

Bradykinin receptors (version 2019.4) in the IUPHAR/BPS Guide to Pharmacology Database

Joseph Coulson¹, Réjean Couture², Alexander Faussner³, Fernand Gobeil Jr⁴, Fredrik Leeb-Lundberg⁵, Francois Marceau⁶, Werner Muller-Esterl⁷, Doug Pettibone⁸ and Bruce Zuraw⁹

1. University of Edinburgh, UK
2. Université de Montréal, Canada
3. Ludwig-Maximilians-Universität, Germany
4. Université de Sherbrooke, Canada
5. Lunds Universitet, Sweden
6. Université Laval, Canada
7. Johann Wolfgang Goethe-University, Germany
8. Merck Research Laboratories, USA
9. University of California San Diego, USA

Abstract

Bradykinin (or kinin) receptors (**nomenclature as agreed by the NC-IUPHAR subcommittee on Bradykinin (kinin) Receptors [76]**) are activated by the endogenous peptides [bradykinin](#) (BK), [\[des-Arg⁹\]bradykinin](#), Lys-BK ([kallidin](#)), [\[des-Arg¹⁰\]kallidin](#), [Phospho-Ser⁶]-Bradykinin, [T-kinin](#) (Ile-Ser-BK), [\[Hyp³\]bradykinin](#) and [Lys-\[Hyp³\]-bradykinin](#). Variation in pharmacology and activity of B₁ and B₂ receptor antagonists at species orthologs has been documented. [icatibant](#) (Hoe140, Firazir) is approved in North America and Europe for the treatment of acute attacks of hereditary angioedema.

Contents

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B₂ receptor

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=42>

References

1. Alfie ME, Alim S, Mehta D, Shesely EG and Carretero OA. (1999) An enhanced effect of arginine vasopressin in bradykinin B2 receptor null mutant mice. *Hypertension* **33**: 1436-40 [PMID:10373229]
2. Alfie ME, Sigmon DH, Pomposiello SI and Carretero OA. (1997) Effect of high salt intake in mutant mice lacking bradykinin-B2 receptors. *Hypertension* **29**: 483-7 [PMID:9039146]
3. Amblard M, Bedos P, Olivier C, Daffix I, Luccarini JM, Dodey P, Pruneau D, Paquet JL and Martinez J. (2000) Synthesis and biological evaluation of bradykinin B(1)/B(2) and selective B(1) receptor antagonists. *J. Med. Chem.* **43**: 2382-6 [PMID:10882364]
4. Amblard M, Daffix I, Bedos P, Bergé G, Pruneau D, Paquet JL, Luccarini JM, Bélichard P, Dodey P and Martinez J. (1999) Design and synthesis of potent bradykinin agonists containing a benzothiazepine moiety. *J. Med. Chem.* **42**: 4185-92 [PMID:10514288]
5. Aramori I, Zenkoh J, Morikawa N, Asano M, Hatori C, Sawai H, Kayakiri H, Satoh S, Inoue T and Abe Y et al.. (1997) Nonpeptide mimic of bradykinin with long-acting properties at the bradykinin B2 receptor. *Mol. Pharmacol.* **52**: 16-20 [PMID:9224807]
6. Aramori I, Zenkoh J, Morikawa N, O'Donnell N, Asano M, Nakamura K, Iwami M, Kojo H and Notsu Y. (1997) Novel subtype-selective nonpeptide bradykinin receptor antagonists FR167344 and FR173657. *Mol. Pharmacol.* **51**: 171-6 [PMID:9203620]
7. Araújo RC, Mori MA, Merino VF, Bascands JL, Schanstra JP, Zollner RL, Villela CA, Nakaie CR, Paiva AC and Pesquero JL et al.. (2006) Role of the kinin B1 receptor in insulin homeostasis and pancreatic islet function. *Biol. Chem.* **387**: 431-6 [PMID:16606341]
8. Austin CE, Faussner A, Robinson HE, Chakravarty S, Kyle DJ, Bathon JM and Proud D. (1997) Stable expression of the human kinin B1 receptor in Chinese hamster ovary cells. Characterization of ligand binding and effector pathways. *J. Biol. Chem.* **272**: 11420-5 [PMID:9111052]
9. Bachvarov DR, Landry M, Pelletier I, Chevrette M, Betard C, Houde I, Bergeron J, Lebel M and Marceau F. (1998) Characterization of two polymorphic sites in the human kinin B1 receptor gene: altered frequency of an allele in patients with a history of end-stage renal failure. *J. Am. Soc. Nephrol.* **9**: 598-604 [PMID:9555662]
10. Bascands JL, Pecher C, Rouaud S, Emond C, Tack JL, Bastie MJ, Burch R, Regoli D and Girolami JP. (1993) Evidence for existence of two distinct bradykinin receptors on rat mesangial cells. *Am. J. Physiol.* **264**: F548-56 [PMID:8384416]
11. Bastian S, Loillier B, Paquet JL and Pruneau D. (1997) Stable expression of human kinin B1 receptor in 293 cells: pharmacological and functional characterization. *Br. J. Pharmacol.* **122**: 393-9 [PMID:9313952]
12. Bertram CM, Baltic S, Misso NL, Bhoola KD, Foster PS, Thompson PJ and Fogel-Petrovic M. (2007) Expression of kinin B1 and B2 receptors in immature, monocyte-derived dendritic cells and bradykinin-mediated increase in intracellular Ca²⁺ and cell migration. *J. Leukoc. Biol.* **81**: 1445-54 [PMID:17327486]
13. Bhoola R, Ramsaroop R, Naidoo S, Müller-Esterl W and Bhoola KD. (1997) Kinin receptor status in normal and inflamed gastric mucosa. *Immunopharmacology* **36**: 161-5 [PMID:9228541]
14. Borkowski JA, Ransom RW, Seabrook GR, Trumbauer M, Chen H, Hill RG, Strader CD and Hess JF.

