

Calcitonin receptors in GtoPdb v.2021.2

Debbie Hay¹, David R. Poyner² and Christopher S. Walker¹

1. University of Auckland, New Zealand
2. Aston University, UK

Abstract

This receptor family comprises a group of receptors for the calcitonin/CGRP family of peptides. The calcitonin (CT), amylin (AMY), calcitonin gene-related peptide (CGRP) and adrenomedullin (AM) receptors (**nomenclature as agreed by the NC-IUPHAR Subcommittee on CGRP, AM, AMY, and CT receptors [131, 74, 71]**) are generated by the genes *CALCR* (which codes for the CT receptor) and *CALCLR* (which codes for the calcitonin receptor-like receptor, CLR, previously known as CRLR). Their function and pharmacology are altered in the presence of RAMPs (receptor activity-modifying proteins), which are single TM domain proteins of *ca.* 150 amino acids, identified as a family of three members; RAMP1, RAMP2 and RAMP3. There are splice variants of the CT receptor; these in turn produce variants of the AMY receptor [131], some of which can be potently activated by CGRP. The endogenous agonists are the peptides calcitonin, α -CGRP (formerly known as CGRP-I), β -CGRP (formerly known as CGRP-II), amylin (occasionally called islet-amyloid polypeptide, diabetes-associated polypeptide), adrenomedullin and adrenomedullin 2/intermedin. There are species differences in peptide sequences, particularly for the CTs. CTR-stimulating peptide (CRSP) is another member of the family with selectivity for the CT receptor but it is not expressed in humans [94]. CLR (calcitonin receptor-like receptor) by itself binds no known endogenous ligand, but in the presence of RAMPs it gives receptors for CGRP, adrenomedullin and adrenomedullin 2/intermedin. There are several approved drugs that target this receptor family, such as pramlintide, erenumab, and the "gepant" class of CGRP receptor antagonists.

Contents

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Database links

Calcitonin receptors

<https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=11>

Introduction to Calcitonin receptors

<https://www.guidetopharmacology.org/GRAC/FamilyIntroductionForward?familyId=11>

Receptors

Complexes

[AMY₁ receptor](#)

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=44>

AMY₂ receptor

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=45>

AMY₃ receptor

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AM₁ receptor

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AM₂ receptor

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=50>

Receptors and Subunits

CT receptor

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=43>

calcitonin receptor-like receptor

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=47>

Accessory Proteins

RAMP1

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=51>

RAMP2

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=52>

RAMP3

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=53>

RAMP1

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=51>

RAMP2

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RAMP3

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=53>

References

1. Aiyar N, Disa J, Pullen M and Nambi P. (2001) Receptor activity modifying proteins interaction with human and porcine calcitonin receptor-like receptor (CRLR) in HEK-293 cells. *Mol Cell Biochem* **224**: 123-33 [PMID:11693189]
2. Aiyar N, Disa J, Stadel JM and Lysko PG. (1999) Calcitonin gene-related peptide receptor independently stimulates 3',5'-cyclic adenosine monophosphate and Ca²⁺ signaling pathways. *Mol Cell Biochem* **197**: 179-85 [PMID:10485337]
3. Albrandt K, Brady EM, Moore CX, Mull E, Sierzega ME and Beaumont K. (1995) Molecular cloning and functional expression of a third isoform of the human calcitonin receptor and partial characterization of the calcitonin receptor gene. *Endocrinology* **136**: 5377-84 [PMID:7588285]
4. Aldecoa A, Gujer R, Fischer JA and Born W. (2000) Mammalian calcitonin receptor-like receptor/receptor activity modifying protein complexes define calcitonin gene-related peptide and adrenomedullin receptors in *Drosophila Schneider 2* cells. *FEBS Lett* **471**: 156-60 [PMID:10767413]
5. Ali N, Yousufzai SY and Abdel-Latif AA. (2000) Activation of particulate guanylate cyclase by adrenomedullin in cultured SV-40 transformed cat iris sphincter smooth muscle (SV-CISM-2) cells. *Cell Signal* **12**: 491-498 [PMID:10989285]
6. Allen MA and Ferguson AV. (1996) In vitro recordings from area postrema neurons demonstrate responsiveness to adrenomedullin. *Am J Physiol* **270**: R920-5 [PMID:8967423]
7. Amara SG, Jonas V, Rosenfeld MG, Ong ES and Evans RM. (1982) Alternative RNA processing in calcitonin gene expression generates mRNAs encoding different polypeptide products. *Nature* **298**: 240-4 [PMID:6283379]
8. Andreis PG, Mazzocchi G, Rebuffat P and Nussdorfer GG. (1997) Effects of adrenomedullin and proadrenomedullin N-terminal 20 peptide on rat zona glomerulosa cells. *Life Sci* **60**: 1693-7 [PMID:9129124]
9. Andreis PG, Neri G, Prayer-Galetti T, Rossi GP, Gottardo G, Malendowicz LK and Nussdorfer GG. (1997) Effects of adrenomedullin on the human adrenal glands: an in vitro study. *J Clin Endocrinol Metab* **82**: 1167-70 [PMID:9100590]
10. Archbold JK, Flanagan JU, Watkins HA, Gingell JJ and Hay DL. (2011) Structural insights into RAMP modification of secretin family G protein-coupled receptors: implications for drug development. *Trends Pharmacol Sci* **32**: 591-600 [PMID:21722971]
11. Armour SL, Foord S, Kenakin T and Chen WJ. (1999) Pharmacological characterization of receptor-activity-modifying proteins (RAMPs) and the human calcitonin receptor. *J Pharmacol Toxicol Methods* **42**: 217-24 [PMID:11033437]
12. Arulmani U, Schuijt MP, Heiligers JP, Willems EW, Villalón CM and Saxena PR. (2004) Effects of

the calcitonin gene-related peptide (CGRP) receptor antagonist BIBN4096BS on alpha-CGRP-induced regional haemodynamic changes in anaesthetised rats. *Basic Clin Pharmacol Toxicol* **94**: 291-7 [PMID:15228501]

