

Endothelin receptors in GtoPdb v.2023.1

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Abstract

Endothelin receptors (**nomenclature as agreed by the NC-IUPHAR Subcommittee on Endothelin Receptors [24]**) are activated by the endogenous 21 amino-acid peptides endothelins 1-3 ([endothelin-1](#), [endothelin-2](#) and [endothelin-3](#)).

Contents

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Database links

Endothelin receptors

<https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=21>

Introduction to Endothelin receptors

<https://www.guidetopharmacology.org/GRAC/FamilyIntroductionForward?familyId=21>

Receptors

ET_A receptor

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ET_B receptor

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=220>

References

1. Adachi M, Yang YY, Furuichi Y and Miyamoto C. (1991) Cloning and characterization of cDNA encoding human A-type endothelin receptor. *Biochem Biophys Res Commun* **180**: 1265-72 [PMID:1719979]
2. Adner M, Cardell LO, Sjöberg T, Ottosson A and Edvinsson L. (1996) Contractile endothelin-B (ETB) receptors in human small bronchi. *Eur Respir J* **9**: 351-5 [PMID:8777976]
3. Arai H, Hori S, Aramori I, Ohkubo H and Nakanishi S. (1990) Cloning and expression of a cDNA encoding an endothelin receptor. *Nature* **348**: 730-2 [PMID:2175396]
4. Arai H, Nakao K, Takaya K, Hosoda K, Ogawa Y, Nakanishi S and Imura H. (1993) The human endothelin-B receptor gene. Structural organization and chromosomal assignment. *J Biol Chem* **268**: 3463-70 [PMID:8429023]
5. Aramori I and Nakanishi S. (1992) Coupling of two endothelin receptor subtypes to differing signal transduction in transfected Chinese hamster ovary cells. *J Biol Chem* **267**: 12468-74 [PMID:1319997]
6. Aramori I, Nirei H, Shoubo M, Sogabe K, Nakamura K, Kojo H, Notsu Y, Ono T and Nakanishi S. (1993) Subtype selectivity of a novel endothelin antagonist, FR139317, for the two endothelin receptors in transfected Chinese hamster ovary cells. *Mol Pharmacol* **43**: 127-31 [PMID:8429819]
7. Bacon CR and Davenport AP. (1996) Endothelin receptors in human coronary artery and aorta. *Br J Pharmacol* **117**: 986-92 [PMID:8851522]
8. Balwierczak JL, Bruseo CW, DelGrande D, Jeng AY, Savage P and Shetty SS. (1995) Characterization of a potent and selective endothelin-B receptor antagonist, IRL 2500. *J Cardiovasc Pharmacol* **26 Suppl 3**: S393-6 [PMID:8587424]
9. Battistini B, Berthiaume N, Kelland NF, Webb DJ and Kohan DE. (2006) Profile of past and current clinical trials involving endothelin receptor antagonists: the novel "-sentan" class of drug. *Exp Biol Med (Maywood)* **231**: 653-695 [PMID:16740981]
10. Battistini B and Dussault P. (1998) Biosynthesis, distribution and metabolism of endothelins in the pulmonary system. *Pulm Pharmacol Ther* **11**: 79-88 [PMID:9918740]
11. Baynash AG, Hosoda K, Giaid A, Richardson JA, Emoto N, Hammer RE and Yanagisawa M. (1994) Interaction of endothelin-3 with endothelin-B receptor is essential for development of epidermal melanocytes and enteric neurons. *Cell* **79**: 1277-85 [PMID:8001160]
12. Bolli MH, Boss C, Binkert C, Buchmann S, Bur D, Hess P, Iglarz M, Meyer S, Rein J and Rey M *et al.* (2012) The discovery of N-[5-(4-bromophenyl)-6-[2-[(5-bromo-2-pyrimidinyl)oxy]ethoxy]-4-pyrimidinyl]-N'-propylsulfamide (Macitentan), an orally active, potent dual endothelin receptor antagonist. *J Med Chem* **55**: 7849-61 [PMID:22862294]
13. Bolli MH, Marfurt J, Grisostomi C, Boss C, Binkert C, Hess P, Treiber A, Thorin E, Morrison K and Buchmann S *et al.* (2004) Novel benzo[1,4]diazepin-2-one derivatives as endothelin receptor antagonists. *J Med Chem* **47**: 2776-95 [PMID:15139756]
14. Breu V, Clozel M, Burri K, Hirth G, Neidhart W and Ramuz H. (1996) In vitro characterisation of Ro 46-8443, the first non-peptide antagonist selective for the endothelin ETB receptor. *FEBS Lett* **383**: 37-41 [PMID:8612786]
15. Breu V *et al.* (2003) Heterocyclic sulfonamides. Patent number: US6521631. Assignee: Hoffmann-La Roche. Priority date: 13/03/2015. Publication date: 18/02/2003.
16. 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]
17. Cai Y, Yamada T, Xin X, Agui T and Matsumoto K. (1995) Mapping of the genes for rat endothelin receptor type A (ETAR) and type B (ETBR) to chromosomes 19 and 15 respectively. *Anim Genet* **26**: 39-41 [PMID:7702211]
18. Cheng HF, Su YM, Yeh JR and Chang KJ. (1993) Alternative transcript of the nonselective-type endothelin receptor from rat brain. *Mol Pharmacol* **44**: 533-8 [PMID:8371713]
19. Clouthier DE, Hosoda K, Richardson JA, Williams SC, Yanagisawa H, Kuwaki T, Kumada M, Hammer RE and Yanagisawa M. (1998) Cranial and cardiac neural crest defects in endothelin-A receptor-deficient mice. *Development* **125**: 813-24 [PMID:9449664]
20. Clozel M, Breu V, Gray GA, Kalina B, Löffler BM, Burri K, Cassal JM, Hirth G, Müller M and Neidhart W *et al.* (1994) Pharmacological characterization of bosentan, a new potent orally active nonpeptide endothelin receptor antagonist. *J Pharmacol Exp Ther* **270**: 228-35 [PMID:8035319]
21. Clozel M, Ramuz H, Clozel JP, Breu V, Hess P, Löffler BM, Coassolo P and Roux S. (1999) Pharmacology of