- (1995) Targeted disruption of a B2 bradykinin receptor gene in mice eliminates bradykinin action in smooth muscle and neurons. *J. Biol. Chem.* **270**: 13706-10 [PMID:7775424]
15. Brull D, Dhamrait S, Myerson S, Erdmann J, Woods D, World M, Pennell D, Humphries S, Regitz-Zagrosek V and Montgomery H. (2001) Bradykinin B2BKR receptor polymorphism and left-ventricular growth response. *Lancet* **358**: 1155-6 [PMID:11597672]
 16. Burch RM and Axelrod J. (1987) Dissociation of bradykinin-induced prostaglandin formation from phosphatidylinositol turnover in Swiss 3T3 fibroblasts: evidence for G protein regulation of phospholipase A2. *Proc. Natl. Acad. Sci. U.S.A.* **84**: 6374-8 [PMID:2888113]
 17. Burgess GM, Perkins MN, Rang HP, Campbell EA, Brown MC, McIntyre P, Urban L, Dziadulewicz EK, Ritchie TJ and Hallett A *et al.*. (2000) Bradyzide, a potent non-peptide B(2) bradykinin receptor antagonist with long-lasting oral activity in animal models of inflammatory hyperalgesia. *Br. J. Pharmacol.* **129**: 77-86 [PMID:10694205]
 18. Busse R and Fleming I. (1995) Regulation and functional consequences of endothelial nitric oxide formation. *Ann Med* **27**: 331-340 [PMID:7546623]
 19. Byron KL, Babnigg G and Villereal ML. (1992) Bradykinin-induced Ca²⁺ entry, release, and refilling of intracellular Ca²⁺ stores. Relationships revealed by image analysis of individual human fibroblasts. *J. Biol. Chem.* **267**: 108-18 [PMID:1730576]
 20. Campos MM, Ongali B, De Souza Buck H, Schanstra JP, Girolami JP, Chabot JG and Couture R. (2005) Expression and distribution of kinin B1 receptor in the rat brain and alterations induced by diabetes in the model of streptozotocin. *Synapse* **57**: 29-37 [PMID:15858836]
 21. Cayla C, Todiras M, Iliescu R, Saul VV, Gross V, Pilz B, Chai G, Merino VF, Pesquero JB and Baltatu OC *et al.*. (2007) Mice deficient for both kinin receptors are normotensive and protected from endotoxin-induced hypotension. *FASEB J.* **21**: 1689-98 [PMID:17289925]
 22. Cervenka L, Harrison-Bernard LM, Dipp S, Primrose G, Imig JD and El-Dahr SS. (1999) Early onset salt-sensitive hypertension in bradykinin B(2) receptor null mice. *Hypertension* **34**: 176-80 [PMID:10454437]
 23. Cervenka L, Maly J, Karasová L, Simová M, Vítko S, Hellerová S, Heller J and El-Dahr SS. (2001) Angiotensin II-induced hypertension in bradykinin B2 receptor knockout mice. *Hypertension* **37**: 967-73 [PMID:11270390]
 24. Chai KX, Ni A, Wang D, Ward DC, Chao J and Chao L. (1996) Genomic DNA sequence, expression, and chromosomal localization of the human B1 bradykinin receptor gene BDKRB1. *Genomics* **31**: 51-7 [PMID:8808279]
 25. Cheuk BL, Ko WH and Wong PY. (2002) COX-dependent and -independent pathways in bradykinin-induced anion secretion in rat epididymis. *J Cell Physiol* **191**: 217-226 [PMID:12064465]
 26. Christopher J, Velarde V and Jaffa AA. (2001) Induction of B(1)-kinin receptors in vascular smooth muscle cells: cellular mechanisms of map kinase activation. *Hypertension* **38**: 602-5 [PMID:11566939]
 27. Cloutier F, de Sousa Buck H, Ongali B and Couture R. (2002) Pharmacologic and autoradiographic evidence for an up-regulation of kinin B(2) receptors in the spinal cord of spontaneously hypertensive rats. *Br. J. Pharmacol.* **135**: 1641-54 [PMID:11934804]
 28. Cockcroft JR, Chowienczyk PJ, Brett SE, Bender N and Ritter JM. (1994) Inhibition of bradykinin-induced vasodilation in human forearm vasculature by icatibant, a potent B2-receptor antagonist. *Br J Clin Pharmacol* **38**: 317-21 [PMID:7833220]
 29. Conley RK, Wheeldon A, Webb JK, DiPardo RM, Homnick CF, Bock MG, Chen TB, Chang RS, Pettibone DJ and Boyce S. (2005) Inhibition of acute nociceptive responses in rat spinal cord by a bradykinin B1 receptor antagonist. *Eur. J. Pharmacol.* **527**: 44-51 [PMID:16310181]
 30. D'Amico DC, Aya T, Human J, Fotsch C, Chen JJ, Biswas K, Riahi B, Norman MH, Willoughby CA and Hungate R *et al.*. (2007) Identification of a nonpeptidic and conformationally restricted bradykinin B1 receptor antagonist with anti-inflammatory activity. *J. Med. Chem.* **50**: 607-10 [PMID:17243660]
 31. De Falco L, Fioravanti A, Galeazzi M and Tenti S. (2013) Bradykinin and its role in osteoarthritis. *Reumatismo* **65**: 97-104 [PMID:23884024]
 32. de Sousa Buck H, Ongali B, Thibault G, Lindsey CJ and Couture R. (2002) Autoradiographic detection of