13. Avgoustou P. *et al.*. (2020) Discovery of a First-in-Class Potent Small Molecule Antagonist against the Adrenomedullin-2 Receptor *ACS Pharmacol Transl Sci*
14. Bailey RJ and Hay DL. (2006) Pharmacology of the human CGRP1 receptor in Cos 7 cells. *Peptides* **27**: 1367-75 [PMID:16375989]
15. Bailey RJ, Walker CS, Ferner AH, Loomes KM, Prijic G, Halim A, Whiting L, Phillips AR and Hay DL. (2012) Pharmacological characterization of rat amylin receptors: implications for the identification of amylin receptor subtypes. *Br J Pharmacol* **166**: 151-67 [PMID:22014233]
16. Barrick CJ, Lenhart PM, Dackor RT, Nagle E and Caron KM. (2012) Loss of receptor activity-modifying protein 3 exacerbates cardiac hypertrophy and transition to heart failure in a sex-dependent manner. *J Mol Cell Cardiol* **52**: 165-74 [PMID:22100352]
17. Becskei C, Riediger T, Zünd D, Wookey P and Lutz TA. (2004) Immunohistochemical mapping of calcitonin receptors in the adult rat brain. *Brain Res* **1030**: 221-33 [PMID:15571671]
18. Bell D and McDermott BJ. (1994) Calcitonin gene-related peptide stimulates a positive contractile response in rat ventricular cardiomyocytes. *J Cardiovasc Pharmacol* **23**: 1011-21 [PMID:7523774]
19. Bell IM and Fraley ME. (2012) Piperidinone carboxamide azaindane CGRP receptor antagonists. Patent number: US20120122911.
20. Bell IM, Fraley ME, Gallicchio SN, Ginnetti A, Mitchell HJ, Paone DV, Staas DD, Stevenson HE, Wang C and Zartman CB. (2012) Piperidinone carboxamide azaindane cgrp receptor antagonists Patent number: WO2012064910A1.
21. Bhogal R, Smith DM and Bloom SR. (1992) Investigation and characterization of binding sites for islet amyloid polypeptide in rat membranes. *Endocrinology* **130**: 906-13 [PMID:1310282]
22. Bomberger JM, Parameswaran N, Hall CS, Aiyar N and Spielman WS. (2005) Novel function for receptor activity-modifying proteins (RAMPs) in post-endocytic receptor trafficking. *J Biol Chem* **280**: 9297-307 [PMID:15613468]
23. Booe JM, Walker CS, Barwell J, Kuteyi G, Simms J, Jamaluddin MA, Warner ML, Bill RM, Harris PW and Brimble MA *et al.*. (2015) Structural Basis for Receptor Activity-Modifying Protein-Dependent Selective Peptide Recognition by a G Protein-Coupled Receptor. *Mol Cell* **58**: 1040-52 [PMID:25982113]
24. Brain SD and Grant AD. (2004) Vascular actions of calcitonin gene-related peptide and adrenomedullin. *Physiol Rev* **84**: 903-34 [PMID:15269340]
25. Brain SD, Poyner DR and Hill RG. (2002) CGRP receptors: a headache to study, but will antagonists prove therapeutic in migraine? *Trends Pharmacol Sci* **23**: 51-3 [PMID:11830255]
26. Bucknell SJ, Ator MA, Brown AJH, Brown J, Cansfield AD, Cansfield JE, Christopher JA, Congreve M, Cseke G and Deflorian F *et al.*. (2020) Structure-Based Drug Discovery of *N*-((*R*)-3-(7-Methyl-1*H*-indazol-5-yl)-1-oxo-1-(((*S*)-1-oxo-3-(piperidin-4-yl)-1-(4-(pyridin-4-yl)piperazin-1-yl)propan-2-yl)amino)propan-2-yl)-2'-oxo-1',2'-dihydrospiro[piperidine-4,4'-pyrido[2,3-*d*][1,3]oxazine]-1-carboxamide (HTL22562): A Calcitonin Gene-Related Peptide Receptor Antagonist for Acute Treatment of Migraine. *J Med Chem* **63**: 7906-7920 [PMID:32558564]
27. Bullock CM, Wookey P, Bennett A, Mobasheri A, Dickerson I and Kelly S. (2014) Peripheral calcitonin gene-related peptide receptor activation and mechanical sensitization of the joint in rat models of osteoarthritis pain. *Arthritis Rheumatol* **66**: 2188-200 [PMID:24719311]
28. 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]
29. Bühlmann N, Leuthäuser K, Muff R, Fischer JA and Born W. (1999) A receptor activity modifying protein (RAMP)2-dependent adrenomedullin receptor is a calcitonin gene-related peptide receptor when coexpressed with human RAMP1. *Endocrinology* **140**: 2883-90 [PMID:10342881]
30. Caron KM and Smithies O. (2001) Extreme hydrops fetalis and cardiovascular abnormalities in mice lacking a functional Adrenomedullin gene. *Proc Natl Acad Sci USA* **98**: 615-9 [PMID:11149956]
31. Chait A, Suaudeau C and De Beaurepaire R. (1995) Extensive brain mapping of calcitonin-induced anorexia. *Brain Res Bull* **36**: 467-472 [PMID:7712209]
32. Chambers TJ and Magnus CJ. (1982) Calcitonin alters behaviour of isolated osteoclasts. *J Pathol* **136**: 27-39 [PMID:7057295]
33. Champion HC, Bivalacqua TJ, Pierce RL, Murphy WA, Coy DH, Hyman AL and Kadowitz PJ. (2003) Responses to human CGRP, ADM, and PAMP in human thymic arteries. *Am J Physiol Regul Integr Comp Physiol* **284**: R531-7 [PMID:12529288]
34. Chaturvedula PV, Mercer SE, Pin SS, Thalody G, Xu C, Conway CM, Keavy D, Signor L, Cantor GH and Mathias N *et al.*. (2013) Discovery of (R)-*N*-(3-(7-methyl-1*H*-indazol-5-yl)-1-(4-(1-methylpiperidin-4-yl)-1-oxopropan-2-yl)-4-(2-oxo-1,2-dihydroquinolin-3-yl)piperidine-1-carboxamide (BMS-742413): a potent human CGRP antagonist with superior safety profile for

the treatment of migraine through intranasal delivery. *Bioorg Med Chem Lett* **23**: 3157-61 [PMID:23632269]

