

Glucagon receptor family in GtoPdb v.2025.3

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Abstract

The glucagon family of receptors (**nomenclature as agreed by the NC-IUPHAR Subcommittee on the Glucagon receptor family [170]**) are activated by the endogenous peptide (27-44 aa) hormones [glucagon](#), [glucagon-like peptide 1](#), [glucagon-like peptide 2](#), glucose-dependent insulintropic polypeptide (also known as [gastric inhibitory polypeptide](#)), [GHRH](#) and [secretin](#). One common precursor (*GCG*) generates [glucagon](#), [glucagon-like peptide 1](#) and [glucagon-like peptide 2](#) peptides [126]. For a recent review on the current understanding of the structures of GLP-1 and GLP-1R, the molecular basis of their interaction, and the associated signaling events see de Graaf *et al.*, 2016 [94].

Contents

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Database links

Glucagon receptor family

<https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=29>

Introduction to Glucagon receptor family

<https://www.guidetopharmacology.org/GRAC/FamilyIntroductionForward?familyId=29>

Receptors

GHRH receptor

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=247>

GIP receptor

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=248>

GLP-1 receptor

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=249>

GLP-2 receptor

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glucagon receptor

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=251>

secretin receptor

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=252>

References

1. Adams EF, Symowski H, Buchfelder M and Poyner DR. (2000) A polymorphism in the growth hormone (GH)-releasing hormone (GHRH) receptor gene is associated with elevated response to GHRH by human pituitary somatotrophinomas in vitro. *Biochem Biophys Res Commun* **275**: 33-6 [PMID:10944436]
2. Ahn JM, Medeiros M, Trivedi D and Hruby VJ. (2001) Development of potent glucagon antagonists: structure-activity relationship study of glycine at position 4. *J Pept Res* **58**: 151-8 [PMID:11532074]
3. Aspnes GE, Bagley SW, Curto JM, Edmonds DJ, Flanagan ME, Futasugi K, Griffith DA, Huard K, Lian Y and Limberakis C *et al.*. (2020) GLP-1 receptor agonists and uses thereof Patent number: US10676465B2. Assignee: Pfizer Corp SRL. Priority date: 08/08/2019. Publication date: 09/06/2020.
4. Baggio LL, Huang Q, Brown TJ and Drucker DJ. (2004) A recombinant human glucagon-like peptide (GLP)-1-albumin protein (albugon) mimics peptidergic activation of GLP-1 receptor-dependent pathways coupled with satiety, gastrointestinal motility, and glucose homeostasis. *Diabetes* **53**: 2492-500 [PMID:15331566]
5. Bagnato A, Moretti C, Ohnishi J, Frajese G and Catt KJ. (1992) Expression of the growth hormone-releasing hormone gene and its peptide product in the rat ovary. *Endocrinology* **130**: 1097-102 [PMID:1537276]
6. Barinaga M, Yamonoto G, Rivier C, Vale W, Evans R and Rosenfeld MG. (1983) Transcriptional regulation of growth hormone gene expression by growth hormone-releasing factor. *Nature* **306**: 84-5 [PMID:6415487]
7. Baumann G and Maheshwari H. (1997) The Dwarfs of Sindh: severe growth hormone (GH) deficiency caused by a mutation in the GH-releasing hormone receptor gene. *Acta Paediatr Suppl* **423**: 33-8 [PMID:9401536]
8. Bayliss WM and Starling EH. (1902) On the causation of the so-called 'peripheral reflex secretion' of the pancreas. *Proc R Soc Lond, B, Biol Sci* **69**: 352-353
9. Beak SA, Small CJ, Ilovaiskaia I, Hurley JD, Ghatel MA, Bloom SR and Smith DM. (1996) Glucagon-like peptide-1 (GLP-1) releases thyrotropin (TSH): characterization of binding sites for GLP-1 on alpha-TSH cells. *Endocrinology* **137**: 4130-8 [PMID:8828468]
10. Beinborn M, Worrall CI, McBride EW and Kopin AS. (2005) A human glucagon-like peptide-1 receptor polymorphism results in reduced agonist responsiveness. *Regul Pept* **130**: 1-6 [PMID:15975668]
11. Bell GI, Sanchez-Pescador R, Laybourn PJ and Najarian RC. (1983) Exon duplication and divergence in the human preproglucagon gene. *Nature* **304**: 368-71 [PMID:6877358]
12. Bell GI, Santerre RF and Mullenbach GT. (1983) Hamster preproglucagon contains the sequence of glucagon and two related peptides. *Nature* **302**: 716-718 [PMID:6835407]
13. Berry SA and Pescovitz OH. (1988) Identification of a rat GHRH-like substance and its messenger RNA in rat testis. *Endocrinology* **123**: 661-3 [PMID:3133203]
14. Billestrup N and Vale W. (1986) Growth hormone-releasing factor stimulates proliferation of somatotrophs *in vitro*. *Proc Natl Acad Sci USA* **83**: 6854-6857 [PMID:3018748]
15. Bode HP, Moormann B, Dabew R and Göke B. (1999) Glucagon-like peptide 1 elevates cytosolic calcium in pancreatic beta-cells independently of protein kinase A. *Endocrinology* **140**: 3919-27 [PMID:10465260]
16. Boer GA, Hunt JE, Gabe MBN, Windeløv JA, Sparre-Ulrich AH, Hartmann B, Holst JJ and Rosenkilde MM. (2022) Glucose-dependent insulinotropic polypeptide receptor antagonist treatment causes a reduction in weight gain in ovariectomised high fat diet-fed mice. *Br J Pharmacol* **179**: 4486-4499 [PMID:35710141]
17. Boisvert C, Paré C, Veyrat-Durebex C, Robert A, Dubuisson S, Morel G and Gaudreau P. (2002) Localization and regulation of a functional GHRH receptor in the rat renal medulla. *Endocrinology* **143**: 1475-84 [PMID:11897706]
18. Bollag RJ, Zhong Q, Phillips P, Min L, Zhong L, Cameron R, Mulloy AL, Rasmussen H, Qin F, Ding KH and Isaacs CM. (2000) Osteoblast-derived cells express functional glucose-dependent insulinotropic peptide receptors. *Endocrinology* **141**: 1228-1235 [PMID:10698200]
19. Boulanger L, Girard N, Strecko J and Gaudreau P. (2002) Characterization of a growth hormone-

- releasing hormone binding site in the rat renal medulla. *Peptides* **23**: 43-50 [PMID:11814616]
20. Boushey RP, Yusta B and Drucker DJ. (1999) Glucagon-like peptide 2 decreases mortality and reduces the severity of indomethacin-induced murine enteritis. *Am J Physiol* **277**: E937-47 [PMID:10567023]
 21. Breyer PR, Rothrock JK, Beaudry N and Pescovitz OH. (1996) A novel peptide from the growth hormone releasing hormone gene stimulates Sertoli cell activity. *Endocrinology* **137**: 2159-62 [PMID:8612561]
 22. Brubaker PL, Izzo A, Hill M and Drucker DJ. (1997) Intestinal function in mice with small bowel growth induced by glucagon-like peptide-2. *Am J Physiol* **272**: E1050-8 [PMID:9227451]
 23. Buchholz S, Schally AV, Engel JB, Hohla F, Heinrich E, Koester F, Varga JL and Halmos G. (2007) Potentiation of mammary cancer inhibition by combination of antagonists of growth hormone-releasing hormone with docetaxel. *Proc Natl Acad Sci USA* **104**: 1943-6 [PMID:17261802]
 24. Bullock BP, Heller RS and Habener JF. (1996) Tissue distribution of messenger ribonucleic acid encoding the rat glucagon-like peptide-1 receptor. *Endocrinology* **137**: 2968-78 [PMID:8770921]
 25. 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]
 26. Bunnett NW. (1994) Gastrin-releasing peptide. In *Gut Peptides* Edited by Walsh JH, Dockray GJ: Raven Press: 423-445 [ISBN: 0781701155]
 27. Burcelin R, Li J and Charron MJ. (1995) Cloning and sequence analysis of the murine glucagon receptor-encoding gene. *Gene* **164**: 305-10 [PMID:7590348]
 28. Busto R, Schally AV, Braczkowski R, Plonowski A, Krupa M, Groot K, Armatis P and Varga JL. (2002) Expression of mRNA for growth hormone-releasing hormone and splice variants of GHRH receptors in human malignant bone tumors. *Regul Pept* **108**: 47-53 [PMID:12220726]
 29. CAHILL Jr GF, EARLE AS and ZOTTU S. (1957) In vivo effects of glucagon on hepatic glycogen, phosphorylase and glucose-6-phosphatase. *Endocrinology* **60**: 265-9 [PMID:13397492]
 30. Cai R, Schally AV, Cui T, Szalontay L, Halmos G, Sha W, Kovacs M, Jaszberenyi M, He J and Rick FG *et al.* (2014) Synthesis of new potent agonistic analogs of growth hormone-releasing hormone (GHRH) and evaluation of their endocrine and cardiac activities. *Peptides* **52**: 104-12 [PMID:24373935]
 31. Campbell RM and Scanes CG. (1992) Evolution of the growth hormone-releasing factor (GRF) family of peptides. *Growth Regul* **2**: 175-91 [PMID:1290954]
 32. Campos RV, Lee YC and Drucker DJ. (1994) Divergent tissue-specific and developmental expression of receptors for glucagon and glucagon-like peptide-1 in the mouse. *Endocrinology* **134**: 2156-64 [PMID:8156917]
 33. Canonico PL, Cronin MJ, Thorner MO and MacLeod RM. (1983) Human pancreatic GRF stimulates phosphatidylinositol labeling in cultured anterior pituitary cells. *Am J Physiol* **245**: E587-90 [PMID:6140852]
 34. Carakushansky M, Whatmore AJ, Clayton PE, Shalet SM, Gleeson HK, Price DA, Levine MA and Salvatori R. (2003) A new missense mutation in the growth hormone-releasing hormone receptor gene in familial isolated GH deficiency. *Eur J Endocrinol* **148**: 25-30 [PMID:12534354]
 35. Carlquist M and Johansson C. (1985) Human secretin is not identical to the porcine/bovine hormone. *IRCS Med Sci* **13**: 217-218
 36. Carlquist M, Jörnvall H and Mutt V. (1981) Isolation and amino acid sequence of bovine secretin. *FEBS Lett* **127**: 71-4 [PMID:7250377]
 37. Cascieri MA, Koch GE, Ber E, Sadowski SJ, Louizides D, de Laszlo SE, Hacker C, Hagmann WK, MacCoss M and Chicchi GG *et al.* (1999) Characterization of a novel, non-peptidyl antagonist of the human glucagon receptor. *J Biol Chem* **274**: 8694-7 [PMID:10085108]
 38. Cervini LA, Donaldson CJ, Koerber SC, Vale WW and Rivier JE. (1998) Human growth hormone-releasing hormone hGHRH(1-29)-NH₂: systematic structure-activity relationship studies. *J Med Chem* **41**: 717-27 [PMID:9513600]
 39. Chance WT, Foley-Nelson T, Thomas I and Balasubramaniam A. (1997) Prevention of parenteral nutrition-induced gut hypoplasia by coinfusion of glucagon-like peptide-2. *Am J Physiol* **273**: G559-63 [PMID:9277438]
 40. Cheeseman CI and Tsang R. (1996) The effect of GIP and glucagon-like peptides on intestinal basolateral membrane hexose transport. *Am J Physiol* **271**: G477-82 [PMID:8843773]
 41. Chen C, Vincent JD and Clarke IJ. (1994) Ion channels and the signal transduction pathways in the regulation of growth hormone secretion. *Trends Endocrinol Metab* **5**: 227-33 [PMID:18407212]
 42. Chow BK. (1995) Molecular cloning and functional characterization of a human secretin receptor. *Biochem Biophys Res Commun* **212**: 204-11 [PMID:7612008]
 43. Chow BK, Cheung KH, Tsang EM, Leung MC, Lee SM and Wong PY. (2004) Secretin controls anion secretion in the rat epididymis in an autocrine/paracrine fashion. *Biol Reprod* **70**: 1594-9 [PMID:14749298]