- kinin receptors in the human medulla of control, hypertensive, and diabetic donors. *Can. J. Physiol. Pharmacol.* **80**: 249-57 [PMID:12025957]
33. Dhamrait SS, Payne JR, Li P, Jones A, Toor IS, Cooper JA, Hawe E, Palmén JM, Wootton PT and Miller GJ *et al.*. (2003) Variation in bradykinin receptor genes increases the cardiovascular risk associated with hypertension. *Eur. Heart J.* **24**: 1672-80 [PMID:14499231]
 34. Doctrow SR, Abelleira SM, Curry LA, Heller-Harrison R, Kozarich JW, Malfroy B, McCarroll LA, Morgan KG, Morrow AR and Musso GF *et al.*. (1994) The bradykinin analog RMP-7 increases intracellular free calcium levels in rat brain microvascular endothelial cells. *J. Pharmacol. Exp. Ther.* **271**: 229-37 [PMID:7965719]
 35. Dray A, Bettaney J, Forster P and Perkins MN. (1988) Activation of a bradykinin receptor in peripheral nerve and spinal cord in the neonatal rat in vitro. *Br. J. Pharmacol.* **95**: 1008-10 [PMID:2905907]
 36. Duka A, Duka I, Gao G, Shenouda S, Gavras I and Gavras H. (2006) Role of bradykinin B1 and B2 receptors in normal blood pressure regulation. *Am. J. Physiol. Endocrinol. Metab.* **291**: E268-74 [PMID:16507603]
 37. Duka I, Shenouda S, Johns C, Kintsurashvili E, Gavras I and Gavras H. (2001) Role of the B(2) receptor of bradykinin in insulin sensitivity. *Hypertension* **38**: 1355-60 [PMID:11751717]
 38. Ehrenfeld P, Millan C, Matus CE, Figueroa JE, Burgos RA, Nualart F, Bhoola KD and Figueroa CD. (2006) Activation of kinin B1 receptors induces chemotaxis of human neutrophils. *J. Leukoc. Biol.* **80**: 117-24 [PMID:16670123]
 39. El-Dahr SS, Harrison-Bernard LM, Dipp S, Yosipiv IV and Meleg-Smith S. (2000) Bradykinin B2 null mice are prone to renal dysplasia: gene-environment interactions in kidney development. *Physiol. Genomics* **3**: 121-31 [PMID:11015607]
 40. Eric J, Gabra BH and Sirois P. (2003) Implication of the bradykinin receptors in antigen-induced pulmonary inflammation in mice. *Br. J. Pharmacol.* **138**: 1589-97 [PMID:12721115]
 41. Ewald DA, Pang IH, Sternweis PC and Miller RJ. (1989) Differential G protein-mediated coupling of neurotransmitter receptors to Ca²⁺ channels in rat dorsal root ganglion neurons in vitro. *Neuron* **2**: 1185-93 [PMID:2560387]
 42. Fallo F, Mulatero P, Vettor R, Scarda A, Della Mea P, Morello F, Veglio F and Williams TA. (2004) Bradykinin B2 receptor gene C-58T polymorphism and insulin resistance. A study on obese patients. *Horm. Metab. Res.* **36**: 243-6 [PMID:15114524]
 43. Fasolato C, Pandiella A, Meldolesi J and Pozzan T. (1988) Generation of inositol phosphates, cytosolic Ca²⁺, and ionic fluxes in PC12 cells treated with bradykinin. *J. Biol. Chem.* **263**: 17350-9 [PMID:3141420]
 44. Ferreira J, Beirith A, Mori MA, Araújo RC, Bader M, Pesquero JB and Calixto JB. (2005) Reduced nerve injury-induced neuropathic pain in kinin B1 receptor knock-out mice. *J. Neurosci.* **25**: 2405-12 [PMID:15745967]
 45. Figueroa CD, Marchant A, Novoa U, Förstermann U, Jarnagin K, Schölkens B and Müller-Esterl W. (2001) Differential Distribution of Bradykinin B(2) Receptors in the Rat and Human Cardiovascular System. *Hypertension* **37**: 110-120 [PMID:11208765]
 46. Fleming I, Fisslthaler B and Busse R. (1996) Interdependence of calcium signaling and protein tyrosine phosphorylation in human endothelial cells. *J. Biol. Chem.* **271**: 11009-15 [PMID:8631922]
 47. Fleming I, Fisslthaler B and Busse R. (1995) Calcium signaling in endothelial cells involves activation of tyrosine kinases and leads to activation of mitogen-activated protein kinases. *Circ Res* **76**: 522-529 [PMID:7895328]
 48. Fox A, Kaur S, Li B, Panesar M, Saha U, Davis C, Dragoni I, Colley S, Ritchie T and Bevan *et al.*. (2005) Antihyperalgesic activity of a novel nonpeptide bradykinin B1 receptor antagonist in transgenic mice expressing the human B1 receptor. *Br. J. Pharmacol.* **144**: 889-99 [PMID:15685199]
 49. Fox A, Wotherspoon G, McNair K, Hudson L, Patel S, Gentry C and Winter J. (2003) Regulation and function of spinal and peripheral neuronal B1 bradykinin receptors in inflammatory mechanical hyperalgesia. *Pain* **104**: 683-91 [PMID:12927641]
 50. Gabra BH, Berthiaume N, Sirois P, Nantel F and Battistini B. (2006) The kinin system mediates