35. Chausmer A, Stuart C and Stevens M. (1980) Identification of testicular cell plasma membrane receptors for calcitonin. *J Lab Clin Med* **96**: 933-8 [PMID:6252270]
36. Chausmer AB, Stevens MD and Severn C. (1982) Autoradiographic evidence for a calcitonin receptor on testicular Leydig cells. *Science* **216**: 735-6 [PMID:6281881]
37. Chiba T, Yamaguchi A, Yamatani T, Nakamura A, Morishita T, Inui T, Fukase M, Noda T and Fujita T. (1989) Calcitonin gene-related peptide receptor antagonist human CGRP-(8-37). *Am J Physiol* **256**: E331-5 [PMID:2537579]
38. Christopoulos G, Perry KJ, Morfis M, Tilakaratne N, Gao Y, Fraser NJ, Main MJ, Foord SM and Sexton PM. (1999) Multiple amylin receptors arise from receptor activity-modifying protein interaction with the calcitonin receptor gene product. *Mol Pharmacol* **56**: 235-42 [PMID:10385705]
39. Clarke MV, Russell PK, Findlay DM, Sastra S, Anderson PH, Skinner JP, Atkins GJ, Zajac JD and Davey RA. (2015) A Role for the Calcitonin Receptor to Limit Bone Loss During Lactation in Female Mice by Inhibiting Osteocytic Osteolysis. *Endocrinology* **156**: 3203-14 [PMID:26135836]
40. Cohen DP, Nussenzveig DR and Gershengorn MC. (1996) Iodocalcitonin binds to human calcitonin receptors with higher affinity than calcitonin. *Endocrinology* **137**: 4507-10 [PMID:8828514]
41. Cooper GJ, Leighton B, Dimitriadis GD, Parry-Billings M, Kowalchuk JM, Howland K, Rothbard JB, Willis AC and Reid KB. (1988) Amylin found in amyloid deposits in human type 2 diabetes mellitus may be a hormone that regulates glycogen metabolism in skeletal muscle. *Proc Natl Acad Sci USA* **85**: 7763-6 [PMID:3051005]
42. Cooper GJ, Willis AC, Clark A, Turner RC, Sim RB and Reid KB. (1987) Purification and characterization of a peptide from amyloid-rich pancreases of type 2 diabetic patients. *Proc Natl Acad Sci USA* **84**: 8628-32 [PMID:3317417]
43. Cornish J, Callon KE, Lin CQ, Xiao CL, Gamble GD, Cooper GJ and Reid IR. (1999) Comparison of the effects of calcitonin gene-related peptide and amylin on osteoblasts. *J Bone Miner Res* **14**: 1302-9 [PMID:10457262]
44. Dackor R, Fritz-Six K, Smithies O and Caron K. (2007) Receptor activity-modifying proteins 2 and 3 have distinct physiological functions from embryogenesis to old age. *J Biol Chem* **282**: 18094-9 [PMID:17470425]
45. Dackor RT, Fritz-Six K, Dunworth WP, Gibbons CL, Smithies O and Caron KM. (2006) Hydrops fetalis, cardiovascular defects, and embryonic lethality in mice lacking the calcitonin receptor-like receptor gene. *Mol Cell Biol* **26**: 2511-8 [PMID:16537897]
46. Dacquin R, Davey RA, Laplace C, Lévassieur R, Morris HA, Goldring SR, Gebre-Medhin S, Galson DL, Zajac JD and Karsenty G. (2004) Amylin inhibits bone resorption while the calcitonin receptor controls bone formation in vivo. *J Cell Biol* **164**: 509-14 [PMID:14970190]
47. Davey RA, Turner A, McManus JF, Chiu WS, Tjahjono F, Moore AJ, Atkins GJ, Anderson PH, Ma C, Glatt V, Maclean HE, Vincent C, Boussein M, Morris HA, Findlay DM and Zajac JD. (2008) The Calcitonin Receptor Plays a Physiological Role to Protect Against Hypercalcemia in Mice. *J Bone Miner Res* **8**: 1182-1193 [PMID:18627265]
48. Dennis T, Fournier A, St Pierre S and Quirion R. (1989) Structure-activity profile of calcitonin gene-related peptide in peripheral and brain tissues. Evidence for receptor multiplicity. *J Pharmacol Exp Ther* **251**: 718-25 [PMID:2553933]
49. Devesa I, Ferrándiz-Huertas C, Mathivanan S, Wolf C, Luján R, Changeux JP and Ferrer-Montiel A. (2014) α CGRP is essential for algescic exocytotic mobilization of TRPV1 channels in peptidergic nociceptors. *Proc Natl Acad Sci USA* **111**: 18345-50 [PMID:25489075]
50. Dong M, Cox RF and Miller LJ. (2009) Juxtamembranous region of the amino terminus of the family B G protein-coupled calcitonin receptor plays a critical role in small-molecule agonist action. *J Biol Chem* **284**: 21839-47 [PMID:19447889]
51. Doods H, Hallermayer G, Wu D, Entzeroth M, Rudolf K, Engel W and Eberlein W. (2000) Pharmacological profile of BIBN4096BS, the first selective small molecule CGRP antagonist. *Br J Pharmacol* **129**: 420-3 [PMID:10711339]
52. Edvinsson L, Gulbenkian S, Barroso CP, Cunha e Sá M, Polak JM, Mortensen A, Jørgensen L and Jansen-Olesen I. (1998) Innervation of the human middle meningeal artery: immunohistochemistry, ultrastructure, and role of endothelium for vasomotility. *Peptides* **19**: 1213-25 [PMID:9786171]
53. Edvinsson L, Sams A, Jansen-Olesen I, Tajti J, Kane SA, Rutledge RZ, Koblan KS, Hill RG and Longmore J. (2001) Characterisation of the effects of a non-peptide CGRP receptor antagonist in SK-N-MC cells and isolated human cerebral arteries. *Eur J Pharmacol* **415**: 39-44 [PMID:11245850]
54. Evans BN, Rosenblatt MI, Mnayer LO, Oliver KR and Dickerson IM. (2000) CGRP-RCP, a novel protein required for signal transduction at calcitonin gene-related peptide and adrenomedullin receptors. *J Biol Chem* **275**: 31438-43 [PMID:10903324]