44. Christopoulos A, Christopoulos G, Morfis M, Udawela M, Laburthe M, Couvineau A, Kuwasako K, Tilakaratne N and Sexton PM. (2003) Novel receptor partners and function of receptor activity-modifying proteins. *J Biol Chem* **278**: 3293-7 [PMID:12446722]
45. Ciampani T, Fabbri A, Isidori A and Dufau ML. (1992) Growth hormone-releasing hormone is produced by rat Leydig cell in culture and acts as a positive regulator of Leydig cell function. *Endocrinology* **131**: 2785-92 [PMID:1332849]
46. Coates DA, Fields T, Ho JD and Qu F. (2020) Glucagon-like peptide 1 receptor agonists Patent number: [WO2020263695A1](#). Assignee: Eli Lilly And Company. Priority date: 19/06/2020. Publication date: 30/12/2020.
47. Coskun T, Sloop KW, Loghin C, Alsina-Fernandez J, Urva S, Bokvist KB, Cui X, Briere DA, Cabrera O and Roell WC *et al.*. (2018) LY3298176, a novel dual GIP and GLP-1 receptor agonist for the treatment of type 2 diabetes mellitus: From discovery to clinical proof of concept. *Mol Metab* **18**: 3-14 [PMID:30473097]
48. Coskun T, Urva S, Roell WC, Qu H, Loghin C, Moyers JS, O'Farrell LS, Briere DA, Sloop KW and Thomas MK *et al.*. (2022) LY3437943, a novel triple glucagon, GIP, and GLP-1 receptor agonist for glycemic control and weight loss: From discovery to clinical proof of concept. *Cell Metab* **34**: 1234-1247.e9 [PMID:35985340]
49. Coy DH, Jiang NY, Fuselier J and Murphy WA. (1996) Structural simplification of potent growth hormone-releasing hormone analogs: implications for other members of the VIP/GHRH/PACAP family. *Ann N Y Acad Sci* **805**: 149-58 [PMID:8993400]
50. Dalle S, Smith P, Blache P, Le-Nguyen D, Le Brigand L, Bergeron F, Ashcroft FM and Bataille D. (1999) Miniglucagon (glucagon 19-29), a potent and efficient inhibitor of secretagogue-induced insulin release through a Ca²⁺ pathway. *J Biol Chem* **274**: 10869-76 [PMID:10196164]
51. Davis RJ, Page KJ, Dos Santos Cruz GJ, Harmer DW, Munday PW, Williams SJ, Picot J, Evans TJ, Sheldrick RL and Coleman RA *et al.*. (2004) Expression and functions of the duodenal peptide secretin and its receptor in human lung. *Am J Respir Cell Mol Biol* **31**: 302-8 [PMID:15191914]
52. Deacon CF, Plamboeck A, Rosenkilde MM, de Heer J and Holst JJ. (2006) GIP-(3-42) does not antagonize insulinotropic effects of GIP at physiological concentrations. *Am J Physiol Endocrinol Metab* **291**: E468-75 [PMID:16608883]
53. DeAlmeida VI and Mayo KE. (1998) Identification of binding domains of the growth hormone-releasing hormone receptor by analysis of mutant and chimeric receptor proteins. *Mol Endocrinol* **12**: 750-65 [PMID:9605937]
54. Dillon JS, Tanizawa Y, Wheeler MB, Leng XH, Ligon BB, Rabin DU, Yoo-Warren H, Permutt MA and Boyd AE. (1993) Cloning and functional expression of the human glucagon-like peptide-1 (GLP-1) receptor. *Endocrinology* **133**: 1907-10 [PMID:8404634]
55. Dong G, Ye Q, Li W, Zhang S, Yang Z, Zhang R, Deng T, Li H, Zhang Y and Zhang X *et al.*. (2025) Discovery and Evaluation of DA-302168S as an Efficacious Oral Small-Molecule Glucagon-Like Peptide-1 Receptor Agonist. *J Med Chem* **68**: 9555-9583 [PMID:40257122]
56. Dong M, Wang Y, Hadac EM, Pinon DI, Holicky E and Miller LJ. (1999) Identification of an interaction between residue 6 of the natural peptide ligand and a distinct residue within the amino-terminal tail of the secretin receptor. *J Biol Chem* **274**: 19161-7 [PMID:10383421]
57. Drucker DJ. (1998) Glucagon-like peptides. *Diabetes* **47**: 159-69 [PMID:9519708]
58. Drucker DJ and Brubaker PL. (1996) Induction of intestinal epithelial proliferation by glucagon-like peptide 2. *Proc Natl Acad Sci USA* **93**: 7911-7916 [PMID:8755576]
59. Drucker DJ, DeForest L and Brubaker PL. (1997) Intestinal response to growth factors administered alone or in combination with human [Gly²]glucagon-like peptide 2. *Am J Physiol* **273**: G1252-62 [PMID:9435550]
60. Drucker DJ, Philippe J, Mojsov S, Chick WL and Habener JF. (1987) Glucagon-like peptide I stimulates insulin gene expression and increases cyclic AMP levels in a rat islet cell line. *Proc Natl Acad Sci USA* **84**: 3434-8 [PMID:3033647]
61. Duffy JL, Kirk BA, Konteatis Z, Campbell EL, Liang R, Brady EJ, Candelore MR, Ding VD, Jiang G and Liu F *et al.*. (2005) Discovery and investigation of a novel class of thiophene-derived antagonists of the human glucagon receptor. *Bioorg Med Chem Lett* **15**: 1401-5 [PMID:15713396]
62. Dunphy JL, Taylor RG and Fuller PJ. (1998) Tissue distribution of rat glucagon receptor and GLP-1 receptor gene expression. *Mol Cell Endocrinol* **141**: 179-86 [PMID:9723898]
63. During MJ, Cao L, Zuzga DS, Francis JS, Fitzsimons HL, Jiao X, Bland RJ, Klugmann M, Banks WA and Drucker DJ *et al.*. (2003) Glucagon-like peptide-1 receptor is involved in learning and neuroprotection. *Nat Med* **9**: 1173-9 [PMID:12925848]
64. Ehses JA, Lee SS, Pederson RA and McIntosh CH. (2001) A new pathway for glucose-dependent insulinotropic polypeptide (GIP) receptor signaling: evidence for the involvement of phospholipase A2 in GIP-stimulated insulin secretion. *J Biol Chem* **276**: 23667-73 [PMID:11323439]
65. Eicher EM and Beamer WG. (1976) Inherited ateliotic dwarfism in mice. Characteristics of the mutation, little, on chromosome 6. *J Hered* **67**: 87-91 [PMID:1270792]