- hyperalgesia through the inducible bradykinin B1 receptor subtype: evidence in various experimental animal models of type 1 and type 2 diabetic neuropathy. *Biol. Chem.* **387**: 127-43 [PMID:16497144]
51. Gabra BH, Merino VF, Bader M, Pesquero JB and Sirois P. (2005) Absence of diabetic hyperalgesia in bradykinin B1 receptor-knockout mice. *Regul. Pept.* **127**: 245-8 [PMID:15680494]
 52. Gabra BH and Sirois P. (2004) Pathways for the bradykinin B1 receptor-mediated diabetic hyperalgesia in mice. *Inflamm. Res.* **53**: 653-7 [PMID:15654512]
 53. Gera L, Fortin JP, Adam A, Stewart JM and Marceau F. (2006) Discovery of a dual-function peptide that combines aminopeptidase N inhibition and kinin B1 receptor antagonism. *J Pharmacol Exp Ther* **317**: 300-308 [PMID:16368899]
 54. Gobeil F, Charland S, Filteau C, Perron SI, Neugebauer W and Regoli D. (1999) Kinin B1 receptor antagonists containing alpha-methyl-L-phenylalanine: in vitro and in vivo antagonistic activities. *Hypertension* **33**: 823-9 [PMID:10082494]
 55. Gobeil F, Neugebauer W, Filteau C, Jukic D, Allogho SN, Pheng LH, Nguyen-Le XK, Blouin D and Regoli D. (1996) Structure-activity studies of B1 receptor-related peptides. Antagonists. *Hypertension* **28**: 833-9 [PMID:8901831]
 56. Gobeil F, Pheng LH, Badini I, Nguyen-Le XK, Pizard A, Rizzi A, Blouin D and Regoli D. (1996) Receptors for kinins in the human isolated umbilical vein. *Br. J. Pharmacol.* **118**: 289-94 [PMID:8735629]
 57. Gohla A, Offermanns S, Wilkie TM and Schultz G. (1999) Differential involvement of Galpha12 and Galpha13 in receptor-mediated stress fiber formation. *J. Biol. Chem.* **274**: 17901-7 [PMID:10364236]
 58. Gougat J, Ferrari B, Sarran L, Planchenault C, Poncelet M, Maruani J, Alonso R, Cudennec A, Croci T and Guagnini F *et al.*. (2004) SSR240612 [(2R)-2-[[[(3R)-3-(1,3-benzodioxol-5-yl)-3-[[[(6-methoxy-2-naphthyl)sulfonyl]amino]propanoyl]amino]-3-(4-[[[2R,6S]-2,6-dimethylpiperidinyl]methyl]phenyl)-N-isopropyl-N-methylpropanamide hydrochloride], a new nonpeptide antagonist of the bradykinin B1 receptor: biochemical and pharmacological characterization. *J. Pharmacol. Exp. Ther.* **309**: 661-9 [PMID:14747609]
 59. Groves P, Kurz S, Just H and Drexler H. (1995) Role of endogenous bradykinin in human coronary vasomotor control. *Circulation* **92**: 3424-30 [PMID:8521563]
 60. Gutowski S, Smrcka A, Nowak L, Wu DG, Simon M and Sternweis PC. (1991) Antibodies to the alpha q subfamily of guanine nucleotide-binding regulatory protein alpha subunits attenuate activation of phosphatidylinositol 4,5-bisphosphate hydrolysis by hormones. *J Biol Chem* **266**: 20519-20524 [PMID:1657928]
 61. Han ED, MacFarlane RC, Mulligan AN, Scafidi J and Davis 3rd AE. (2002) Increased vascular permeability in C1 inhibitor-deficient mice mediated by the bradykinin type 2 receptor. *J. Clin. Invest.* **109**: 1057-63 [PMID:11956243]
 62. Hayashi R, Yamashita N, Matsui S, Fujita T, Araya J, Sassa K, Arai N, Yoshida Y, Kashii T and Maruyama M *et al.*. (2000) Bradykinin stimulates IL-6 and IL-8 production by human lung fibroblasts through ERK- and p38 MAPK-dependent mechanisms. *Eur. Respir. J.* **16**: 452-8 [PMID:11028659]
 63. Hess JF, Borkowski JA, MacNeil T, Stonesifer GY, Fraher J, Strader CD and Ransom RW. (1994) Differential pharmacology of cloned human and mouse B2 bradykinin receptors. *Mol Pharmacol* **45**: 1-8 [PMID:8302267]
 64. Hess JF, Derrick AW, MacNeil T and Borkowski JA. (1996) The agonist selectivity of a mouse B1 bradykinin receptor differs from human and rabbit B1 receptors. *Immunopharmacology* **33**: 1-8 [PMID:8856107]
 65. Higashida H, Streaty RA, Klee W and Nirenberg M. (1986) Bradykinin-activated transmembrane signals are coupled via No or Ni to production of inositol 1,4,5-trisphosphate, a second messenger in NG108-15 neuroblastoma-glioma hybrid cells. *Proc Natl Acad Sci U S A* **83**: 942-946 [PMID:3081891]
 66. Horlick RA, Ohlmeyer MH, Stroke IL, Strohl B, Pan G, Schilling AE, Paradkar V, Quintero JG, You M and Riviello C *et al.*. (1999) Small molecule antagonists of the bradykinin B1 receptor. *Immunopharmacology* **43**: 169-77 [PMID:10596850]
 67. Houle S, Landry M, Audet R, Bouthillier J, Bachvarov DR and Marceau F. (2000) Effect of allelic