55. Felsenfeld AJ and Levine BS. (2015) Calcitonin, the forgotten hormone: does it deserve to be forgotten? *Clin Kidney J* **8**: 180-7 [PMID:25815174]
56. Fraser NJ, Wise A, Brown J, McLatchie LM, Main MJ and Foord SM. (1999) The amino terminus of receptor activity modifying proteins is a critical determinant of glycosylation state and ligand binding of calcitonin receptor-like receptor. *Mol Pharmacol* **55**: 1054-1059 [PMID:10347248]
57. Fritz-Six KL, Dunworth WP, Li M and Caron KM. (2008) Adrenomedullin signaling is necessary for murine lymphatic vascular development. *J Clin Invest* **118**: 40-50 [PMID:18097475]
58. Galvin RJ, Bryan P, Venugopalan M, Smith DP and Thomas JE. (1998) Calcitonin responsiveness and receptor expression in porcine and murine osteoclasts: a comparative study. *Bone* **23**: 233-40 [PMID:9737345]
59. Gebre-Medhin S, Mulder H, Pekny M, Westermarck G, Törnell J, Westermarck P, Sundler F, Ahrén B and Betsholtz C. (1998) Increased insulin secretion and glucose tolerance in mice lacking islet amyloid polypeptide (amylin). *Biochem Biophys Res Commun* **250**: 271-7 [PMID:9753619]
60. Gingell JJ, Burns ER and Hay DL. (2014) Activity of pramlintide, rat and human amylin but not A β 1-42 at human amylin receptors. *Endocrinology* **155**: 21-6 [PMID:24169554]
61. Gorn AH, Lin HY, Yamin M, Auron PE, Flannery MR, Tapp DR, Manning CA, Lodish HF, Krane SM and Goldring SR. (1992) Cloning, characterization, and expression of a human calcitonin receptor from an ovarian carcinoma cell line. *J Clin Invest* **90**: 1726-35 [PMID:1331173]
62. Gorn AH, Rudolph SM, Flannery MR, Morton CC, Weremowicz S, Wang TZ, Krane SM and Goldring SR. (1995) Expression of two human skeletal calcitonin receptor isoforms cloned from a giant cell tumor of bone. The first intracellular domain modulates ligand binding and signal transduction. *J Clin Invest* **95**: 2680-2691 [PMID:7769107]
63. Gydesen S, Andreassen KV, Hjulster ST, Christensen JM, Karsdal MA and Henriksen K. (2016) KBP-088, a novel DACRA with prolonged receptor activation, is superior to davalintide in terms of efficacy on body weight. *Am J Physiol Endocrinol Metab* **310**: E821-7 [PMID:26908506]
64. Han SP, Naes L and Westfall TC. (1990) Calcitonin gene-related peptide is the endogenous mediator of nonadrenergic-noncholinergic vasodilation in rat mesentery. *J Pharmacol Exp Ther* **255**: 423-8 [PMID:2243334]
65. Hay DL. (2019) CGRP Receptor Biology: Is There More Than One Receptor? *Handb Exp Pharmacol* **255**: 13-22 [PMID:29797087]
66. Hay DL. (2007) What makes a CGRP2 receptor? *Clin Exp Pharmacol Physiol* **34**: 963-71 [PMID:17714080]
67. Hay DL, Chen S, Lutz TA, Parkes DG and Roth JD. (2015) Amylin: Pharmacology, Physiology, and Clinical Potential. *Pharmacol Rev* **67**: 564-600 [PMID:26071095]
68. Hay DL, Christopoulos G, Christopoulos A, Poyner DR and Sexton PM. (2005) Pharmacological discrimination of calcitonin receptor: receptor activity-modifying protein complexes. *Mol Pharmacol* **67**: 1655-65 [PMID:15692146]
69. Hay DL, Christopoulos G, Christopoulos A and Sexton PM. (2006) Determinants of 1-piperidinecarboxamide, N-[2-[[5-amino-1-[[4-(4-pyridinyl)-1-piperazinyl]carbonyl]pentyl]amino]-1-[(3,5-dibromo-4-hydroxyphenyl)methyl]-2-oxoethyl]-4-(1,4-dihydro-2-oxo-3(2H)-quinazoliny)] (BIBN4096BS) affinity for calcitonin gene-related peptide and amylin receptors--the role of receptor activity modifying protein 1. *Mol Pharmacol* **70**: 1984-1991 [PMID:16959943]
70. Hay DL, Conner AC, Howitt SG, Takhshid MA, Simms J, Mahmoud K and Poyner DR. (2004) The pharmacology of CGRP-responsive receptors in cultured and transfected cells. *Peptides* **25**: 2019-2026 [PMID:15501536]
71. Hay DL, Garelja ML, Poyner DR and Walker CS. (2018) Update on the pharmacology of calcitonin/CGRP family of peptides: IUPHAR Review 25. *Br J Pharmacol* **175**: 3-17 [PMID:29059473]
72. Hay DL, Howitt SG, Conner AC, Schindler M, Smith DM and Poyner DR. (2003) CL/RAMP2 and CL/RAMP3 produce pharmacologically distinct adrenomedullin receptors: a comparison of effects of adrenomedullin22-52, CGRP8-37 and BIBN4096BS. *Br J Pharmacol* **140**: 477-86 [PMID:12970090]
73. Hay DL and Pioszak AA. (2016) Receptor Activity-Modifying Proteins (RAMPs): New Insights and Roles. *Annu Rev Pharmacol Toxicol* **56**: 469-87 [PMID:26514202]
74. Hay DL, Poyner DR, Quirion R and International Union of Pharmacology. (2008) International Union of Pharmacology. LXIX. Status of the calcitonin gene-related peptide subtype 2 receptor. *Pharmacol Rev* **60**: 143-5 [PMID:18552275]
75. Hay DL, Poyner DR and Sexton PM. (2006) GPCR modulation by RAMPs. *Pharmacol Ther* **109**: 173-97 [PMID:16111761]
76. Haynes JM and Cooper ME. (1995) Adrenomedullin and calcitonin gene-related peptide in the rat isolated kidney and in the anaesthetised rat: in vitro and in vivo effects. *Eur J Pharmacol* **280**: 91-4 [PMID:7498258]
77. Hilton JM, Dowton M, Houssami S and Sexton PM. (2000) Identification of key components in the irreversibility of salmon calcitonin binding to calcitonin receptors. *J Endocrinol* **166**: 213-26 [PMID:10856900]