66. Escobar DC, Vicentini LM, Ghigo E, Ciccarelli E, Usellini L, Capella C and Cocchi D. (1986) Growth hormone-releasing factor does not stimulate phosphoinositides breakdown in primary cultures of rat and human pituitary cells. *Acta Endocrinol* **112**: 345-50 [PMID:3019052]
67. Exton JH and Park CR. (1966) The stimulation of gluconeogenesis from lactate by epinephrine, glucagon and cyclic 3i-5i-adenylate in the perfused rat liver. *Pharmacol Rev* **18**: 181-188 [PMID:5904135]
68. Fan H, Gong N, Li TF, Ma AN, Wu XY, Wang MW and Wang YX. (2015) The non-peptide GLP-1 receptor agonist WB4-24 blocks inflammatory nociception by stimulating β -endorphin release from spinal microglia. *Br J Pharmacol* **172**: 64-79 [PMID:25176008]
69. Fehmman HC, Göke R and Göke B. (1995) Cell and molecular biology of the incretin hormones glucagon-like peptide-I and glucose-dependent insulin releasing polypeptide. *Endocr Rev* **16**: 390-410 [PMID:7671853]
70. Fehmman HC and Habener JF. (1992) Insulinotropic hormone glucagon-like peptide-I(7-37) stimulation of proinsulin gene expression and proinsulin biosynthesis in insulinoma beta TC-1 cells. *Endocrinology* **130**: 159-66 [PMID:1309325]
71. Fehmman HC and Habener JF. (1991) Functional receptors for the insulinotropic hormone glucagon-like peptide-I(7-37) on a somatostatin secreting cell line. *FEBS Lett* **279**: 335-40 [PMID:1672112]
72. French MB, Lussier BT, Moor BC and Kraicer J. (1990) Effect of growth hormone-releasing factor on phosphoinositide hydrolysis in somatotrophs. *Mol Cell Endocrinol* **72**: 221-6 [PMID:1963157]
73. Frohman LA, Downs TR, Heimer EP and Felix AM. (1989) Dipeptidylpeptidase IV and trypsin-like enzymatic degradation of human growth hormone-releasing hormone in plasma. *J Clin Invest* **83**: 1533-40 [PMID:2565342]
74. Frohman LA and Jansson JO. (1986) Growth hormone-releasing hormone. *Endocr Rev* **7**: 223-53 [PMID:2874984]
75. Frohman LA and Szabo M. (1981) Ectopic production of growth hormone-releasing factor by carcinoid and pancreatic islet tumors associated with acromegaly. *Prog Clin Biol Res* **74**: 259-71 [PMID:6275403]
76. Frohman MA, Downs TR, Chomczynski P and Frohman LA. (1989) Cloning and characterization of mouse growth hormone-releasing hormone (GRH) complementary DNA: increased GRH messenger RNA levels in the growth hormone-deficient lit/lit mouse. *Mol Endocrinol* **3**: 1529-36 [PMID:2481813]
77. Göke R and Conlon JM. (1988) Receptors for glucagon-like peptide-1(736) amide on rat insulinoma-derived cells. *J Endocrinol* **116**: 357-362 [PMID:2832504]
78. Göke R and Göke B. (1994) Glycosylation of the GLP-1 receptor is a prerequisite for regular receptor function. *Peptides* **15**: 675-681 [PMID:7937345]
79. Galehshahi FS, Göke B and Lankat-Buttgereit B. (1998) Contribution of a PS1-like element to the tissue- and cell-specific expression of the human GLP-1 receptor gene. *FEBS Lett* **436**: 163-8 [PMID:9781671]
80. Gallwitz B, Witt M, Morys-Wortmann C, Fölsch UR and Schmidt WE. (1996) GLP-1/GIP chimeric peptides define the structural requirements for specific ligand-receptor interaction of GLP-1. *Regul Pept* **63**: 17-22 [PMID:8795084]
81. Ganguli SC, Park CG, Holtmann MH, Hadac EM, Kenakin TP and Miller LJ. (1998) Protean effects of a natural peptide agonist of the G protein-coupled secretin receptor demonstrated by receptor mutagenesis. *J Pharmacol Exp Ther* **286**: 593-8 [PMID:9694908]
82. Gaudreau P, Boulanger L and Abribat T. (1992) Affinity of human growth hormone-releasing factor (1-29)NH₂ analogues for GRF binding sites in rat adenopituitary. *J Med Chem* **35**: 1864-9 [PMID:1534126]
83. Gault VA, O'Harte FP, Harriott P, Mooney MH, Green BD and Flatt PR. (2003) Effects of the novel (Pro3)GIP antagonist and exendin(9-39)amide on GIP- and GLP-1-induced cyclic AMP generation, insulin secretion and postprandial insulin release in obese diabetic (ob/ob) mice: evidence that GIP is the major physiological incretin. *Diabetologia* **46**: 222-30 [PMID:12627321]
84. Gaylinn BD. (1999) Molecular and cell biology of the growth hormone-releasing hormone receptor. *Growth Horm IGF Res* **9**: 37-44 [PMID:10429879]
85. Gaylinn BD, Dealmeida VI, Lyons Jr CE, Wu KC, Mayo KE and Thorner MO. (1999) The mutant growth hormone-releasing hormone (GHRH) receptor of the little mouse does not bind GHRH. *Endocrinology* **140**: 5066-74 [PMID:10537133]
86. Gaylinn BD, Harrison JK, Zysk JR, Lyons CE, Lynch KR and Thorner MO. (1993) Molecular cloning and expression of a human anterior pituitary receptor for growth hormone-releasing hormone. *Mol Endocrinol* **7**: 77-84 [PMID:7680413]
87. Gaylinn BD, von Kap-Herr C, Golden WL and Thorner MO. (1994) Assignment of the human growth hormone-releasing hormone receptor gene (GHRHR) to 7p14 by in situ hybridization. *Genomics* **19**: 193-5 [PMID:8188233]
88. Gelling RW, Coy DH, Pederson RA, Wheeler MB, Hinke S, Kwan T and McIntosh CH. (1997)

- GIP(6-30amide) contains the high affinity binding region of GIP and is a potent inhibitor of GIP1-42 action in vitro. *Regul Pept* **69**: 151-4 [PMID:9226399]
89. Gelling RW, Du XQ, Dichmann DS, Romer J, Huang H, Cui L, Obici S, Tang B, Holst JJ and Fledelius C *et al.*. (2003) Lower blood glucose, hyperglucagonemia, and pancreatic alpha cell hyperplasia in glucagon receptor knockout mice. *Proc Natl Acad Sci USA* **100**: 1438-43 [PMID:12552113]
 90. Gick GG, Zeytin FN, Brazeau P, Ling NC, Esch FS and Bancroft C. (1984) Growth hormone-releasing factor regulates growth hormone mRNA in primary cultures of rat pituitary cells. *Proc Natl Acad Sci USA* **81**: 1553-5 [PMID:6424119]
 91. Godfrey P, Rahal JO, Beamer WG, Copeland NG, Jenkins NA and Mayo KE. (1993) GHRH receptor of little mice contains a missense mutation in the extracellular domain that disrupts receptor function. *Nat Genet* **4**: 227-32 [PMID:8395283]
 92. Gossen D, Vandermeers A, Vandermeers-Piret MC, Rathé J, Cauvin A, Robberecht P and Christophe J. (1989) Isolation and primary structure of rat secretin. *Biochem Biophys Res Commun* **160**: 862-7 [PMID:2719704]
 93. Gourlet P, Vandermeers A, Vertongen P, Rathe J, De Neef P, Cnudde J, Waelbroeck M and Robberecht P. (1997) Development of high affinity selective VIP1 receptor agonists. *Peptides* **18**: 1539-45 [PMID:9437714]
 94. Graaf Cd, Donnelly D, Wootten D, Lau J, Sexton PM, Miller LJ, Ahn JM, Liao J, Fletcher MM and Yang D *et al.*. (2016) Glucagon-Like Peptide-1 and Its Class B G Protein-Coupled Receptors: A Long March to Therapeutic Successes. *Pharmacol Rev* **68**: 954-1013 [PMID:27630114]
 95. Graziano MP and Strader CD. (1993) Cloning and functional expression of a human glucagon-like peptide-1 receptor. *Biochem Biophys Res Commun* **196**: 141-146 [PMID:8216285]
 96. Griffith DA, Edmonds DJ, Fortin JP, Kalgutkar AS, Kuzmiski JB, Loria PM, Saxena AR, Bagley SW, Buckeridge C and Curto JM *et al.*. (2022) A Small-Molecule Oral Agonist of the Human Glucagon-like Peptide-1 Receptor. *J Med Chem* **65**: 8208-8226 [PMID:35647711]
 97. Gromada J, Rorsman P, Dissing S and Wulff BS. (1995) Stimulation of cloned human glucagon-like peptide 1 receptor expressed in HEK 293 cells induces cAMP-dependent activation of calcium-induced calcium release. *FEBS Lett* **373**: 182-6 [PMID:7589461]
 98. Gros L, Demiprence E, Bataille D and Kervra A. (1992) Characterization of high affinity receptors for glucagon-like peptide-1 (7-36) amide on a somatostatin-secreting cell line. *Biomed Res* **13**: 143-150
 99. Gros R, You X, Baggio LL, Kabir MG, Sadi AM, Mungrue IN, Parker TG, Huang Q, Drucker DJ and Husain M. (2003) Cardiac function in mice lacking the glucagon-like peptide-1 receptor. *Endocrinology* **144**: 2242-52 [PMID:12746281]
 100. Gubler U, Monahan JJ, Lomedico PT, Bhatt RS, Collier KJ, Hoffman BJ, Böhlen P, Esch F, Ling N and Zeytin F *et al.*. (1983) Cloning and sequence analysis of cDNA for the precursor of human growth hormone-releasing factor, somatocrinin. *Proc Natl Acad Sci USA* **80**: 4311-4 [PMID:6192430]
 101. Guillemín R, Brazeau P, Böhlen P, Esch F, Ling N and Wehrenberg WB. (1982) Growth hormone-releasing factor from a human pancreatic tumor that caused acromegaly. *Science* **218**: 585-7 [PMID:6812220]
 102. Guo W, Xu Z, Zou H, Li F, Li Y, Feng J, Zhu Z, Zheng Q, Zhu R and Wang B *et al.*. (2023) Discovery of ecnoglutide - A novel, long-acting, cAMP-biased glucagon-like peptide-1 (GLP-1) analog. *Mol Metab* **75**: 101762 [PMID:37364710]
 103. Gutzwiller JP, Drewe J, Göke B, Schmidt H, Rohrer B, Lareida J and Beglinger C. (1999) Glucagon-like peptide-1 promotes satiety and reduces food intake in patients with diabetes mellitus type 2. *Am J Physiol* **276**: R1541-4 [PMID:10233049]
 104. Göke B, Leferink J, Göke R and Adler G. (1989) Effect of a low-molecular weight serine proteinase inhibitor (camostat) on amylase release from isolated pancreatic acini. *Res Exp Med (Berl.)* **189**: 33-8 [PMID:2469115]
 105. Göke R, Cole T and Conlon JM. (1989) Characterization of the receptor for glucagon-like peptide-1(7-36)amide on plasma membranes from rat insulinoma-derived cells by covalent cross-linking. *J Mol Endocrinol* **2**: 93-8 [PMID:2550026]
 106. Göke R, Fehmann HC, Linn T, Schmidt H, Krause M, Eng J and Göke B. (1993) Exendin-4 is a high potency agonist and truncated exendin-(9-39)-amide an antagonist at the glucagon-like peptide 1-(7-36)-amide receptor of insulin-secreting beta-cells. *J Biol Chem* **268**: 19650-5 [PMID:8396143]
 107. Göke R, Larsen PJ, Mikkelsen JD and Sheikh SP. (1995) Identification of specific binding sites for glucagon-like peptide-1 on the posterior lobe of the rat pituitary. *Neuroendocrinology* **62**: 130-4 [PMID:8584112]
 108. Göke R, Oltmer B, Sheikh SP and Göke B. (1992) Solubilization of active GLP-1 (7-36)amide receptors from RINm5F plasma membranes. *FEBS Lett* **300**: 232-6 [PMID:1313374]
 109. Haffar BM, Hocart SJ, Coy DH, Mantey S, Chiang HC and Jensen RT. (1991) Reduced peptide bond pseudopeptide analogues of secretin. A new class of secretin receptor antagonists. *J Biol*