- polymorphism of the B(1) and B(2) receptor genes on the contractile responses of the human umbilical vein to kinins. *J. Pharmacol. Exp. Ther.* **294**: 45-51 [PMID:10871294]
68. Imig JD, Zhao X, Orengo SR, Dipp S and El-Dahr SS. (2003) The Bradykinin B2 receptor is required for full expression of renal COX-2 and renin. *Peptides* **24**: 1141-7 [PMID:14612184]
 69. Jones C, Phillips E, Davis C, Arbuckle J, Yaqoob M, Burgess GM, Docherty RJ, Webb M, Bevan SJ and McIntyre P. (1999) Molecular characterisation of cloned bradykinin B1 receptors from rat and human. *Eur J Pharmacol* **374**: 423-433 [PMID:10422787]
 70. Kusser B, Braun A, Praun M, Illi S, von Mutius E and Roscher AA. (2001) Polymorphisms in the bradykinin B2 receptor gene and childhood asthma. *Biol. Chem.* **382**: 885-9 [PMID:11517947]
 71. Lagneux C, Bader M, Pesquero JB, Demenge P and Ribouot C. (2002) Detrimental implication of B1 receptors in myocardial ischemia: evidence from pharmacological blockade and gene knockout mice. *Int. Immunopharmacol.* **2**: 815-22 [PMID:12095172]
 72. LaMorte VJ, Harootunian AT, Spiegel AM, Tsien RY and Feramisco JR. (1993) Mediation of growth factor induced DNA synthesis and calcium mobilization by Gq and Gi2. *J Cell Biol* **121**: 91-99 [PMID:8458876]
 73. Lawson SR, Gabra BH, Guérin B, Neugebauer W, Nantel F, Battistini B and Sirois P. (2005) Enhanced dermal and retinal vascular permeability in streptozotocin-induced type 1 diabetes in Wistar rats: blockade with a selective bradykinin B1 receptor antagonist. *Regul. Pept.* **124**: 221-4 [PMID:15544863]
 74. Lawson SR, Gabra BH, Nantel F, Battistini B and Sirois P. (2005) Effects of a selective bradykinin B1 receptor antagonist on increased plasma extravasation in streptozotocin-induced diabetic rats: distinct vasculopathic profile of major key organs. *Eur. J. Pharmacol.* **514**: 69-78 [PMID:15878326]
 75. Leeb T, Mathis SA and Leeb-Lundberg LM. (1997) The sixth transmembrane domains of the human B1 and B2 bradykinin receptors are structurally compatible and involved in discriminating between subtype-selective agonists. *J Biol Chem* **272**: 311-317 [PMID:8995263]
 76. Leeb-Lundberg LM, Marceau F, Müller-Esterl W, Pettibone DJ and Zuraw BL. (2005) International union of pharmacology. XLV. Classification of the kinin receptor family: from molecular mechanisms to pathophysiological consequences. *Pharmacol. Rev.* **57**: 27-77 [PMID:15734727]
 77. Leeb-Lundberg LM, Song XH and Mathis SA. (1994) Focal adhesion-associated proteins p125FAK and paxillin are substrates for bradykinin-stimulated tyrosine phosphorylation in Swiss 3T3 cells. *J. Biol. Chem.* **269**: 24328-34 [PMID:7929090]
 78. Liao JK and Homcy CJ. (1993) The G proteins of the G alpha i and G alpha q family couple the bradykinin receptor to the release of endothelium-derived relaxing factor. *J Clin Invest* **92**: 2168-2172 [PMID:8227332]
 79. Linder ME, Ewald DA, Miller RJ and Gilman AG. (1990) Purification and characterization of Go alpha and three types of Gi alpha after expression in Escherichia coli. *J. Biol. Chem.* **265**: 8243-51 [PMID:2159473]
 80. MacNeil T, Feighner S, Hreniuk DL, Hess JF and Van der Ploeg LH. (1997) Partial agonists and full antagonists at the human and murine bradykinin B1 receptors. *Can J Physiol Pharmacol* **75**: 735-740 [PMID:9276157]
 81. Maltais I, Bachvarova M, Maheux P, Perron P, Marceau F and Bachvarov D. (2002) Bradykinin B2 receptor gene polymorphism is associated with altered urinary albumin/creatinine values in diabetic patients. *Can J Physiol Pharmacol* **80**: 323-327 [PMID:12025967]
 82. Marceau F, Hess JF and Bachvarov DR. (1998) The B1 receptors for kinins. *Pharmacol. Rev.* **50**: 357-86 [PMID:9755287]
 83. Marceau F, Levesque L, Drapeau G, Rioux F, Salvino JM, Wolfe HR, Seoane PR and Sawutz DG. (1994) Effects of peptide and nonpeptide antagonists of bradykinin B2 receptors on the venoconstrictor action of bradykinin. *J. Pharmacol. Exp. Ther.* **269**: 1136-43 [PMID:8014858]
 84. McEachern AE, Shelton ER, Bhakta S, Obernolte R, Bach C, Zuppan P, Fujisaki J, Aldrich RW and Jarnagin K. (1991) Expression cloning of a rat B2 bradykinin receptor. *Proc. Natl. Acad. Sci. U.S.A.* **88**: 7724-8 [PMID:1715575]
 85. Menke JG, Borkowski JA, Bierilo KK, MacNeil T, Derrick AW, Schneck KA, Ransom RW, Strader CD, Linemeyer DL and Hess JF. (1994) Expression cloning of a human B1 bradykinin receptor. *J Biol Chem* **269**: 21583-21586 [PMID:8063797]