78. Hinson JP, Kapas S and Smith DM. (2000) Adrenomedullin, a multifunctional regulatory peptide. *Endocr Rev* **21**: 138-67 [PMID:10782362]
79. Hoare SR. (2005) Mechanisms of peptide and nonpeptide ligand binding to Class B G-protein-coupled receptors. *Drug Discov Today* **10**: 417-27 [PMID:15808821]
80. Hong Y, Hay DL, Quirion R and Poyner DR. (2012) The pharmacology of adrenomedullin 2/intermedin. *Br J Pharmacol* **166**: 110-20 [PMID:21658025]
81. Hoshiya H, Meguro M, Kashiwagi A, Okita C and Oshimura M. (2003) Calcr, a brain-specific imprinted mouse calcitonin receptor gene in the imprinted cluster of the proximal region of chromosome 6. *J Hum Genet* **48**: 208-11 [PMID:12730726]
82. Husmann K, Born W, Fischer JA and Muff R. (2003) Three receptor-activity-modifying proteins define calcitonin gene-related peptide or adrenomedullin selectivity of the mouse calcitonin-like receptor in COS-7 cells. *Biochem Pharmacol* **66**: 2107-15 [PMID:14609735]
83. Husmann K, Sexton PM, Fischer JA and Born W. (2000) Mouse receptor-activity-modifying proteins 1, -2 and -3: amino acid sequence, expression and function. *Mol Cell Endocrinol* **162**: 35-43 [PMID:10854696]
84. Ichikawa I and Brenner BM. (1976) Of unglazed pottery and glomerular sieving. *Kidney Int* **10**: 264-7 [PMID:787620]
85. Ichikawa-Shindo Y, Sakurai T, Kamiyoshi A, Kawate H, Iinuma N, Yoshizawa T, Koyama T, Fukuchi J, Iimuro S and Moriyama N *et al.*. (2008) The GPCR modulator protein RAMP2 is essential for angiogenesis and vascular integrity. *J Clin Invest* **118**: 29-39 [PMID:18097473]
86. Igarashi K, Sakurai T, Kamiyoshi A, Ichikawa-Shindo Y, Kawate H, Yamauchi A, Toriyama Y, Tanaka M, Liu T and Xian X *et al.*. (2014) Pathophysiological roles of adrenomedullin-RAMP2 system in acute and chronic cerebral ischemia. *Peptides* **62**: 21-31 [PMID:25252154]
87. Joshi P, Anderson C, Binch H, Hadida S, Yoo S, Bergeron D, Decker C, terHaar E, Moore J and Garcia-Guzman M *et al.*. (2014) Identification of potent CNS-penetrant thiazolidinones as novel CGRP receptor antagonists. *Bioorg Med Chem Lett* **24**: 845-9 [PMID:24405707]
88. Jusek G, Reim D, Tsujikawa K and Holzmann B. (2012) Deficiency of the CGRP receptor component RAMP1 attenuates immunosuppression during the early phase of septic peritonitis. *Immunobiology* **217**: 761-7 [PMID:22656887]
89. Kahn ML. (2008) Blood is thicker than lymph. *J Clin Invest* **118**: 23-6 [PMID:18097477]
90. Kano H, Kohno M, Yasunari K, Yokokawa K, Horio T, Ikeda M, Minami M, Hanehira T, Takeda T and Yoshikawa J. (1996) Adrenomedullin as a novel antiproliferative factor of vascular smooth muscle cells. *J Hypertens* **14**: 209-13 [PMID:8728298]
91. Kapoor K, Arulmani U, Heiligers JP, Garrelds IM, Willems EW, Doods H, Villalón CM and Saxena PR. (2003) Effects of the CGRP receptor antagonist BIBN4096BS on capsaicin-induced carotid haemodynamic changes in anaesthetised pigs. *Br J Pharmacol* **140**: 329-38 [PMID:12970078]
92. Kapoor K, Arulmani U, Heiligers JP, Willems EW, Doods H, Villalón CM and Saxena PR. (2003) Effects of BIBN4096BS on cardiac output distribution and on CGRP-induced carotid haemodynamic responses in the pig. *Eur J Pharmacol* **475**: 69-77 [PMID:12954361]
93. Katafuchi T, Hamano K, Kikumoto K and Minamino N. (2003) Identification of second and third calcitonin receptor-stimulating peptides in porcine brain. *Biochem Biophys Res Commun* **308**: 445-51 [PMID:12914769]
94. Katafuchi T, Kikumoto K, Hamano K, Kangawa K, Matsuo H and Minamino N. (2003) Calcitonin receptor-stimulating peptide, a new member of the calcitonin gene-related peptide family. Its isolation from porcine brain, structure, tissue distribution, and biological activity. *J Biol Chem* **278**: 12046-54 [PMID:12556539]
95. Kiriya Y, Tsuchiya H, Murakami T, Satoh K and Tokumitsu Y. (2001) Calcitonin induces IL-6 production via both PKA and PKC pathways in the pituitary folliculo-stellate cell line. *Endocrinology* **142**: 3563-9 [PMID:11459804]
96. Kitamura K, Kangawa K, Kawamoto M, Ichiki Y, Nakamura S, Matsuo H and Eto T. (1993) Adrenomedullin: a novel hypotensive peptide isolated from human pheochromocytoma. *Biochem Biophys Res Commun* **192**: 553-60 [PMID:8387282]
97. Kurashige C, Hosono K, Matsuda H, Tsujikawa K, Okamoto H and Majima M. (2014) Roles of receptor activity-modifying protein 1 in angiogenesis and lymphangiogenesis during skin wound healing in mice. *FASEB J* **28**: 1237-47 [PMID:24308973]
98. Kusano S, Kukimoto-Niino M, Akasaka R, Toyama M, Terada T, Shirouzu M, Shindo T and Yokoyama S. (2008) Crystal structure of the human receptor activity-modifying protein 1 extracellular domain. *Protein Sci* **17**: 1907-14 [PMID:18725456]
99. Kusano S, Kukimoto-Niino M, Hino N, Ohsawa N, Okuda K, Sakamoto K, Shirouzu M, Shindo T and Yokoyama S. (2012) Structural basis for extracellular interactions between calcitonin receptor-like receptor and receptor activity-modifying protein 2 for adrenomedullin-specific binding. *Protein Sci* **21**: 199-210 [PMID:22102369]
100. Kuwasako K, Cao YN, Nagoshi Y, Tsuruda T, Kitamura K and Eto T. (2004) Characterization of the human calcitonin gene-related peptide receptor subtypes associated with receptor activity-modifying proteins. *Mol Pharmacol* **65**: 207-13 [PMID:14722252]