- Chem* **266**: 316-22 [PMID:1702423]
110. Hager J, Hansen L, Vaisse C, Vionnet N, Philippi A, Poller W, Velho G, Carcassi C, Contu L and Julier C *et al.*. (1995) A missense mutation in the glucagon receptor gene is associated with non-insulin-dependent diabetes mellitus. *Nat Genet* **9**: 299-304 [PMID:7773293]
 111. Hammer RE, Brinster RL, Rosenfeld MG, Evans RM and Mayo KE. (1985) Expression of human growth hormone-releasing factor in transgenic mice results in increased somatic growth. *Nature* **315**: 413-6 [PMID:3923368]
 112. Hansen AB, Gespach CP, Rosselin GE and Holst JJ. (1988) Effect of truncated glucagon-like peptide 1 on cAMP in rat gastric glands and HGT-1 human gastric cancer cells. *FEBS Lett* **236**: 119-22 [PMID:2841160]
 113. Hansen LH, Abrahamsen N and Nishimura E. (1995) Glucagon receptor mRNA distribution in rat tissues. *Peptides* **16**: 1163-6 [PMID:8532603]
 114. Hansen LS, Sparre-Ulrich AH, Christensen M, Knop FK, Hartmann B, Holst JJ and Rosenkilde MM. (2016) N-terminally and C-terminally truncated forms of glucose-dependent insulinotropic polypeptide are high-affinity competitive antagonists of the human GIP receptor. *Br J Pharmacol* **173**: 826-38 [PMID:26572091]
 115. Hargrove DM, Alagarsamy S, Croston G, Laporte R, Qi S, Srinivasan K, Sueiras-Diaz J, Wiśniewski K, Hartwig J and Lu M *et al.*. (2020) Pharmacological Characterization of Apraglutide, a Novel Long-Acting Peptidic Glucagon-Like Peptide-2 Agonist, for the Treatment of Short Bowel Syndrome. *J Pharmacol Exp Ther* **373**: 193-203 [PMID:32075870]
 116. Hashimoto K, Koga M, Motomura T, Kasayama S, Kouhara H, Ohnishi T, Arita N, Hayakawa T, Sato B and Kishimoto T. (1995) Identification of alternatively spliced messenger ribonucleic acid encoding truncated growth hormone-releasing hormone receptor in human pituitary adenomas. *J Clin Endocrinol Metab* **80**: 2933-9 [PMID:7559877]
 117. Hassan HA, Hsiung HM, Zhang XY, Smith DP, Smiley DL and Heiman ML. (1995) Characterization of growth hormone-releasing hormone (GHRH) binding to cloned porcine GHRH receptor. *Peptides* **16**: 1469-73 [PMID:8745060]
 118. Hatton TW, Yip CC and Vranic M. (1985) Biosynthesis of glucagon (IRG3500) in canine gastric mucosa. *Diabetes* **34**: 38-46 [PMID:3880548]
 119. Heinrich G, Gros P, Lund PK, Bentley RC and Habener JF. (1984) Pre-proglucagon messenger ribonucleic acid: nucleotide and encoded amino acid sequences of the rat pancreatic complementary deoxyribonucleic acid. *Endocrinology* **115**: 2176-81 [PMID:6548696]
 120. Holl RW, Thorner MO and Leong DA. (1988) Intracellular calcium concentration and growth hormone secretion in individual somatotropes: effects of growth hormone-releasing factor and somatostatin. *Endocrinology* **122**: 2927-32 [PMID:2453353]
 121. Holtmann MH, Hadac EM, Ulrich CD and Miller LJ. (1996) Molecular basis and species specificity of high affinity binding of vasoactive intestinal polypeptide by the rat secretin receptor. *J Pharmacol Exp Ther* **279**: 555-60 [PMID:8930157]
 122. Holz 4th GG, Leech CA and Habener JF. (1995) Activation of a cAMP-regulated Ca(2+)-signaling pathway in pancreatic beta-cells by the insulinotropic hormone glucagon-like peptide-1. *J Biol Chem* **270**: 17749-57 [PMID:7543091]
 123. Holz GG and Habener JF. (1993) Pancreatic β -cells are rendered glucose-competent by the insulinotropic hormone glucagon-like peptide-1(7-37). *Nature* **361**: 362-365 [PMID:8381211]
 124. Horváth JE, Zarándi M, Groot K and Schally AV. (1995) Effect of long-acting antagonists of growth hormone (GH)-releasing hormone on GH and cyclic adenosine 3',5'-monophosphate release in superfused rat pituitary cells. *Endocrinology* **136**: 3849-55 [PMID:7649091]
 125. Hsiung HM, Smith DP, Zhang XY, Bennett T, Rosteck Jr PR and Lai MH. (1993) Structure and functional expression of a complementary DNA for porcine growth hormone-releasing hormone receptor. *Neuropeptides* **25**: 1-10 [PMID:8413847]
 126. Irwin DM. (2001) Molecular evolution of proglucagon. *Regul Pept* **98**: 1-12 [PMID:11179772]
 127. Ishihara T, Nakamura S, Kaziro Y, Takahashi T, Takahashi K and Nagata S. (1991) Molecular cloning and expression of a cDNA encoding the secretin receptor. *EMBO J* **10**: 1635-41 [PMID:1646711]
 128. Jazayeri A, Doré AS, Lamb D, Krishnamurthy H, Southall SM, Baig AH, Bortolato A, Koglin M, Robertson NJ and Errey JC *et al.*. (2016) Extra-helical binding site of a glucagon receptor antagonist. *Nature* **533**: 274-7 [PMID:27111510]
 129. Jazayeri A, Rappas M, Brown AJH, Kean J, Errey JC, Robertson NJ, Fiez-Vandal C, Andrews SP, Congreve M and Bortolato A *et al.*. (2017) Crystal structure of the GLP-1 receptor bound to a peptide agonist. *Nature* **546**: 254-258 [PMID:28562585]
 130. Jelinek LJ, Lok S, Rosenberg GB, Smith RA, Grant FJ, Biggs S, Bensch PA, Kuijper JL, Sheppard PO and Sprecher CA *et al.*. (1993) Expression cloning and signaling properties of the rat glucagon receptor. *Science* **259**: 1614-6 [PMID:8384375]
 131. Jensen RT and Gardner JD. (1980) Interaction of cholecystokinin with specific membrane receptors on pancreatic acinar cells. *Proc Natl Acad Sci USA* **77**: 2079-2083 [PMID:6246521]
 132. Jiang S and Ulrich C. (1995) Molecular cloning and functional expression of a human pancreatic

- secretin receptor. *Biochem Biophys Res Commun* **207**: 883-90 [PMID:7864894]
133. Jorgensen R, Martini L, Schwartz TW and Elling CE. (2005) Characterization of glucagon-like peptide-1 receptor beta-arrestin 2 interaction: a high-affinity receptor phenotype. *Mol Endocrinol* **19**: 812-23 [PMID:15528268]
 134. Kanashiro-Takeuchi RM, Tziomalos K, Takeuchi LM, Treuer AV, Lamirault G, Dulce R, Hurtado M, Song Y, Block NL and Rick F *et al.*. (2010) Cardioprotective effects of growth hormone-releasing hormone agonist after myocardial infarction. *Proc Natl Acad Sci USA* **107**: 2604-9 [PMID:20133784]
 135. Kawai K, Yokota C, Ohashi S, Watanabe Y and Yamashita K. (1995) Evidence that glucagon stimulates insulin secretion through its own receptor in rats. *Diabetologia* **38**: 274-6 [PMID:7758872]
 136. Kawai T, Sun B, Yoshino H, Feng D, Suzuki Y, Fukazawa M, Nagao S, Wainscott DB, Showalter AD and Droz BA *et al.*. (2020) Structural basis for GLP-1 receptor activation by LY3502970, an orally active nonpeptide agonist. *Proc Natl Acad Sci U S A* **117**: 29959-29967 [PMID:33177239]
 137. Kazda CM, Ding Y, Kelly RP, Garhyan P, Shi C, Lim CN, Fu H, Watson DE, Lewin AJ and Landschulz WH *et al.*. (2016) Evaluation of Efficacy and Safety of the Glucagon Receptor Antagonist LY2409021 in Patients With Type 2 Diabetes: 12- and 24-Week Phase 2 Studies. *Diabetes Care* **39**: 1241-9 [PMID:26681715]
 138. Kelly RP, Garhyan P, Raddad E, Fu H, Lim CN, Prince MJ, Pinaire JA, Loh MT and Deeg MA. (2015) Short-term administration of the glucagon receptor antagonist LY2409021 lowers blood glucose in healthy people and in those with type 2 diabetes. *Diabetes Obes Metab* **17**: 414-22 [PMID:25656305]
 139. Kieffer TJ, McIntosh CH and Pederson RA. (1995) Degradation of glucose-dependent insulinotropic polypeptide and truncated glucagon-like peptide 1 in vitro and in vivo by dipeptidyl peptidase IV. *Endocrinology* **136**: 3585-96 [PMID:7628397]
 140. Knudsen LB, Nielsen PF, Huusfeldt PO, Johansen NL, Madsen K, Pedersen FZ, Thøgersen H, Wilken M and Agersø H. (2000) Potent derivatives of glucagon-like peptide-1 with pharmacokinetic properties suitable for once daily administration. *J Med Chem* **43**: 1664-9 [PMID:10794683]
 141. Kostic TS, Tomić M, Andric SA and Stojilkovic SS. (2002) Calcium-independent and cAMP-dependent modulation of soluble guanylyl cyclase activity by G protein-coupled receptors in pituitary cells. *J Biol Chem* **277**: 16412-8 [PMID:11867632]
 142. Koth CM, Murray JM, Mukund S, Madjidi A, Minn A, Clarke HJ, Wong T, Chiang V, Luis E and Estevez A *et al.*. (2012) Molecular basis for negative regulation of the glucagon receptor. *Proc Natl Acad Sci USA* **109**: 14393-8 [PMID:22908259]
 143. Kovacs M, Schally AV, Lee EJ, Busto R, Armatis P, Groot K and Varga JL. (2002) Inhibitory effects of antagonistic analogs of GHRH on GH3 pituitary cells overexpressing the human GHRH receptor. *J Endocrinol* **175**: 425-34 [PMID:12429040]
 144. Lance VA, Murphy WA, Sueiras-Diaz J and Coy DH. (1984) Super-active analogs of growth hormone-releasing factor (1-29)-amide. *Biochem Biophys Res Commun* **119**: 265-72 [PMID:6231028]
 145. Lankat-Buttgereit B and Göke B. (1997) Cloning and characterization of the 5' flanking sequences (promoter region) of the human GLP-1 receptor gene. *Peptides* **18**: 617-24 [PMID:9213353]
 146. Lankat-Buttgereit B, Göke R, Fehmann HC, Richter G and Göke B. (1994) Molecular cloning of a cDNA encoding for the GLP-1 receptor expressed in rat lung. *Exp Clin Endocrinol* **102**: 341-7 [PMID:7813606]
 147. Larsen PJ, Tang-Christensen M and Jessop DS. (1997) Central administration of glucagon-like peptide-1 activates hypothalamic neuroendocrine neurons in the rat. *Endocrinology* **138**: 4445-55 [PMID:9322962]
 148. Lau J, Bloch P, Schäffer L, Pettersson I, Spetzler J, Kofoed J, Madsen K, Knudsen LB, McGuire J and Steensgaard DB *et al.*. (2015) Discovery of the Once-Weekly Glucagon-Like Peptide-1 (GLP-1) Analogue Semaglutide. *J Med Chem* **58**: 7370-80 [PMID:26308095]
 149. Lee SM, Chen L, Chow BK and Yung WH. (2005) Endogenous release and multiple actions of secretin in the rat cerebellum. *Neuroscience* **134**: 377-86 [PMID:15963647]
 150. Lefebvre P. (1966) The physiological effect of glucagon on fat mobilization. *Diabetologia* **2**: 130-132 [PMID:6005201]
 151. Li B, Xi X, Roane DS, Ryan DH and Martin RJ. (2003) Distribution of glucokinase, glucose transporter GLUT2, sulfonylurea receptor-1, glucagon-like peptide-1 receptor and neuropeptide Y messenger RNAs in rat brain by quantitative real time RT-PCR. *Brain Res Mol Brain Res* **113**: 139-42 [PMID:12750016]
 152. Lin C, Lin SC, Chang CP and Rosenfeld MG. (1992) Pit-1-dependent expression of the receptor for growth hormone releasing factor mediates pituitary cell growth. *Nature* **360**: 765-8 [PMID:1334535]
 153. Lin SC, Lin CR, Gukovsky I, Lusis AJ, Sawchenko PE and Rosenfeld MG. (1993) Molecular basis

