand of the G protein-coupled receptor GPR103 regulates feeding, behavioral arousal, and blood pressure in mice. *Proc Natl Acad Sci USA* **103**: 7438-43 [PMID:16648250]
  28. Zhang Q, Qiu P, Arreaza MG, Simon JS, Golovko A, Lavery M, Vassileva G, Gustafson EL, Rojas-Triana A and Bober LA *et al.*. (2007) P518/Qrfp sequence polymorphisms in SAMP6 osteopenic mouse. *Genomics* **90**: 629-35 [PMID:17869477]