86. Moniwa N, Agata J, Hagiwara M, Ura N and Shimamoto K. (2006) The role of bradykinin B1 receptor on cardiac remodeling in stroke-prone spontaneously hypertensive rats (SHR-SP). *Biol. Chem.* **387**: 203-9 [PMID:16497153]
87. Morissette G, Sabourin T, Adam A and Marceau F. (2006) Inhibition of human and rabbit arterial smooth muscle cell migration mediated by the kinin B1 receptor: role of receptor density and released mediators. *Can. J. Physiol. Pharmacol.* **84**: 1107-19 [PMID:17218975]
88. Mulatero P, Williams TA, Milan A, Paglieri C, Rabbia F, Fallo F and Veglio F. (2002) Blood pressure in patients with primary aldosteronism is influenced by bradykinin B(2) receptor and alpha-adducin gene polymorphisms. *J. Clin. Endocrinol. Metab.* **87**: 3337-43 [PMID:12107246]
89. Ni A, Chai KX, Chao L and Chao J. (1998) Molecular cloning and expression of rat bradykinin B1 receptor. *Biochim. Biophys. Acta* **1442**: 177-85 [PMID:9804950]
90. Ongali B, Campos MM, Bregola G, Rodi D, Regoli D, Thibault G, Simonato M and Couture R. (2003) Autoradiographic analysis of rat brain kinin B1 and B2 receptors: normal distribution and alterations induced by epilepsy. *J Comp Neurol* **461**: 506-519 [PMID:12746865]
91. Pan ZK, Zuraw BL, Lung CC, Prossnitz ER, Browning DD and Ye RD. (1996) Bradykinin stimulates NF-kappaB activation and interleukin 1beta gene expression in cultured human fibroblasts. *J. Clin. Invest.* **98**: 2042-9 [PMID:8903323]
92. Perkins MN and Kelly D. (1993) Induction of bradykinin B1 receptors in vivo in a model of ultra-violet irradiation-induced thermal hyperalgesia in the rat. *Br. J. Pharmacol.* **110**: 1441-4 [PMID:8306084]
93. Perosa SR, Argañaraz GA, Goto EM, Costa LG, Konno AC, Varella PP, Santiago JF, Pesquero JB, Canzian M and Amado D *et al.*. (2007) Kinin B1 and B2 receptors are overexpressed in the hippocampus of humans with temporal lobe epilepsy. *Hippocampus* **17**: 26-33 [PMID:17094085]
94. Pesquero JB, Araujo RC, Heppenstall PA, Stucky CL, Silva Jr JA, Walther T, Oliveira SM, Pesquero JL, Paiva AC and Calixto JB *et al.*. (2000) Hypoalgesia and altered inflammatory responses in mice lacking kinin B1 receptors. *Proc. Natl. Acad. Sci. U.S.A.* **97**: 8140-5 [PMID:10859349]
95. Pesquero JB, Pesquero JL, Oliveira SM, Roscher AA, Metzger R, Ganten D and Bader M. (1996) Molecular cloning and functional characterization of a mouse bradykinin B1 receptor gene. *Biochem. Biophys. Res. Commun.* **220**: 219-25 [PMID:8602848]
96. Powell SJ, Slynn G, Thomas C, Hopkins B, Briggs I and Graham A. (1993) Human bradykinin B2 receptor: nucleotide sequence analysis and assignment to chromosome 14. *Genomics* **15**: 435-8 [PMID:7916737]
97. Prat A, Weinrib L, Becher B, Poirier J, Duquette P, Couture R and Antel JP. (1999) Bradykinin B1 receptor expression and function on T lymphocytes in active multiple sclerosis. *Neurology* **53**: 2087-92 [PMID:10599786]
98. Pruneau D, Paquet JL, Luccarini JM, Defrêne E, Fouchet C, Franck RM, Lollhier B, Robert C, Bélichard P and Duclos H *et al.*. (1999) Pharmacological profile of LF 16-0687, a new potent non-peptide bradykinin B2 receptor antagonist. *Immunopharmacology* **43**: 187-94 [PMID:10596852]
99. Pyne NJ, Tolan D and Pyne S. (1997) Bradykinin stimulates cAMP synthesis via mitogen-activated protein kinase-dependent regulation of cytosolic phospholipase A2 and prostaglandin E2 release in airway smooth muscle. *Biochem. J.* **328 (Pt 2)**: 689-94 [PMID:9371732]
100. Regoli D, Nsa Allogho S, Rizzi A and Gobeil FJ. (1998) Bradykinin receptors and their antagonists. *Eur. J. Pharmacol.* **348**: 1-10 [PMID:9650825]
101. Ricupero DA, Romero JR, Rishikof DC and Goldstein RH. (2000) Des-Arg(10)-kallidin engagement of the B1 receptor stimulates type I collagen synthesis via stabilization of connective tissue growth factor mRNA. *J. Biol. Chem.* **275**: 12475-80 [PMID:10777533]
102. Ritchie TJ, Dziadulewicz EK, Culshaw AJ, Müller W, Burgess GM, Bloomfield GC, Drake GS, Dunstan AR, Beattie D and Hughes GA *et al.*. (2004) Potent and orally bioavailable non-peptide antagonists at the human bradykinin B(1) receptor based on a 2-alkylamino-5-sulfamoylbenzamide core. *J. Med. Chem.* **47**: 4642-4 [PMID:15341478]
103. Rizzi A, Gobeil F, Calò G, Inamura N and Regoli D. (1997) FR 173657: a new, potent, nonpeptide kinin B2 receptor antagonist. An in vitro study. *Hypertension* **29**: 951-6 [PMID:9095082]