of the little mouse phenotype and implications for cell type-specific growth. *Nature* **364**: 208-13 [PMID:8391647]

154. Ling N, Baird A, Wehrenberg WB, Ueno N, Munegumi T and Brazeau P. (1984) Synthesis and in vitro bioactivity of C-terminal deleted analogs of human growth hormone-releasing factor. *Biochem Biophys Res Commun* **123**: 854-61 [PMID:6435620]
155. Ling N, Esch F, Böhlen P, Brazeau P, Wehrenberg WB and Guillemin R. (1984) Isolation, primary structure, and synthesis of human hypothalamic somatocrinin: growth hormone-releasing factor. *Proc Natl Acad Sci USA* **81**: 4302-6 [PMID:6431406]
156. Lok S, Kuijper JL, Jelinek LJ, Kramer JM, Whitmore TE, Sprecher CA, Mathewes S, Grant FJ, Biggs SH and Rosenberg GB *et al.*. (1994) The human glucagon receptor encoding gene: structure, cDNA sequence and chromosomal localization. *Gene* **140**: 203-9 [PMID:8144028]
157. Lovshin J, Yusta B, Iliopoulos I, Migirdicyan A, Dableh L, Brubaker PL and Drucker DJ. (2000) Ontogeny of the glucagon-like peptide-2 receptor axis in the developing rat intestine. *Endocrinology* **141**: 4194-201 [PMID:11089553]
158. Lu M, Wheeler MB, Leng XH and Boyd 3rd AE. (1993) The role of the free cytosolic calcium level in beta-cell signal transduction by gastric inhibitory polypeptide and glucagon-like peptide I(7-37). *Endocrinology* **132**: 94-100 [PMID:8380389]
159. Lussier BT, French MB, Moore BC and Kraicer J. (1991) Free intracellular Ca²⁺ concentration ([Ca²⁺]_i) and growth hormone release from purified rat somatotrophs. I. GH-releasing factor-induced Ca²⁺ influx raises [Ca²⁺]_i. *Endocrinology* **128**: 570-82 [PMID:1846113]
160. MacLusky NJ, Cook S, Scrocchi L, Shin J, Kim J, Vaccarino F, Asa SL and Drucker DJ. (2000) Neuroendocrine function and response to stress in mice with complete disruption of glucagon-like peptide-1 receptor signaling. *Endocrinology* **141**: 752-62 [PMID:10650957]
161. MacNeil DJ, Occi JL, Hey PJ, Strader CD and Graziano MP. (1994) Cloning and expression of a human glucagon receptor. *Biochem Biophys Res Commun* **198**: 328-34 [PMID:7507321]
162. Madsen P, Knudsen LB, Wiberg FC and Carr RD. (1998) Discovery and structure-activity relationship of the first non-peptide competitive human glucagon receptor antagonists. *J Med Chem* **41**: 5150-7 [PMID:9857085]
163. Margioris AN, Brockmann G, Bohler Jr HC, Grino M, Vamvakopoulos N and Chrousos GP. (1990) Expression and localization of growth hormone-releasing hormone messenger ribonucleic acid in rat placenta: in vitro secretion and regulation of its peptide product. *Endocrinology* **126**: 151-8 [PMID:2104584]
164. Mark HF and Chow BK. (1995) Localization of the gene encoding the secretin receptor, SCTR, on human chromosome 2q14.1 by fluorescence in situ hybridization and chromosome morphometry. *Genomics* **29**: 817-8 [PMID:8575789]
165. Matsubara S, Sato M, Mizobuchi M, Niimi M and Takahara J. (1995) Differential gene expression of growth hormone (GH)-releasing hormone (GRH) and GRH receptor in various rat tissues. *Endocrinology* **136**: 4147-50 [PMID:7649123]
166. Mayo KE. (1992) Molecular cloning and expression of a pituitary-specific receptor for growth hormone-releasing hormone. *Mol Endocrinol* **6**: 1734-44 [PMID:1333056]
167. Mayo KE, Cerelli GM, Rosenfeld MG and Evans RM. (1985) Characterization of cDNA and genomic clones encoding the precursor to rat hypothalamic growth hormone-releasing factor. *Nature* **314**: 464-7 [PMID:3920534]
168. Mayo KE and Godfrey PA. (1996) The growth-hormone-releasing hormone receptor: signal transduction, gene expression, and physiological function in growth regulation. *Ann NY Acad Sci* **805**: 184-203 [PMID:8993403]
169. Mayo KE, Godfrey PA, Suhr ST, Kulik DJ and Rahal JO. (1995) Growth hormone-releasing hormone: synthesis and signaling. *Recent Prog Horm Res* **50**: 35-73 [PMID:7740167]
170. Mayo KE, Miller LJ, Bataille D, Dalle S, Göke B, Thorens B and Drucker DJ. (2003) International Union of Pharmacology. XXXV. The glucagon receptor family. *Pharmacol Rev* **55**: 167-94 [PMID:12615957]
171. Mayo KE, Vale W, Rivier J, Rosenfeld MG and Evans RM. (1983) Expression-cloning and sequence of a cDNA encoding human growth hormone-releasing factor. *Nature* **306**: 86-8 [PMID:6415488]
172. McIntosh CH, Bremsak I, Lynn FC, Gill R, Hinke SA, Gelling R, Nian C, McKnight G, Jaspers S and Pederson RA. (1999) Glucose-dependent insulinotropic polypeptide stimulation of lipolysis in differentiated 3T3-L1 cells: wortmannin-sensitive inhibition by insulin. *Endocrinology* **140**: 398-404 [PMID:9886851]
173. McKeage K. (2015) Teduglutide: a guide to its use in short bowel syndrome. *Clin Drug Investig* **35**: 335-40 [PMID:25859983]
174. Menzel S, Stoffel M, Espinosa 3rd R, Fernald AA, Le Beau MM and Bell GI. (1994) Localization of the glucagon receptor gene to human chromosome band 17q25. *Genomics* **20**: 327-8 [PMID:8020989]
175. Merchenthaler I, Vigh S, Schally AV and Petrusz P. (1984) Immunocytochemical localization of growth hormone-releasing factor in the rat hypothalamus. *Endocrinology* **114**: 1082-5

[PMID:6423368]