101. Kuwasako K, Kitamura K, Nagoshi Y and Eto T. (2003) Novel calcitonin-(8-32)-sensitive adrenomedullin receptors derived from co-expression of calcitonin receptor with receptor activity-modifying proteins. *Biochem Biophys Res Commun* **301**: 460-4 [PMID:12565884]
102. Leighton B and Cooper GJ. (1988) Pancreatic amylin and calcitonin gene-related peptide cause resistance to insulin in skeletal muscle in vitro. *Nature* **335**: 632-5 [PMID:3050530]
103. Leuthauser K, Gujer R, Aldecoa A, McKinney RA, Muff R, Fischer JA and Born W. (2000) Receptor-activity-modifying protein 1 forms heterodimers with two G-protein-coupled receptors to define ligand recognition. *Biochem J* **351**: 347-351 [PMID:11023820]
104. Lin HY, Harris TL, Flannery MS, Aruffo A, Kaji EH, Gorn A, Kolakowski Jr LF, Lodish HF and Goldring SR. (1991) Expression cloning of an adenylate cyclase-coupled calcitonin receptor. *Science* **254**: 1022-4 [PMID:1658940]
105. Luo G, Chen L, Conway CM, Denton R, Keavy D, Signor L, Kostich W, Lentz KA, Santone KS and Schartman R *et al.*. (2012) Discovery of (5S,6S,9R)-5-amino-6-(2,3-difluorophenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-9-yl 4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)piperidine-1-carboxylate (BMS-927711): an oral calcitonin gene-related peptide (CGRP) antagonist in clinical trials for treating migraine. *J Med Chem* **55**: 10644-51 [PMID:23153230]
106. Lutz TA. (2006) Amylinergic control of food intake. *Physiol Behav* **89**: 465-71 [PMID:16697020]
107. Main MJ, Brown J, Brown S, Fraser NJ and Foord SM. (1998) The CGRP receptor can couple via pertussis toxin sensitive and insensitive G proteins. *FEBS Lett* **441**: 6-10 [PMID:9877154]
108. Mallee JJ, Salvatore CA, LeBourdelle B, Oliver KR, Longmore J, Koblan KS and Kane SA. (2002) Receptor activity-modifying protein 1 determines the species selectivity of non-peptide CGRP receptor antagonists. *J Biol Chem* **277**: 14294-8 [PMID:11847213]
109. Martínez V, Cuttitta F and Taché Y. (1997) Central action of adrenomedullin to inhibit gastric emptying in rats. *Endocrinology* **138**: 3749-55 [PMID:9275061]
110. Masi L, Becherini L, Gennari L, Colli E, Mansani R, Falchetti A, Cepollaro C, Gonnelli S, Tanini A and Brandi ML. (1998) Allelic variants of human calcitonin receptor: distribution and association with bone mass in postmenopausal Italian women. *Biochem Biophys Res Commun* **245**: 622-6 [PMID:9571205]
111. McLatchie LM, Fraser NJ, Main MJ, Wise A, Brown J, Thompson N, Solari R, Lee MG and Foord SM. (1998) RAMPs regulate the transport and ligand specificity of the calcitonin-receptor-like receptor. *Nature* **393**: 333-9 [PMID:9620797]
112. Mercer SE, Chaturvedula PV, Conway CM, Cook DA, Davis CD, Pin SS, Macci R, Schartman R, Signor LJ and Widmann KA *et al.*. (2021) Azepino-indazoles as calcitonin gene-related peptide (CGRP) receptor antagonists. *Bioorg Med Chem Lett* **31**: 127624 [PMID:33096162]
113. Mikami N, Watanabe K, Hashimoto N, Miyagi Y, Sueda K, Fukada S, Yamamoto H and Tsujikawa K. (2012) Calcitonin gene-related peptide enhances experimental autoimmune encephalomyelitis by promoting Th17-cell functions. *Int Immunol* **24**: 681-91 [PMID:22843730]
114. Mitsikostas DD and Rapoport AM. (2015) New players in the preventive treatment of migraine. *BMC Med* **13**: 279 [PMID:26555040]
115. Mogil JS, Miermeister F, Seifert F, Strasburg K, Zimmermann K, Reinold H, Austin JS, Bernardini N, Chesler EJ and Hofmann HA *et al.*. (2005) Variable sensitivity to noxious heat is mediated by differential expression of the CGRP gene. *Proc Natl Acad Sci USA* **102**: 12938-43 [PMID:16118273]
116. Moore EL and Salvatore CA. (2012) Targeting a family B GPCR/RAMP receptor complex: CGRP receptor antagonists and migraine. *Br J Pharmacol* **166**: 66-78 [PMID:21871019]
117. Morfis M, Tilakaratne N, Furness SG, Christopoulos G, Werry TD, Christopoulos A and Sexton PM. (2008) Receptor activity-modifying proteins differentially modulate the G protein-coupling efficiency of amylin receptors. *Endocrinology* **149**: 5423-31 [PMID:18599553]
118. Muff R, Bühlmann N, Fischer JA and Born W. (1999) An amylin receptor is revealed following co-transfection of a calcitonin receptor with receptor activity modifying proteins-1 or -3. *Endocrinology* **140**: 2924-7 [PMID:10342886]
119. Mulderry PK, Ghatei MA, Spokes RA, Jones PM, Pierson AM, Hamid QA, Kanse S, Amara SG, Burrin JM and Legon S *et al.*. (1988) Differential expression of alpha-CGRP and beta-CGRP by primary sensory neurons and enteric autonomic neurons of the rat. *Neuroscience* **25**: 195-205 [PMID:2839796]
120. Nakamura M, Zhang ZQ, Shan L, Hisa T, Sasaki M, Tsukino R, Yokoi T, Kaname A and Kakudo K. (1997) Allelic variants of human calcitonin receptor in the Japanese population. *Hum Genet* **99**: 38-41 [PMID:9003491]
121. Nakamuta H, Fukuda Y, Koida M, Fujii N, Otaka A, Funakoshi S, Yajima H, Mitsuyasu N and Orłowski RC. (1986) Binding sites of calcitonin gene-related peptide (CGRP): abundant occurrence in visceral organs. *Jpn J Pharmacol* **42**: 175-80 [PMID:3025489]
122. Nishimatsu H, Suzuki E, Nagata D, Moriyama N, Satonaka H, Walsh K, Sata M, Kangawa K, Matsuo H and Goto A *et al.*. (2001) Adrenomedullin induces endothelium-dependent vasorelaxation via the phosphatidylinositol 3-kinase/Akt-dependent pathway in rat aorta. *Circ Res* **89**: 63-70 [PMID:11440979]

123. Nodin C, Vauquelin G and von Mentzer B. (2005) Cys^{2,7}EtalphaCGRP is a potent agonist for CGRP1 receptors in SK-N-MC cells. *Biochem Pharmacol* **69**: 1235-40 [PMID:15794944]
124. Offermanns S, Iida-Klein A, Segre GV and Simon MI. (1996) G alpha q family members couple parathyroid hormone (PTH)/PTH-related peptide and calcitonin receptors to phospholipase C in COS-7 cells. *Mol Endocrinol* **10**: 566-74 [PMID:8732687]
125. Oliver KR, Kane SA, Salvatore CA, Mallee JJ, Kinsey AM, Koblan KS, Keyvan-Fouladi N, Heavens RP, Wainwright A and Jacobson M *et al.*. (2001) Cloning, characterization and central nervous system distribution of receptor activity modifying proteins in the rat. *Eur J Neurosci* **14**: 618-28 [PMID:11556887]
126. Owji AA, Smith DM, Coppock HA, Morgan DG, Bhogal R, Ghatei MA and Bloom SR. (1995) An abundant and specific binding site for the novel vasodilator adrenomedullin in the rat. *Endocrinology* **136**: 2127-34 [PMID:7720662]
127. Parameswaran N, Disa J, Spielman WS, Brooks DP, Nambi P and Aiyar N. (2000) Activation of multiple mitogen-activated protein kinases by recombinant calcitonin gene-related peptide receptor. *Eur J Pharmacol* **389**: 125-30 [PMID:10688975]
128. Petersen KA, Birk S, Lassen LH, Kruuse C, Jonassen O, Lesko L and Olesen J. (2005) The CGRP-antagonist, BIBN4096BS does not affect cerebral or systemic haemodynamics in healthy volunteers. *Cephalalgia* **25**: 139-47 [PMID:15658951]
129. Pham V, Wade JD, Purdue BW and Sexton PM. (2004) Spatial proximity between a photolabile residue in position 19 of salmon calcitonin and the amino terminus of the human calcitonin receptor. *J Biol Chem* **279**: 6720-9 [PMID:14623894]
130. Piao FL, Cao C, Han JH, Kim SZ, Cho KW and Kim SH. (2004) Amylin-induced suppression of ANP secretion through receptors for CGRP1 and salmon calcitonin. *Regul Pept* **117**: 159-166 [PMID:14749035]
131. Poyner DR, Sexton PM, Marshall I, Smith DM, Quirion R, Born W, Muff R, Fischer JA and Foord SM. (2002) International Union of Pharmacology. XXXII. The mammalian calcitonin gene-related peptides, adrenomedullin, amylin, and calcitonin receptors. *Pharmacol Rev* **54**: 233-46 [PMID:12037140]
132. Purdue BW, Tilakaratne N and Sexton PM. (2002) Molecular pharmacology of the calcitonin receptor. *Recept Channels* **8**: 243-55 [PMID:12529940]
133. Pérez Jurado LA, Li X and Francke U. (1995) The human calcitonin receptor gene (CALCR) at 7q21.3 is outside the deletion associated with the Williams syndrome. *Cytogenet Cell Genet* **70**: 246-9 [PMID:7789182]
134. Qi T, Dong M, Watkins HA, Wootten D, Miller LJ and Hay DL. (2013) Receptor activity-modifying protein-dependent impairment of calcitonin receptor splice variant Δ(1-47)hCT((a)) function. *Br J Pharmacol* **168**: 644-57 [PMID:22946511]
135. Qing X and Keith IM. (2003) Targeted blocking of gene expression for CGRP receptors elevates pulmonary artery pressure in hypoxic rats. *Am J Physiol Lung Cell Mol Physiol* **285**: L86-96 [PMID:12626334]
136. Quigley A, Pike ACW, Burgess-Brown N, Krojer T, Shrestha L, Goubin S, Kim J, Das S, Muniz JRC, Canning P, Chaikuad A, Vollmar M, Von Delft F, Arrowsmith CH, Weigelt J, Edwards AM, Bountra C, Barr AJ and Carpenter EP. Structure of the Extracellular Domain of Human Ramp2.
137. Roh J, Chang CL, Bhalla A, Klein C and Hsu SY. (2004) Intermedin is a calcitonin/calcitonin gene-related peptide family peptide acting through the calcitonin receptor-like receptor/receptor activity-modifying protein receptor complexes. *J Biol Chem* **279**: 7264-74 [PMID:14615490]
138. Roth JD, Erickson MR, Chen S and Parkes DG. (2012) GLP-1R and amylin agonism in metabolic disease: complementary mechanisms and future opportunities. *Br J Pharmacol* **166**: 121-36 [PMID:21671898]
139. Russell FA, King R, Smillie SJ, Kodji X and Brain SD. (2014) Calcitonin gene-related peptide: physiology and pathophysiology. *Physiol Rev* **94**: 1099-142 [PMID:25287861]
140. Saetrum Opgaard O, Hasbak P, de Vries R, Saxena PR and Edvinsson L. (2000) Positive inotropy mediated via CGRP receptors in isolated human myocardial trabeculae. *Eur J Pharmacol* **397**: 373-82 [PMID:10844137]
141. Salvatore CA, Hershey JC, Corcoran HA, Fay JF, Johnston VK, Moore EL, Mosser SD, Burgey CS, Paone DV and Shaw AW *et al.*. (2008) Pharmacological characterization of MK-0974 [N-[(3R,6S)-6-(2,3-difluorophenyl)-2-oxo-1-(2,2,2-trifluoroethyl)azepan-3-yl]-4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)piperidine-1-carboxamide], a potent and orally active calcitonin gene-related peptide receptor antagonist for the treatment of migraine. *J Pharmacol Exp Ther* **324**: 416-21 [PMID:18039958]
142. Schütz B, Mauer D, Salmon AM, Changeux JP and Zimmer A. (2004) Analysis of the cellular expression pattern of beta-CGRP in alpha-CGRP-deficient mice. *J Comp Neurol* **476**: 32-43 [PMID:15236465]
143. Sexton PM, Houssami S, Hilton JM, O'Keeffe LM, Center RJ, Gillespie MT, Darcy P and Findlay DM. (1993) Identification of brain isoforms of the rat calcitonin receptor. *Mol Endocrinol* **7**: 815-