104. Rodriguez JA, De la Cerda P, Collyer E, Decap V, Vio CP and Velarde V. (2006) Cyclooxygenase-2 induction by bradykinin in aortic vascular smooth muscle cells. *Am. J. Physiol. Heart Circ. Physiol.* **290**: H30-6 [PMID:16143655]
105. Ross D and Joyner WL. (1997) Resting distribution and stimulated translocation of protein kinase C isoforms alpha, epsilon and zeta in response to bradykinin and TNF in human endothelial cells. *Endothelium* **5**: 321-32 [PMID:9588823]
106. Salvino JM, Seoane PR, Douty BD, Awad MM, Dolle RE, Houck WT, Faunce DM and Sawutz DG. (1993) Design of potent non-peptide competitive antagonists of the human bradykinin B2 receptor. *J. Med. Chem.* **36**: 2583-4 [PMID:8394936]
107. Samadfam R, Teixeira C, Bkaily G, Sirois P, de Brum-Fernandes A and D'Orleans-Juste P. (2000) Contribution of B(2) receptors for bradykinin in arthus reaction-induced plasma extravasation in wild-type or B(2) transgenic knockout mice. *Br. J. Pharmacol.* **129**: 1732-8 [PMID:10780980]
108. Sawada Y, Kayakiri H, Abe Y, Mizutani T, Inamura N, Asano M, Hatori C, Aramori I, Oku T and Tanaka H. (2004) Discovery of the first non-peptide full agonists for the human bradykinin B(2) receptor incorporating 4-(2-picolyl)oxyquinoline and 1-(2-picolyl)benzimidazole frameworks. *J. Med. Chem.* **47**: 2853-63 [PMID:15139763]
109. Sawutz DG, Salvino JM, Dolle RE, Casiano F, Ward SJ, Houck WT, Faunce DM, Douty BD, Baizman E and Awad MM *et al.* (1994) The nonpeptide WIN 64338 is a bradykinin B2 receptor antagonist. *Proc. Natl. Acad. Sci. U.S.A.* **91**: 4693-7 [PMID:8197121]
110. Schanstra JP, Duchene J, Praddaude F, Bruneval P, Tack I, Chevalier J, Girolami JP and Bascands JL. (2003) Decreased renal NO excretion and reduced glomerular tuft area in mice lacking the bradykinin B2 receptor. *Am. J. Physiol. Heart Circ. Physiol.* **284**: H1904-8 [PMID:12560214]
111. Schanstra JP, Neau E, Drogoz P, Arevalo Gomez MA, Lopez Novoa JM, Calise D, Pecher C, Bader M, Girolami JP and Bascands JL. (2002) In vivo bradykinin B2 receptor activation reduces renal fibrosis. *J. Clin. Invest.* **110**: 371-9 [PMID:12163456]
112. Sevcik MA, Ghilardi JR, Halvorson KG, Lindsay TH, Kubota K and Mantyh PW. (2005) Analgesic efficacy of bradykinin B1 antagonists in a murine bone cancer pain model. *J Pain* **6**: 771-5 [PMID:16275602]
113. Souza DG, Lomez ES, Pinho V, Pesquero JB, Bader M, Pesquero JL and Teixeira MM. (2004) Role of bradykinin B2 and B1 receptors in the local, remote, and systemic inflammatory responses that follow intestinal ischemia and reperfusion injury. *J. Immunol.* **172**: 2542-8 [PMID:14764727]
114. Steranka LR, Manning DC, DeHaas CJ, Ferkany JW, Borosky SA, Connor JR, Vavrek RJ, Stewart JM and Snyder SH. (1988) Bradykinin as a pain mediator: receptors are localized to sensory neurons, and antagonists have analgesic actions. *Proc Natl Acad Sci U S A* **85**: 3245-3249 [PMID:2896357]
115. Stewart JM, Gera L, Hanson W, Zuzak JS, Burkard M, McCullough R and Whalley ET. (1996) A new generation of bradykinin antagonists. *Immunopharmacology* **33**: 51-60 [PMID:8856115]
116. Su DS, Markowitz MK, DiPardo RM, Murphy KL, Harrell CM, O'Malley SS, Ransom RW, Chang RS, Ha S and Hess FJ *et al.* (2003) Discovery of a potent, non-peptide bradykinin B1 receptor antagonist. *J. Am. Chem. Soc.* **125**: 7516-7 [PMID:12812482]
117. Taub JS, Guo R, Leeb-Lundberg LM, Madden JF and Daaka Y. (2003) Bradykinin receptor subtype 1 expression and function in prostate cancer. *Cancer Res.* **63**: 2037-41 [PMID:12727816]
118. Tilly BC, van Paridon PA, Verlaan I, Wirtz KW, de Laat SW and Moolenaar WH. (1987) Inositol phosphate metabolism in bradykinin-stimulated human A431 carcinoma cells. Relationship to calcium signalling. *Biochem. J.* **244**: 129-35 [PMID:3663107]
119. Tippmer S, Qwitterer U, Kolm V, Faussner A, Roscher A, Mosthaf L, Müller-Esterl W and Häring H. (1994) Bradykinin induces translocation of the protein kinase C isoforms alpha, epsilon, and zeta. *Eur. J. Biochem.* **225**: 297-304 [PMID:7925449]
120. Trabold F, Pons S, Hagege AA, Bloch-Faure M, Alhenc-Gelas F, Giudicelli JF, Richer-Giudicelli C and Meneton P. (2002) Cardiovascular phenotypes of kinin B2 receptor- and tissue kallikrein-deficient mice. *Hypertension* **40**: 90-5 [PMID:12105144]
121. Uknis AB, DeLa Cadena RA, Janardham R, Sartor RB, Whalley ET and Colman RW. (2001) Bradykinin