176. Mezo AR, Chen Y, Valenzuela FA and Qu H. (2018) Glucagon and GLP-1 co-agonist compounds Patent number: [US9938335B2](#). Assignee: Eli Lilly and Co. Priority date: 16/06/2016. Publication date: 10/04/2018.
177. Miao L, Lou J, Xu S, Zhang J, Zhong Y, Wang G, Li Y, Lei S, Shao S and Wang J *et al.*. (2025) Discovery of New Difluorocyclobutyl Derivatives as Effective Glucagon-Like Peptide-1 Receptor Agonists with Reduced hERG Inhibitory Activities. *J Med Chem* **68**: 7662-7692 [PMID:40167442]
178. Miller TL, Godfrey PA, Dealmeida VI and Mayo KE. (1999) The rat growth hormone-releasing hormone receptor gene: structure, regulation, and generation of receptor isoforms with different signaling properties. *Endocrinology* **140**: 4152-65 [PMID:10465288]
179. Miranda LP, Winters KA, Gegg CV, Patel A, Aral J, Long J, Zhang J, Diamond S, Guido M and Stanislaus S *et al.*. (2008) Design and synthesis of conformationally constrained glucagon-like peptide-1 derivatives with increased plasma stability and prolonged in vivo activity. *J Med Chem* **51**: 2758-65 [PMID:18412318]
180. Mitchell ML, Byrne MJ and Silver J. (1969) Growth-hormone release by glucagon. *Lancet* **1**: 289-90 [PMID:4178983]
181. Miyawaki K, Yamada Y, Yano H, Niwa H, Ban N, Ihara Y, Kubota A, Fujimoto S, Kajikawa M and Kuroe A *et al.*. (1999) Glucose intolerance caused by a defect in the entero-insular axis: a study in gastric inhibitory polypeptide receptor knockout mice. *Proc Natl Acad Sci USA* **96**: 14843-7 [PMID:10611300]
182. Moens K, Heimberg H, Flamez D, Huypens P, Quartier E, Ling Z, Pipeleers D, Gremlich S, Thorens B and Schuit F. (1996) Expression and functional activity of glucagon, glucagon-like peptide I, and glucose-dependent insulinotropic peptide receptors in rat pancreatic islet cells. *Diabetes* **45**: 257-61 [PMID:8549871]
183. Montrose-Rafizadeh C, Yang H, Rodgers BD, Beday A, Pritchette LA and Eng J. (1997) High potency antagonists of the pancreatic glucagon-like peptide-1 receptor. *J Biol Chem* **272**: 21201-6 [PMID:9261127]
184. Montrose-Rafizadeh C, Yang H, Wang Y, Roth J, Montrose MH and Adams LG. (1997) Novel signal transduction and peptide specificity of glucagon-like peptide receptor in 3T3-L1 adipocytes. *J Cell Physiol* **172**: 275-83 [PMID:9284947]
185. Moore MC, Connolly CC and Cherrington AD. (1998) Autoregulation of hepatic glucose production. *Eur J Endocrinol* **138**: 240-8 [PMID:9539293]
186. Motomura T, Hashimoto K, Koga M, Arita N, Hayakawa T, Kishimoto T and Kasayama S. (1998) Inhibition of signal transduction by a splice variant of the growth hormone-releasing hormone receptor expressed in human pituitary adenomas. *Metab Clin Exp* **47**: 804-8 [PMID:9667225]
187. Munroe DG, Gupta AK, Kooshesh F, Vyas TB, Rizkalla G, Wang H, Demchyshyn L, Yang ZJ, Kamboj RK and Chen H *et al.*. (1999) Prototypic G protein-coupled receptor for the intestinotrophic factor glucagon-like peptide 2. *Proc Natl Acad Sci USA* **96**: 1569-73 [PMID:9990065]
188. Mutt V, Jorpes JE and Magnusson S. (1970) Structure of porcine secretin. The amino acid sequence. *Eur J Biochem* **15**: 513-9 [PMID:5465996]
189. Mühlhauser I, Koch J and Berger M. (1985) Pharmacokinetics and bioavailability of injected glucagon: differences between intramuscular, subcutaneous, and intravenous administration. *Diabetes Care* **8**: 39-42 [PMID:3971846]
190. Netchine I, Talon P, Dastot F, Vitaux F, Goossens M and Amselem S. (1998) Extensive phenotypic analysis of a family with growth hormone (GH) deficiency caused by a mutation in the GH-releasing hormone receptor gene. *J Clin Endocrinol Metab* **83**: 432-6 [PMID:9467553]
191. Ng SS, Pang RT, Chow BK and Cheng CH. (1999) Real-time evaluation of human secretin receptor activity using cytosensor microphysiometry. *J Cell Biochem* **72**: 517-27 [PMID:10022611]
192. Nilsson A, Carlquist M, Jörnvall H and Mutt V. (1980) Isolation and characterization of chicken secretin. *Eur J Biochem* **112**: 383-8 [PMID:7460928]
193. Nolte WM, Fortin JP, Stevens BD, Aspnes GE, Griffith DA, Hoth LR, Ruggeri RB, Mathiowetz AM, Limberakis C and Hepworth D *et al.*. (2014) A potentiator of orthosteric ligand activity at GLP-1R acts via covalent modification. *Nat Chem Biol* **10**: 629-31 [PMID:24997604]
194. Northup JK, Smigel MD, Sternweis PC and Gilman AG. (1983) The subunits of the stimulatory regulatory component of adenylate cyclase. Resolution of the activated 45,000-dalton (α) subunit. *J Biol Chem* **258**: 11369-11376 [PMID:6309844]
195. Nyström T, Gonon AT, Sjöholm A and Pernow J. (2005) Glucagon-like peptide-1 relaxes rat conduit arteries via an endothelium-independent mechanism. *Regul Pept* **125**: 173-7 [PMID:15582729]
196. Ohlsson L and Lindström P. (1990) The correlation between calcium outflow and growth hormone release in perfused rat somatotrophs. *Endocrinology* **126**: 488-97 [PMID:1688413]
197. Okamoto H, Kim J, Aglione J, Lee J, Cavino K, Na E, Rafique A, Kim JH, Harp J and Valenzuela DM *et al.*. (2015) Glucagon Receptor Blockade With a Human Antibody Normalizes Blood

- Glucose in Diabetic Mice and Monkeys. *Endocrinology* **156**: 2781-94 [PMID:26020795]
198. Parker JC, Andrews KM, Allen MR, Stock JL and McNeish JD. (2002) Glycemic control in mice with targeted disruption of the glucagon receptor gene. *Biochem Biophys Res Commun* **290**: 839-843 [PMID:11785978]
 199. Parthier C, Kleinschmidt M, Neumann P, Rudolph R, Manhart S, Schlénzig D, Fanghänel J, Rahfeld JU, Demuth HU and Stubbs MT. (2007) Crystal structure of the incretin-bound extracellular domain of a G protein-coupled receptor. *Proc Natl Acad Sci USA* **104**: 13942-7 [PMID:17715056]
 200. Petersen KF and Sullivan JT. (2001) Effects of a novel glucagon receptor antagonist (Bay 27-9955) on glucagon-stimulated glucose production in humans. *Diabetologia* **44**: 2018-24 [PMID:11719833]
 201. Petersenn S, Rasch AC, Heyens M and Schulte HM. (1998) Structure and regulation of the human growth hormone-releasing hormone receptor gene. *Mol Endocrinol* **12**: 233-47 [PMID:9482665]
 202. Pohl SL, Birnbaumer L and Rodbell M. (1969) Glucagon-sensitive adenylyl cyclase in plasma membrane of hepatic parenchymal cells. *Science* **164**: 566-7 [PMID:4305077]
 203. Pohl SL, Birnbaumer L and Rodbell M. (1971) The glucagon-sensitive adenylyl cyclase system in plasma membranes of rat liver. I. Properties. *J Biol Chem* **246**: 1849-56 [PMID:4993961]
 204. Preitner F, Ibberson M, Franklin I, Binnert C, Pende M, Gjinovci A, Hansotia T, Drucker DJ, Wollheim C and Burcelin R *et al.*. (2004) Gluco-incretins control insulin secretion at multiple levels as revealed in mice lacking GLP-1 and GIP receptors. *J Clin Invest* **113**: 635-45 [PMID:14966573]
 205. Qureshi SA, Rios Candelore M, Xie D, Yang X, Tota LM, Ding VD, Li Z, Bansal A, Miller C and Cohen SM *et al.*. (2004) A novel glucagon receptor antagonist inhibits glucagon-mediated biological effects. *Diabetes* **53**: 3267-73 [PMID:15561959]
 206. Ramírez JL, Castaño JP, Torronteras R, Martínez-Fuentes AJ, Frawley LS, García-Navarro S and Gracia-Navarro F. (1999) Growth hormone (GH)-releasing factor differentially activates cyclic adenosine 3',5'-monophosphate- and inositol phosphate-dependent pathways to stimulate GH release in two porcine somatotrope subpopulations. *Endocrinology* **140**: 1752-9 [PMID:10098512]
 207. Raufman JP, Singh L and Eng J. (1991) Exendin-3, a novel peptide from *Heloderma horridum* venom, interacts with vasoactive intestinal peptide receptors and a newly described receptor on dispersed acini from guinea pig pancreas. Description of exendin-3(9-39) amide, a specific exendin receptor antagonist. *J Biol Chem* **266**: 2897-902 [PMID:1704369]
 208. Richter G, Göke R, Göke B and Arnold R. (1990) Characterization of receptors for glucagon-like peptide-1(7-36)amide on rat lung membranes. *FEBS Lett* **267**: 78-80 [PMID:2163902]
 209. Richter G, Göke R, Göke B, Schmidt H and Arnold R. (1991) Characterization of glucagon-like peptide-I(7-36)amide receptors of rat lung membranes by covalent cross-linking. *FEBS Lett* **280**: 247-50 [PMID:1849486]
 210. Rivier J and Vale W. (1982) Characterization of a growth hormone-releasing factor from a human pancreatic islet tumour. *Nature* **300**: 276-278 [PMID:6292724]
 211. Robberecht P, Coy DH, Waelbroeck M, Heiman ML, de Neef P, Camus JC and Christophe J. (1985) Structural requirements for the activation of rat anterior pituitary adenylate cyclase by growth hormone-releasing factor (GRF): discovery of (N-Ac-Tyr¹, D-Arg²)-GRF(1-29)-NH₂ as a GRF antagonist on membranes. *Endocrinology* **117**: 1759-64 [PMID:2994998]
 212. Robberecht P, De Neef P, Waelbroeck M, Camus JC, Scemama JL, Fourmy D, Pradayrol L, Vaysse N and Christophe J. (1988) Secretin receptors in human pancreatic membranes. *Pancreas* **3**: 529-35 [PMID:3186683]
 213. Runge S, Thøgersen H, Madsen K, Lau J and Rudolph R. (2008) Crystal structure of the ligand-bound glucagon-like peptide-1 receptor extracellular domain. *J Biol Chem* **283**: 11340-7 [PMID:18287102]
 214. Salvatori R, Hayashida CY, Aguiar-Oliveira MH, Phillips 3rd JA, Souza AH, Gondo RG, Toledo SP, Conceição MM, Prince M and Maheshwari HG *et al.*. (1999) Familial dwarfism due to a novel mutation of the growth hormone-releasing hormone receptor gene. *J Clin Endocrinol Metab* **84**: 917-23 [PMID:10084571]
 215. Samols E, Marri G and Marks V. (1966) Interrelationship of glucagon, insulin and glucose. The insulinogenic effect of glucagon. *Diabetes* **15**: 855-66 [PMID:5957476]
 216. Sawchenko PE, Swanson LW, Rivier J and Vale WW. (1985) The distribution of growth-hormone-releasing factor (GRF) immunoreactivity in the central nervous system of the rat: an immunohistochemical study using antisera directed against rat hypothalamic GRF. *J Comp Neurol* **237**: 100-15 [PMID:3930577]
 217. Schaffalitzky de Muckadell OB and Fahrenkrug J. (1978) Secretion pattern of secretin in man: regulation by gastric acid. *Gut* **19**: 812-8 [PMID:30682]
 218. Schally AV and Varga JL. (1999) Antagonistic Analogs of Growth Hormone-releasing Hormone: New Potential Antitumor Agents. *Trends Endocrinol Metab* **10**: 383-391 [PMID:10542394]