- 21 [PMID:8395656]
144. Sheward WJ, Lutz EM and Harmar AJ. (1994) The expression of the calcitonin receptor gene in the brain and pituitary gland of the rat. *Neurosci Lett* **181**: 31-4 [PMID:7898764]
145. Shi L, Lehto SG, Zhu DX, Sun H, Zhang J, Smith BP, Immke DC, Wild KD and Xu C. (2016) Pharmacologic Characterization of AMG 334, a Potent and Selective Human Monoclonal Antibody against the Calcitonin Gene-Related Peptide Receptor. *J Pharmacol Exp Ther* **356**: 223-31 [PMID:26559125]
146. Shindo T, Kurihara Y, Nishimatsu H, Moriyama N, Kakoki M, Wang Y, Imai Y, Ebihara A, Kuwaki T and Ju KH *et al.*. (2001) Vascular abnormalities and elevated blood pressure in mice lacking adrenomedullin gene. *Circulation* **104**: 1964-71 [PMID:11602502]
147. Smillie SJ and Brain SD. (2011) Calcitonin gene-related peptide (CGRP) and its role in hypertension. *Neuropeptides* **45**: 93-104 [PMID:21269690]
148. Sonne N, Larsen AT, Andreassen KV, Karsdal MA and Henriksen K. (2020) The Dual Amylin and Calcitonin Receptor Agonist, KBP-066, Induces an Equally Potent Weight Loss Across a Broad Dose Range While Higher Doses May Further Improve Insulin Action. *J Pharmacol Exp Ther* **373**: 92-102 [PMID:31992608]
149. Taboulet J, Frenkian M, Frenco JL, Feingold N, Jullienne A and de Vernejoul MC. (1998) Calcitonin receptor polymorphism is associated with a decreased fracture risk in postmenopausal women. *Hum Mol Genet* **7**: 2129-33 [PMID:9817931]
150. Takei Y, Inoue K, Ogoshi M, Kawahara T, Bannai H and Miyano S. (2004) Identification of novel adrenomedullin in mammals: a potent cardiovascular and renal regulator. *FEBS Lett* **556**: 53-8 [PMID:14706825]
151. Tam CW, Husmann K, Clark NC, Clark JE, Lazar Z, Ittner LM, Götz J, Douglas G, Grant AD and Sugden D *et al.*. (2006) Enhanced vascular responses to adrenomedullin in mice overexpressing receptor-activity-modifying protein 2. *Circ Res* **98**: 262-70 [PMID:16373602]
152. Taylor GM, Meeran K, O'Shea D, Smith DM, Ghatei MA and Bloom SR. (1996) Adrenomedullin inhibits feeding in the rat by a mechanism involving calcitonin gene-related peptide receptors. *Endocrinology* **137**: 3260-4 [PMID:8754748]
153. ter Haar E, Koth CM, Abdul-Manan N, Swenson L, Coll JT, Lippke JA, Lepre CA, Garcia-Guzman M and Moore JM. (2010) Crystal structure of the ectodomain complex of the CGRP receptor, a class-B GPCR, reveals the site of drug antagonism. *Structure* **18**: 1083-93 [PMID:20826335]
154. Tilakaratne N, Christopoulos G, Zumpe ET, Foord SM and Sexton PM. (2000) Amylin receptor phenotypes derived from human calcitonin receptor/RAMP coexpression exhibit pharmacological differences dependent on receptor isoform and host cell environment. *J Pharmacol Exp Ther* **294**: 61-72 [PMID:10871296]
155. Tsujikawa K, Yayama K, Hayashi T, Matsushita H, Yamaguchi T, Shigeno T, Ogitani Y, Hirayama M, Kato T and Fukada S *et al.*. (2007) Hypertension and dysregulated proinflammatory cytokine production in receptor activity-modifying protein 1-deficient mice. *Proc Natl Acad Sci USA* **104**: 16702-7 [PMID:17923674]
156. Uetake R, Sakurai T, Kamiyoshi A, Ichikawa-Shindo Y, Kawate H, Iesato Y, Yoshizawa T, Koyama T, Yang L and Toriyama Y *et al.*. (2014) Adrenomedullin-RAMP2 system suppresses ER stress-induced tubule cell death and is involved in kidney protection. *PLoS ONE* **9**: e87667 [PMID:24505304]
157. Uezono Y, Nakamura E, Ueda Y, Shibuya I, Ueta Y, Yokoo H, Yanagita T, Toyohira Y, Kobayashi H and Yanagihara N *et al.*. (2001) Production of cAMP by adrenomedullin in human oligodendroglial cell line KG1C: comparison with calcitonin gene-related peptide and amylin. *Brain Res Mol Brain Res* **97**: 59-69 [PMID:11744163]
158. Upton PD, Austin C, Taylor GM, Nandha KA, Clark AJ, Ghatei MA, Bloom SR and Smith DM. (1997) Expression of adrenomedullin (ADM) and its binding sites in the rat uterus: increased number of binding sites and ADM messenger ribonucleic acid in 20-day pregnant rats compared with nonpregnant rats. *Endocrinology* **138**: 2508-14 [PMID:9165042]
159. Venkatanarayan A, Raulji P, Norton W, Chakravarti D, Coarfa C, Su X, Sandur SK, Ramirez MS, Lee J and Kingsley CV *et al.*. (2015) IAPP-driven metabolic reprogramming induces regression of p53-deficient tumours in vivo. *Nature* **517**: 626-30 [PMID:25409149]
160. Villa I, Melzi R, Pagani F, Ravasi F, Rubinacci A and Guidobono F. (2000) Effects of calcitonin gene-related peptide and amylin on human osteoblast-like cells proliferation. *Eur J Pharmacol* **409**: 273-278 [PMID:11108821]
161. Walker CS, Conner AC, Poyner DR and Hay DL. (2010) Regulation of signal transduction by calcitonin gene-related peptide receptors. *Trends Pharmacol Sci* **31**: 476-83 [PMID:20633935]
162. Walker CS, Eftekhari S, Bower RL, Wilderman A, Insel PA, Edvinsson L, Waldvogel HJ, Jamaluddin MA, Russo AF and Hay DL. (2015) A second trigeminal CGRP receptor: function and expression of the AMY1 receptor. *Ann Clin Transl Neurol* **2**: 595-608 [PMID:26125036]
163. Walker CS and Hay DL. (2013) CGRP in the trigeminovascular system: a role for CGRP, adrenomedullin and amylin receptors? *Br J Pharmacol* **170**: 1293-307 [PMID:23425327]
164. Walker CS, Li X, Whiting L, Glyn-Jones S, Zhang S, Hickey AJ, Sewell MA, Ruggiero K, Phillips

