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Bile acid receptor (version 2019.4) in the IUPHAR/BPS Guide to Pharmacology Database

Tom I. Bonner[1], Anthony P. Davenport[2], Rebecca Hills[3], Janet J. Maguire[2] and Edward Rosser[3]

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

Abstract

The bile acid receptor (GPBA) responds to bile acids produced during the liver metabolism of cholesterol. Selective agonists are promising drugs for the treatment of metabolic disorders, such as type II diabetes, obesity and atherosclerosis.

Contents

This is a citation summary for Bile acid 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.

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Database links

Bile acid receptor
http://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=8
Introduction to Bile acid receptor
http://www.guidetopharmacology.org/GRAC/FamilyIntroductionForward?familyId=8

Receptors

GPBA receptor
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=37

References

1. Baxter JD and Webb P. (2006) Metabolism: bile acids heat things up.*Nature* **439**: 402-403 [PMID:16437098]
2. de Oliveira MC, Gilglioni EH, de Boer BA, Runge JH, de Waart DR, Salgueiro CL, Ishii-Iwamoto EL, Oude Elferink RP and Gaemers IC. (2016) Bile acid receptor agonists INT747 and INT777 decrease oestrogen deficiency-related postmenopausal obesity and hepatic steatosis in mice. *Biochim. Biophys. Acta* **1862**: 2054-2062 [PMID:27475255]
3. Evans KA, Budzik BW, Ross SA, Wisnoski DD, Jin J, Rivero RA, Vimal M, Szewczyk GR, Jayawickreme C and Moncol DL *et al.*. (2009) Discovery of 3-aryl-4-isoxazolecarboxamides as TGR5 receptor agonists.*J. Med. Chem.* **52**: 7962-5 [PMID:19902954]
4. Fiorucci S, Cipriani S, Baldelli F and Mencarelli A. (2010) Bile acid-activated receptors in the treatment of dyslipidemia and related disorders. *Prog. Lipid Res.* **49**: 171-85 [PMID:19932133]
5. Fiorucci S, Mencarelli A, Palladino G and Cipriani S. (2009) Bile-acid-activated receptors: targeting TGR5 and farnesoid-X-receptor in lipid and glucose disorders. *Trends Pharmacol. Sci.* **30**: 570-80 [PMID:19758712]
6. Genet C, Strehle A, Schmidt C, Boudjelal G, Lobstein A, Schoonjans K, Souchet M, Auwerx J, Saladin R and Wagner A. (2010) Structure-activity relationship study of betulinic acid, a novel and selective TGR5 agonist, and its synthetic derivatives: potential impact in diabetes. *J. Med. Chem.* **53**: 178-90 [PMID:19911773]
7. Guo C, Chen WD and Wang YD. (2016) TGR5, Not Only a Metabolic Regulator.*Front Physiol* **7**: 646 [PMID:28082913]
8. Guo C, Xie S, Chi Z, Zhang J, Liu Y, Zhang L, Zheng M, Zhang X, Xia D and Ke Y *et al.*. (2016) Bile Acids Control Inflammation and Metabolic Disorder through Inhibition of NLRP3 Inflammasome. *Immunity* **45**: 802-816 [PMID:27692610]
9. Houten SM, Watanabe M and Auwerx J. (2006) Endocrine functions of bile acids.*EMBO J.* **25**: 1419-25 [PMID:16541101]
10. Högenauer K, Arista L, Schmiedeberg N, Werner G, Jaksche H, Bouhelal R, Nguyen DG, Bhat BG, Raad L and Rauld C *et al.*. (2014) G-protein-coupled bile acid receptor 1 (GPBAR1, TGR5) agonists reduce the production of proinflammatory cytokines and stabilize the alternative macrophage phenotype. *J. Med. Chem.* **57**: 10343-54 [PMID:25411721]
11. Katsuma S, Hirasawa A and Tsujimoto G. (2005) Bile acids promote glucagon-like peptide-1 secretion through TGR5 in a murine enteroendocrine cell line STC-1. *Biochem. Biophys. Res. Commun.* **329**: 386-90 [PMID:15721318]
12. Kawamata Y, Fujii R, Hosoya M, Harada M, Yoshida H, Miwa M, Fukusumi S, Habata Y, Itoh T, Shintani Y, Hinuma S, Fujisawa Y and Fujino M. (2003) A G protein-coupled receptor responsive to bile acids. *J Biol Chem.* **278**: 9435-9440 [PMID:12524422]
13. Keitel V, Reinehr R, Gatsios P, Rupprecht C, Görg B, Selbach O, Häussinger D and Kubitz R. (2007) The G-protein coupled bile salt receptor TGR5 is expressed in liver sinusoidal endothelial cells. *Hepatology* **45**: 695-704 [PMID:17326144]
14. Lefebvre P, Cariou B, Lien F, Kuipers F and Staels B. (2009) Role of bile acids and bile acid receptors in metabolic regulation. *Physiol. Rev.* **89**: 147-91 [PMID:19126757]
15. Li B, Yang N, Li C, Li C, Gao K, Xie X, Dong X, Yang J, Yang Q and Tong Z *et al.*. (2018) INT-777, a bile acid receptor agonist, extenuates pancreatic acinar cells necrosis in a mouse model of acute pancreatitis. *Biochem. Biophys. Res. Commun.* **503**: 38-44 [PMID:29859191]
16. Li T and Chiang JY. (2012) Bile Acid signaling in liver metabolism and diseases.*J Lipids* **2012**: 754067 [PMID:21991404]
17. Londregan AT, Piotrowski DW, Futatsugi K, Warmus JS, Boehm M, Carpino PA, Chin JE, Janssen AM, Roush NS and Buxton J *et al.*. (2013) Discovery of 5-phenoxy-1,3-dimethyl-1H-pyrazole-4-carboxamides as potent agonists of TGR5 via sequential combinatorial libraries. *Bioorg. Med. Chem. Lett.* **23**: 1407-11 [PMID:23337601]