219. Schirra J, Kuwert P, Wank U, Leicht P, Arnold R, Göke B and Katschinski M. (1997) Differential effects of subcutaneous GLP-1 on gastric emptying, antroduodenal motility, and pancreatic function in men. *Proc Assoc Am Physicians* **109**: 84-97 [PMID:9010920]
220. Schmidtler J, Dehne K, Offermanns S, Rosenthal W, Classen M and Schepp W. (1994) Stimulation of rat parietal cell function by histamine and GLP-1-(7-36) amide is mediated by Gs alpha. *Am J Physiol* **266**: G775-82 [PMID:8203524]
221. Scott RB, Kirk D, MacNaughton WK and Meddings JB. (1998) GLP-2 augments the adaptive response to massive intestinal resection in rat. *Am J Physiol* **275**: G911-21 [PMID:9815019]
222. Sebokova E, Christ AD, Wang H, Sewing S, Dong JZ, Taylor J, Cawthorne MA and Culler MD. (2010) Taspoglutide, an analog of human glucagon-like Peptide-1 with enhanced stability and in vivo potency. *Endocrinology* **151**: 2474-82 [PMID:20382695]
223. Shimizu I, Hirota M, Ohboshi C and Shima K. (1987) Identification and localization of glucagon-like peptide-1 and its receptor in rat brain. *Endocrinology* **121**: 1076-82 [PMID:3040376]
224. Shinomura Y, Eng J and Yalow RS. (1987) Dog secretin: sequence and biologic activity. *Life Sci* **41**: 1243-8 [PMID:3626755]
225. Shughrue PJ, Lane MV and Merchenthaler I. (1996) Glucagon-like peptide-1 receptor (GLP1-R) mRNA in the rat hypothalamus. *Endocrinology* **137**: 5159-62 [PMID:8895391]
226. Siani A, Iacone R, Russo O, Barba G, Russo P, Cappuccio FP, Galletti F and Strazzullo P. (2001) Gly40Ser polymorphism of the glucagon receptor gene is associated with central adiposity in men. *Obes Res* **9**: 722-6 [PMID:11707539]
227. Siu FY, He M, de Graaf C, Han GW, Yang D, Zhang Z, Zhou C, Xu Q, Wacker D and Joseph JS *et al.*. (2013) Structure of the human glucagon class B G-protein-coupled receptor. *Nature* **499**: 444-9 [PMID:23863937]
228. Skoglund G, Hussain MA and Holz GG. (2000) Glucagon-like peptide 1 stimulates insulin gene promoter activity by protein kinase A-independent activation of the rat insulin I gene cAMP response element. *Diabetes* **49**: 1156-1164 [PMID:10909973]
229. Slim GM, Lansing M, Wizzard P, Nation PN, Wheeler SE, Brubaker PL, Jeppesen PB, Wales PW and Turner JM. (2019) Novel Long-Acting GLP-2 Analogue, FE 203799 (Apraglutide), Enhances Adaptation and Linear Intestinal Growth in a Neonatal Piglet Model of Short Bowel Syndrome with Total Resection of the Ileum. *JPEN J Parenter Enteral Nutr* **43**: 891-898 [PMID:30614011]
230. Song G, Yang D, Wang Y, de Graaf C, Zhou C, Jiang S, Liu K, Cai X, Dai A and Lin G *et al.*. (2017) Human GLP-1 receptor transmembrane domain structure in complex with allosteric modulators. *Nature* **546**: 312-315 [PMID:28514449]
231. Spiess J, Rivier J and Vale W. (1983) Characterization of rat hypothalamic growth hormone-releasing factor. *Nature* **303**: 532-5 [PMID:6406907]
232. Stefanescu L, Kovacs K, Horvath E, Asa SL, Losinski NE, Billestrup N, Price J and Vale W. (1989) Adenohypophysial changes in mice transgenic for human growth hormone-releasing factor: a histological, immunocytochemical, and electron microscopic investigation. *Endocrinology* **125**: 2710-8 [PMID:2507296]
233. Stephanou A, Knight RA and Lightman SL. (1991) Production of a growth hormone-releasing hormone-like peptide and its mRNA by human lymphocytes. *Neuroendocrinology* **53**: 628-33 [PMID:1876239]
234. Stoffel M, Espinosa 3rd R, Le Beau MM and Bell GI. (1993) Human glucagon-like peptide-1 receptor gene. Localization to chromosome band 6p21 by fluorescence in situ hybridization and linkage of a highly polymorphic simple tandem repeat DNA polymorphism to other markers on chromosome 6. *Diabetes* **42**: 1215-8 [PMID:8392011]
235. Suhr ST, Rahal JO and Mayo KE. (1989) Mouse growth-hormone-releasing hormone: precursor structure and expression in brain and placenta. *Mol Endocrinol* **3**: 1693-700 [PMID:2514346]
236. Svoboda M and Christophe J. (1993) A cDNA construct allowing the expression of rat hepatic glucagon receptors. *Biochem Biophys Res Commun* **192**: 135-142 [PMID:8386505]
237. Szpirer C, Szpirer J, Vanvooren P, Rivière M, Maget B, Svoboda M, Shiozawa M, Simon JS, Jacob HJ and Koike G. (1997) Localization of the rat genes encoding glucagon, glucagon receptor, and insulin receptor, candidates for diabetes mellitus susceptibility loci. *Mamm Genome* **8**: 586-8 [PMID:9250867]
238. Takahashi T and Chihara K. (1995) Regional distribution of growth hormone-releasing hormone (GHRH) receptor mRNA in the rat brain. *Endocrinology* **136**: 4721-4724 [PMID:7664697]
239. Takano K, Takei T, Teramoto A and Yamashita N. (1996) GHRH activates a nonselective cation current in human GH-secreting adenoma cells. *Am J Physiol* **270**: E1050-7 [PMID:8764191]
240. Tang J, Lagacé G, Castagné J and Collu R. (1995) Identification of human growth hormone-releasing hormone receptor splicing variants. *J Clin Endocrinol Metab* **80**: 2381-7 [PMID:7629234]
241. Tay J, Goulet M, Rusche J and Boismenu R. (2004) Age-related and regional differences in secretin and secretin receptor mRNA levels in the rat brain. *Neurosci Lett* **366**: 176-81 [PMID:15276242]
242. Thorens B. (1992) Expression cloning of the pancreatic beta cell receptor for the gluco-incretin

- hormone glucagon-like peptide 1. *Proc Natl Acad Sci USA* **89**: 8641-5 [PMID:1326760]
243. Thorens B, Porret A, Bühler L, Deng SP, Morel P and Widmann C. (1993) Cloning and functional expression of the human islet GLP-1 receptor. Demonstration that exendin-4 is an agonist and exendin-(9-39) an antagonist of the receptor. *Diabetes* **42**: 1678-82 [PMID:8405712]
 244. Thorens B and Widmann C. (1996) Structure and function of the glucagon-like peptide-1 receptor. In *Handbook of Experimental Pharmacology Glucagon III* Edited by Lefebvre PJ: Springer: 255-273 [ISBN: 354060989X]
 245. Thulesen J, Knudsen LB, Hartmann B, Hastrup S, Kissow H, Jeppesen PB, Ørskov C, Holst JJ and Poulsen SS. (2002) The truncated metabolite GLP-2 (3-33) interacts with the GLP-2 receptor as a partial agonist. *Regul Pept* **103**: 9-15 [PMID:11738243]
 246. Tibaduiza EC, Chen C and Beinborn M. (2001) A small molecule ligand of the glucagon-like peptide 1 receptor targets its amino-terminal hormone binding domain. *J Biol Chem* **276**: 37787-93 [PMID:11498540]
 247. Trümper A, Trümper K, Trusheim H, Arnold R, Göke B and Hörsch D. (2001) Glucose-dependent insulinotropic polypeptide is a growth factor for beta (INS-1) cells by pleiotropic signaling. *Mol Endocrinol* **15**: 1559-70 [PMID:11518806]
 248. Tsai CH, Hill M, Asa SL, Brubaker PL and Drucker DJ. (1997) Intestinal growth-promoting properties of glucagon-like peptide-2 in mice. *Am J Physiol* **273**: E77-84 [PMID:9252482]
 249. Tsai CH, Hill M and Drucker DJ. (1997) Biological determinants of intestinotrophic properties of GLP-2 in vivo. *Am J Physiol* **272**: G662-8 [PMID:9124589]
 250. Tseng CC, Kieffer TJ, Jarboe LA, Usdin TB and Wolfe MM. (1996) Postprandial stimulation of insulin release by glucose-dependent insulinotropic polypeptide (GIP). Effect of a specific glucose-dependent insulinotropic polypeptide receptor antagonist in the rat. *J Clin Invest* **98**: 2440-5 [PMID:8958204]
 251. Tseng CC, Zhang XY and Wolfe MM. (1999) Effect of GIP and GLP-1 antagonists on insulin release in the rat. *Am J Physiol* **276**: E1049-54 [PMID:10362617]
 252. Turton MD, O'Shea D, Gunn I, Beak SA, Edwards CM, Meeran K, Choi SJ, Taylor GM, Heath MM and Lambert PD *et al.*. (1996) A role for glucagon-like peptide-1 in the central regulation of feeding. *Nature* **379**: 69-72 [PMID:8538742]
 253. Ulrich 2nd CD, Wood P, Hadac EM, Koprass E, Whitcomb DC and Miller LJ. (1998) Cellular distribution of secretin receptor expression in rat pancreas. *Am J Physiol* **275**: G1437-44 [PMID:9843782]
 254. Unson CG, Andreu D, Gurzenda EM and Merrifield RB. (1987) Synthetic peptide antagonists of glucagon. *Proc Natl Acad Sci USA* **84**: 4083-7 [PMID:3035568]
 255. Unson CG, Gurzenda EM and Merrifield RB. (1989) Biological activities of des-His1[Glu9]glucagon amide, a glucagon antagonist. *Peptides* **10**: 1171-7 [PMID:2560175]
 256. Usdin TB and Bonner TI. (1993) Gastric inhibitory polypeptide receptor, a member of the secretin- vasoactive intestinal peptide receptor family, is widely distributed in peripheral organs and the brain. *Endocrinology* **133**: 2861-2870 [PMID:8243312]
 257. Uttenthal LO and Blázquez E. (1990) Characterization of high-affinity receptors for truncated glucagon-like peptide-1 in rat gastric glands. *FEBS Lett* **262**: 139-41 [PMID:2156728]
 258. Uttenthal LO, Toledano A and Blázquez E. (1992) Autoradiographic localization of receptors for glucagon-like peptide-1 (7-36) amide in rat brain. *Neuropeptides* **21**: 143-6 [PMID:1352862]
 259. Véniant MM, Lu SC, Atangan L, Komorowski R, Stanislaus S, Cheng Y, Wu B, Falsey JR, Hager T and Thomas VA *et al.*. (2024) A GIPR antagonist conjugated to GLP-1 analogues promotes weight loss with improved metabolic parameters in preclinical and phase 1 settings. *Nat Metab* **6**: 290-303 [PMID:38316982]
 260. Vajda EG, Potter SC, Fujitaki JM, Reddy RK, Van Poelje PD, Lee YH, Henderson I, Zhi L and Marschke KB. (2012) LGD-6972, a potent, orally-bioavailable, small molecule glucagon receptor antagonist for the treatment of type 2 diabetes *Diabetes* **61**: A252
 261. Valverde I, Mérida E, Delgado E, Trapote MA and Villanueva-Peñacarrillo ML. (1993) Presence and characterization of glucagon-like peptide-1(7-36) amide receptors in solubilized membranes of rat adipose tissue. *Endocrinology* **132**: 75-9 [PMID:8380388]
 262. van Eyll B, Lankat-Buttgereit B, Bode HP, Göke R and Göke B. (1994) Signal transduction of the GLP-1-receptor cloned from a human insulinoma. *FEBS Lett* **348**: 7-13 [PMID:7517895]
 263. Varga JL, Schally AV, Csernus VJ, Zarándi M, Halmos G, Groot K and Rékási Z. (1999) Synthesis and biological evaluation of antagonists of growth hormone-releasing hormone with high and protracted in vivo activities. *Proc Natl Acad Sci USA* **96**: 692-7 [PMID:9892695]
 264. Varga JL, Schally AV, Horvath JE, Kovacs M, Halmos G, Groot K, Toller GL, Rekasi Z and Zarandi M. (2004) Increased activity of antagonists of growth hormone-releasing hormone substituted at positions 8, 9, and 10. *Proc Natl Acad Sci USA* **101**: 1708-13 [PMID:14755056]
 265. Volz A, Göke R, Lankat-Buttgereit B, Fehmann HC, Bode HP and Göke B. (1995) Molecular cloning, functional expression, and signal transduction of the GIP-receptor cloned from a human insulinoma. *FEBS Lett* **373**: 23-9 [PMID:7589426]
 266. Wajnarajch MP, Chua SC, Green ED and Leibell RL. (1994) Human growth hormone-releasing