- receptor antagonists type 2 attenuate the inflammatory changes in peptidoglycan-induced acute arthritis in the Lewis rat. *Inflamm. Res.* **50**: 149-55 [PMID:11339503]
122. Wang DZ, Chao L and Chao J. (1997) Hypotension in transgenic mice overexpressing human bradykinin B2 receptor. *Hypertension* **29**: 488-93 [PMID:9039147]
 123. Wilk-Blaszczak MA, Singer WD, Gutowski S, Sternweis PC and Belardetti F. (1994) The G protein G13 mediates inhibition of voltage-dependent calcium current by bradykinin. *Neuron* **13**: 1215-24 [PMID:7946358]
 124. Windischhofer W and Leis HJ. (1997) [³H]bradykinin receptor-binding, receptor-recycling, and receptor-internalization of the B2 bradykinin receptor in the murine osteoblast-like cell line MC3T3-E1. *J. Bone Miner. Res.* **12**: 1615-25 [PMID:9333122]
 125. Wood MR, Kim JJ, Han W, Dorsey BD, Homnick CF, DiPardo RM, Kuduk SD, MacNeil T, Murphy KL and Lis EV *et al.*. (2003) Benzodiazepines as potent and selective bradykinin B1 antagonists. *J. Med. Chem.* **46**: 1803-6 [PMID:12723943]
 126. Wotherspoon G and Winter J. (2000) Bradykinin B1 receptor is constitutively expressed in the rat sensory nervous system. *Neurosci. Lett.* **294**: 175-8 [PMID:11072143]
 127. Wu J, Akaike T, Hayashida K, Miyamoto Y, Nakagawa T, Miyakawa K, Müller-Esterl W and Maeda H. (2002) Identification of bradykinin receptors in clinical cancer specimens and murine tumor tissues. *Int J Cancer* **98**: 29-35 [PMID:11857381]
 128. Yanaga F, Hirata M and Koga T. (1991) Evidence for coupling of bradykinin receptors to a guanine-nucleotide binding protein to stimulate arachidonate liberation in the osteoblast-like cell line, MC3T3-E1. *Biochim. Biophys. Acta* **1094**: 139-46 [PMID:1654114]
 129. Yang XP, Liu YH, Scicli GM, Webb CR and Carretero OA. (1997) Role of kinins in the cardioprotective effect of preconditioning: study of myocardial ischemia/reperfusion injury in B2 kinin receptor knockout mice and kininogen-deficient rats. *Hypertension* **30**: 735-40 [PMID:9323015]
 130. Yano K, Higashida H, Hattori H and Nozawa Y. (1985) Bradykinin-induced transient accumulation of inositol trisphosphate in neuron-like cell line NG108-15 cells. *FEBS Lett.* **181**: 403-6 [PMID:2857660]
 131. Zhang SP and Codd EE. (1998) Characterization of bradykinin receptors in human lung fibroblasts using the binding of [³H][Des-Arg¹⁰,Leu⁹]kallidin and [³H]NPC17731. *Life Sci.* **62**: 2303-14 [PMID:9651119]
 132. Zhang SP, Wang HY, Lovenberg TW and Codd EE. (2001) Functional studies of bradykinin receptors in Chinese hamster ovary cells stably expressing the human B2 bradykinin receptor. *Int. Immunopharmacol.* **1**: 955-65 [PMID:11379050]
 133. Zuccollo A, Navarro M, Frontera M, Cueva F, Carattino M and Catanzaro OL. (1999) The involvement of kallikrein-kinin system in diabetes type I (insulinitis). *Immunopharmacology* **45**: 69-74 [PMID:10614992]
 134. Zwick E, Daub H, Aoki N, Yamaguchi-Aoki Y, Tinhofer I, Maly K and Ullrich A. (1997) Critical role of calcium-dependent epidermal growth factor receptor transactivation in PC12 cell membrane depolarization and bradykinin signaling. *J. Biol. Chem.* **272**: 24767-70 [PMID:9312072]