- AR and Kraegen EW *et al.*. (2010) Mice lacking the neuropeptide alpha-calcitonin gene-related peptide are protected against diet-induced obesity. *Endocrinology* **151**: 4257-69 [PMID:20610563]
165. Wang Z, Martorell BC, Wälchli T, Vogel O, Fischer J, Born W and Vogel J. (2015) Calcitonin gene-related peptide (CGRP) receptors are important to maintain cerebrovascular reactivity in chronic hypertension. *PLoS ONE* **10**: e0123697 [PMID:25860809]
166. Warshawsky H, Goltzman D, Rouleau MF and Bergeron JJ. (1980) Direct in vivo demonstration by radioautography of specific binding sites for calcitonin in skeletal and renal tissues of the rat. *J Cell Biol* **85**: 682-94 [PMID:7391137]
167. Wolfe 3rd LA, Fling ME, Xue Z, Armour S, Kerner SA, Way J, Rimele T and Cox RF. (2003) In vitro characterization of a human calcitonin receptor gene polymorphism. *Mutat Res* **522**: 93-105 [PMID:12517415]
168. Wunder F, Rebmann A, Geerts A and Kalthof B. (2008) Pharmacological and kinetic characterization of adrenomedullin 1 and calcitonin gene-related peptide 1 receptor reporter cell lines. *Mol Pharmacol* **73**: 1235-43 [PMID:18174292]
169. Yamaguchi M. (1991) Stimulatory effect of calcitonin on Ca²⁺ inflow in isolated rat hepatocytes. *Mol Cell Endocrinol* **75**: 65-70 [PMID:1646739]
170. Yamaguchi M, Watanabe Y, Ohtani T, Uezumi A, Mikami N, Nakamura M, Sato T, Ikawa M, Hoshino M and Tsuchida K *et al.*. (2015) Calcitonin Receptor Signaling Inhibits Muscle Stem Cells from Escaping the Quiescent State and the Niche. *Cell Rep* **13**: 302-14 [PMID:26440893]
171. Yamauchi A, Sakurai T, Kamiyoshi A, Ichikawa-Shindo Y, Kawate H, Igarashi K, Toriyama Y, Tanaka M, Liu T and Xian X *et al.*. (2014) Functional differentiation of RAMP2 and RAMP3 in their regulation of the vascular system. *J Mol Cell Cardiol* **77**: 73-85 [PMID:25264174]
172. Yamin M, Gorn AH, Flannery MR, Jenkins NA, Gilbert DJ, Copeland NG, Tapp DR, Krane SM and Goldring SR. (1994) Cloning and characterization of a mouse brain calcitonin receptor complementary deoxyribonucleic acid and mapping of the calcitonin receptor gene. *Endocrinology* **135**: 2635-43 [PMID:7988453]
173. Yoshizawa T, Sakurai T, Kamiyoshi A, Ichikawa-Shindo Y, Kawate H, Iesato Y, Koyama T, Uetake R, Yang L and Yamauchi A *et al.*. (2013) Novel regulation of cardiac metabolism and homeostasis by the adrenomedullin-receptor activity-modifying protein 2 system. *Hypertension* **61**: 341-51 [PMID:23297372]
174. Young AA, Gedulin B, Gaeta LS, Prickett KS, Beaumont K, Larson E and Rink TJ. (1994) Selective amylin antagonist suppresses rise in plasma lactate after intravenous glucose in the rat. Evidence for a metabolic role of endogenous amylin. *FEBS Lett* **343**: 237-41 [PMID:8174707]
175. Young AA, Gedulin B, Vine W, Percy A and Rink TJ. (1995) Gastric emptying is accelerated in diabetic BB rats and is slowed by subcutaneous injections of amylin. *Diabetologia* **38**: 642-8 [PMID:7672483]
176. Zhang Z, Liu X, Morgan DA, Kuburas A, Thedens DR, Russo AF and Rahmouni K. (2011) Neuronal receptor activity-modifying protein 1 promotes energy expenditure in mice. *Diabetes* **60**: 1063-71 [PMID:21357463]
177. Zhang Z, Winborn CS, Marquez de Prado B and Russo AF. (2007) Sensitization of calcitonin gene-related peptide receptors by receptor activity-modifying protein-1 in the trigeminal ganglion. *J Neurosci* **27**: 2693-703 [PMID:17344407]
178. Zimmermann U, Fluehmann B, Born W, Fischer JA and Muff R. (1997) Coexistence of novel amylin-binding sites with calcitonin receptors in human breast carcinoma MCF-7 cells. *J Endocrinol* **155**: 423-31 [PMID:9487987]