- hormone receptor (GHRHR) maps to a YAC at chromosome 7p15. *Mamm Genome* **5**: 595 [PMID:8000149]
267. Wajnrajch MP, Gertner JM, Harbison MD, Chua Jr SC and Leibel RL. (1996) Nonsense mutation in the human growth hormone-releasing hormone receptor causes growth failure analogous to the little (lit) mouse. *Nat Genet* **12**: 88-90 [PMID:8528260]
 268. Wakelam MJ, Murphy GJ, Hruby VJ and Houslay MD. (1986) Activation of two signal-transduction systems in hepatocytes by glucagon. *Nature* **323**: 68-71 [PMID:3018586]
 269. Walsh NA, Yusta B, DaCampa MP, Anini Y, Drucker DJ and Brubaker PL. (2003) Glucagon-like peptide-2 receptor activation in the rat intestinal mucosa. *Endocrinology* **144**: 4385-92 [PMID:12960094]
 270. Wei Y and Mojsov S. (1995) Tissue-specific expression of the human receptor for glucagon-like peptide-I: brain, heart and pancreatic forms have the same deduced amino acid sequences. *FEBS Lett* **358**: 219-24 [PMID:7843404]
 271. Werner U, Haschke G, Herling AW and Kramer W. (2010) Pharmacological profile of lixisenatide: A new GLP-1 receptor agonist for the treatment of type 2 diabetes. *Regul Pept* **164**: 58-64 [PMID:20570597]
 272. Wheeler MB, Gelling RW, McIntosh CH, Georgiou J, Brown JC and Pederson RA. (1995) Functional expression of the rat pancreatic islet glucose-dependent insulinotropic polypeptide receptor: ligand binding and intracellular signaling properties. *Endocrinology* **136**: 4629-39 [PMID:7664683]
 273. Wheeler MB, Lu M, Dillon JS, Leng XH, Chen C and Boyd 3rd AE. (1993) Functional expression of the rat glucagon-like peptide-I receptor, evidence for coupling to both adenyl cyclase and phospholipase-C. *Endocrinology* **133**: 57-62 [PMID:8391428]
 274. White CM. (1999) A review of potential cardiovascular uses of intravenous glucagon administration. *J Clin Pharmacol* **39**: 442-7 [PMID:10234590]
 275. Widmann C, Dolci W and Thorens B. (1997) Internalization and homologous desensitization of the GLP-1 receptor depend on phosphorylation of the receptor carboxyl tail at the same three sites. *Mol Endocrinol* **11**: 1094-102 [PMID:9212057]
 276. Wildhage I, Trusheim H, Göke B and Lankat-Buttgereit B. (1999) Gene expression of the human glucagon-like peptide-1 receptor is regulated by Sp1 and Sp3. *Endocrinology* **140**: 624-31 [PMID:9927286]
 277. Willard FS, Wainscott DB, Showalter AD, Stutsman C, Ma W, Cardona GR, Zink RW, Corkins CM, Chen Q and Yumibe N *et al.*. (2021) Discovery of an Orally Efficacious Positive Allosteric Modulator of the Glucagon-like Peptide-1 Receptor. *J Med Chem* **64**: 3439-3448 [PMID:33721487]
 278. Wiśniewski K, Sueiras-Diaz J, Jiang G, Galyean R, Lu M, Thompson D, Wang YC, Croston G, Posch A and Hargrove DM *et al.*. (2016) Synthesis and Pharmacological Characterization of Novel Glucagon-like Peptide-2 (GLP-2) Analogues with Low Systemic Clearance. *J Med Chem* **59**: 3129-39 [PMID:26986178]
 279. Wright DE, Hruby VJ and Rodbell M. (1978) A reassessment of structure-function relationships in glucagon. Glucagon1-21 is a full agonist. *J Biol Chem* **253**: 6338-40 [PMID:210180]
 280. Wright DE and Rodbell M. (1979) Glucagon1-6 binds to the glucagon receptor and activates hepatic adenylate cyclase. *J Biol Chem* **254**: 268-269 [PMID:216670]
 281. Xiong X, Ke X, Wang L, Yao Z, Guo Y, Zhang X, Chen Y, Pang CP, Schally AV and Zhang H. (2020) Splice variant of growth hormone-releasing hormone receptor drives esophageal squamous cell carcinoma conferring a therapeutic target. *Proc Natl Acad Sci USA* **117**: 6726-6732 [PMID:32156725]
 282. Xiong Y, Guo J, Candelore MR, Liang R, Miller C, Dallas-Yang Q, Jiang G, McCann PE, Qureshi SA and Tong X *et al.*. (2012) Discovery of a novel glucagon receptor antagonist N-[(4-{(1S)-1-[3-(3, 5-dichlorophenyl)-5-(6-methoxynaphthalen-2-yl)-1H-pyrazol-1-yl]ethyl}phenyl)carbonyl]-β-alanine (MK-0893) for the treatment of type II diabetes. *J Med Chem* **55**: 6137-48 [PMID:22708876]
 283. Yada T and Nakata M. (1993) Glucagon-like peptide-1-(7-36)amide and a rise in cyclic adenosine 3', 5'-monophosphate increase cytosolic free Ca²⁺ in rat pancreatic β-cells by enhancing Ca²⁺ channel activity. *Endocrinology* **133**: 1685-1692 [PMID:8404610]
 284. Yang PY, Zou H, Lee C, Muppidi A, Chao E, Fu Q, Luo X, Wang D, Schultz PG and Shen W. (2018) Stapled, Long-Acting Glucagon-like Peptide 2 Analog with Efficacy in Dextran Sodium Sulfate Induced Mouse Colitis Models. *J Med Chem* **61**: 3218-3223 [PMID:29528634]
 285. You CH, Rominger JM and Chey WY. (1983) Potentiation effect of cholecystokinin-octapeptide on pancreatic bicarbonate secretion stimulated by a physiologic dose of secretin in humans. *Gastroenterology* **85**: 40-5 [PMID:6303892]
 286. Yusta B, Somwar R, Wang F, Munroe D, Grinstein S, Klip A and Drucker DJ. (1999) Identification of glucagon-like peptide-2 (GLP-2)-activated signaling pathways in baby hamster kidney fibroblasts expressing the rat GLP-2 receptor. *J Biol Chem* **274**: 30459-67 [PMID:10521425]

- 287. Zarandi M, Horvath JE, Halmos G, Pinski J, Nagy A, Groot K, Rekasi Z and Schally AV. (1994) Synthesis and biological activities of highly potent antagonists of growth hormone-releasing hormone. *Proc Natl Acad Sci USA* **91**: 12298-302 [PMID:7991622]
- 288. Zarandi M, Kovacs M, Horvath JE, Toth K, Halmos G, Groot K, Nagy A, Kele Z and Schally AV. (1997) Synthesis and in vitro evaluation of new potent antagonists of growth hormone-releasing hormone (GH-RH). *Peptides* **18**: 423-430 [PMID:9145431]
- 289. Zeitler P, Stevens P and Siriwardana G. (1998) Functional GHRH receptor carboxyl terminal isoforms in normal and dwarf (dw) rats. *J Mol Endocrinol* **21**: 363-71 [PMID:9845677]
- 290. Zhang H, Qiao A, Yang D, Yang L, Dai A, de Graaf C, Reedtz-Runge S, Dharmarajan V, Zhang H and Han GW *et al.*. (2017) Structure of the full-length glucagon class B G-protein-coupled receptor. *Nature* **546**: 259-264 [PMID:28514451]
- 291. Zhang H, Qiao A, Yang L, Van Eps N, Frederiksen KS, Yang D, Dai A, Cai X, Zhang H and Yi C *et al.*. (2018) Structure of the glucagon receptor in complex with a glucagon analogue. *Nature* **553**: 106-110 [PMID:29300013]
- 292. Zhong Q, Bollag RJ, Dransfield DT, Gasalla-Herraiz J, Ding KH, Min L and Isales CM. (2000) Glucose-dependent insulinotropic peptide signaling pathways in endothelial cells. *Peptides* **21**: 1427-32 [PMID:11072131]
- 293. Zimmermann T, Thomas L, Baader-Pagler T, Haebel P, Simon E, Reindl W, Bajrami B, Rist W, Uphues I and Drucker DJ *et al.*. (2022) BI 456906: Discovery and preclinical pharmacology of a novel GCGR/GLP-1R dual agonist with robust anti-obesity efficacy. *Mol Metab* **66**: 101633 [PMID:36356832]