18. Maruyama T, Miyamoto Y, Nakamura T, Tamai Y, Okada H, Sugiyama E, Nakamura T, Itadani H and Tanaka K. (2002) Identification of membrane-type receptor for bile acids (M-BAR). *Biochem. Biophys. Res. Commun.* **298**: 714-9 [PMID:12419312]
19. Pellicciari R, Gioiello A, Macchiarulo A, Thomas C, Rosatelli E, Natalini B, Sardella R, Pruzanski M, Roda A and Pastorini E *et al.*. (2009) Discovery of 6alpha-ethyl-23(S)-methylcholic acid (S-EMCA, INT-777) as a potent and selective agonist for the TGR5 receptor, a novel target for diabesity. *J. Med. Chem.* **52**: 7958-61 [PMID:20014870]
20. Pellicciari R, Sato H, Gioiello A, Costantino G, Macchiarulo A, Sadeghpour BM, Giorgi G, Schoonjans K and Auwerx J. (2007) Nongenomic actions of bile acids. Synthesis and preliminary characterization of 23- and 6,23-alkyl-substituted bile acid derivatives as selective modulators for the G-protein coupled receptor TGR5. *J. Med. Chem.* **50**: 4265-8 [PMID:17685603]
21. Pols TW, Nomura M, Harach T, Lo Sasso G, Oosterveer MH, Thomas C, Rizzo G, Gioiello A, Adorini L and Pellicciari R *et al.*. (2011) TGR5 activation inhibits atherosclerosis by reducing macrophage inflammation and lipid loading. *Cell Metab.* **14**: 747-57 [PMID:22152303]
22. Pols TW, Noriega LG, Nomura M, Auwerx J and Schoonjans K. (2011) The bile acid membrane receptor TGR5 as an emerging target in metabolism and inflammation. *J. Hepatol.* **54**: 1263-72 [PMID:21145931]
23. Sato H, Genet C, Strehle A, Thomas C, Lobstein A, Wagner A, Mioskowski C, Auwerx J and Saladin R. (2007) Anti-hyperglycemic activity of a TGR5 agonist isolated from Olea europaea. *Biochem. Biophys. Res. Commun.* **362**: 793-8 [PMID:17825251]
24. Sato H, Macchiarulo A, Thomas C, Gioiello A, Une M, Hofmann AF, Saladin R, Schoonjans K, Pellicciari R and Auwerx J. (2008) Novel potent and selective bile acid derivatives as TGR5 agonists: biological screening, structure-activity relationships, and molecular modeling studies. *J. Med. Chem.* **51**: 1831-41 [PMID:18307294]
25. Takada Y and Aggarwal BB. (2003) Betulinic acid suppresses carcinogen-induced NF-kappa B activation through inhibition of I kappa B alpha kinase and p65 phosphorylation: abrogation of cyclooxygenase-2 and matrix metalloprotease-9. *J. Immunol.* **171**: 3278-86 [PMID:12960358]
26. Takeda S, Kadowaki S, Haga T, Takaesu H and Mitaku S. (2002) Identification of G protein-coupled receptor genes from the human genome sequence. *FEBS Lett.* **520**: 97-101 [PMID:12044878]
27. Thomas C, Auwerx J and Schoonjans K. (2008) Bile acids and the membrane bile acid receptor TGR5--connecting nutrition and metabolism. *Thyroid* **18**: 167-74 [PMID:18279017]
28. Tiwari A and Maiti P. (2009) TGR5: an emerging bile acid G-protein-coupled receptor target for the potential treatment of metabolic disorders. *Drug Discov. Today* **14**: 523-30 [PMID:19429513]
29. Vassileva G, Golovko A, Markowitz L, Abbondanzo SJ, Zeng M, Yang S, Hoos L, Tetzloff G, Levitan D and Murgolo NJ *et al.*. (2006) Targeted deletion of Gpbar1 protects mice from cholesterol gallstone formation. *Biochem. J.* **398**: 423-30 [PMID:16724960]
30. Wang XX, Edelstein MH, Gafter U, Qiu L, Luo Y, Dobrinskikh E, Lucia S, Adorini L, D'Agati VD and Levi J *et al.*. (2016) G Protein-Coupled Bile Acid Receptor TGR5 Activation Inhibits Kidney Disease in Obesity and Diabetes. *J. Am. Soc. Nephrol.* **27**: 1362-78 [PMID:26424786]
31. Watanabe M, Houten SM, Mataki C, Christoffolete MA, Kim BW, Sato H, Messaddeq N, Harney JW, Ezaki O and Kodama T *et al.*. (2006) Bile acids induce energy expenditure by promoting intracellular thyroid hormone activation. *Nature* **439**: 484-9 [PMID:16400329]
32. Yang JI, Yoon JH, Myung SJ, Gwak GY, Kim W, Chung GE, Lee SH, Lee SM, Kim CY and Lee HS. (2007) Bile acid-induced TGR5-dependent c-Jun-N terminal kinase activation leads to enhanced caspase 8 activation in hepatocytes. *Biochem Biophys Res Commun* **361**: 156-161 [PMID:17659258]
33. Yasuda H, Hirata S, Inoue K, Mashima H, Ohnishi H and Yoshiba M. (2007) Involvement of membrane-type bile acid receptor M-BAR/TGR5 in bile acid-induced activation of epidermal growth factor receptor and mitogen-activated protein kinases in gastric carcinoma cells. *Biochem. Biophys. Res. Commun.* **354**: 154-9 [PMID:17214962]