- tezosentan, new endothelin receptor antagonist designed for parenteral use. *J Pharmacol Exp Ther* **290**: 840-846 [PMID:10411600]
22. Cyr C, Huebner K, Druck T and Kris R. (1991) Cloning and chromosomal localization of a human endothelin ETA receptor. *Biochem Biophys Res Commun* **181**: 184-90 [PMID:1659806]
 23. Dasgupta F, Mukherjee AK and Gangadhar N. (2002) Endothelin receptor antagonists--an overview. *Curr Med Chem* **9**: 549-75 [PMID:11945124]
 24. Davenport AP. (2002) International Union of Pharmacology. XXIX. Update on endothelin receptor nomenclature. *Pharmacol Rev* **54**: 219-26 [PMID:12037137]
 25. Davenport AP. (1997) Distribution of endothelin receptors. In *Endothelins in Biology and Medicine* Edited by Mille R, Pelton JT, Huggins J: CRC Press.: 45-68 [ISBN: 0849369754]
 26. Davenport AP and Battistini B. (2002) Classification of endothelin receptors and antagonists in clinical development. *Clin Sci* **103 Suppl 48**: 1S-3S [PMID:12193042]
 27. Davenport AP, Kuc RE, Ashby MJ, Patt WC and Doherty AM. (1998) Characterization of [125I]-PD164333, an ETA selective non-peptide radiolabelled antagonist, in normal and diseased human tissues. *Br J Pharmacol* **123**: 223-30 [PMID:9489609]
 28. Davenport AP, Kuc RE, Fitzgerald F, Maguire JJ, Berryman K and Doherty AM. (1994) [125I]-PD151242: a selective radioligand for human ETA receptors. *Br J Pharmacol* **111**: 4-6 [PMID:8012722]
 29. Davenport AP and Maguire JJ. (2002) Of mice and men: advances in endothelin research and first antagonist gains FDA approval. *Trends Pharmacol Sci* **23**: 155-7 [PMID:11931980]
 30. Davenport AP and Maguire JJ. (2006) Endothelin. *Handb Exp Pharmacol*: 295-329 [PMID:16999223]
 31. Davenport AP, O'Reilly G and Kuc RE. (1995) Endothelin ETA and ETB mRNA and receptors expressed by smooth muscle in the human vasculature: majority of the ETA sub-type. *Br J Pharmacol* **114**: 1110-6 [PMID:7620699]
 32. Davenport AP and Russell FD. (2001) Endothelin converting enzymes and endothelin receptor localisation in human tissues. *Handb Exp Pharmacol* **152**: 209-237
 33. de Nucci G, Thomas R, D'Orleans-Juste P, Antunes E, Walder C, Warner TD and Vane JR. (1988) Pressor effects of circulating endothelin are limited by its removal in the pulmonary circulation and by the release of prostacyclin and endothelium-derived relaxing factor. *Proc Natl Acad Sci USA* **85**: 9797-800 [PMID:3059352]
 34. De Oliveira AM, Viswanathan M, Capsoni S, Heemskerk FM, Correa FM and Saavedra JM. (1995) Characterization of endothelinA receptors in cerebral and peripheral arteries of the rat. *Peptides* **16**: 139-44 [PMID:7716066]
 35. Dhein S, Giessler C, Wangemann T, Silber RE, Zerkowski HR and Brodde OE. (2000) Differential pattern of endothelin-1-induced inotropic effects in right atria and left ventricles of the human heart. *J Cardiovasc Pharmacol* **36**: 564-9 [PMID:11065215]
 36. Doherty AM, Patt WC, Edmunds JJ, Berryman KA, Reisdorph BR, Plummer MS, Shahripour A, Lee C, Cheng XM and Walker DM *et al.*. (1995) Discovery of a novel series of orally active non-peptide endothelin-A (ETA) receptor-selective antagonists. *J Med Chem* **38**: 1259-63 [PMID:7731010]
 37. Douglas SA, Beck Jr GR, Elliott JD and Ohlstein EH. (1995) Pharmacologic evidence for the presence of three functional endothelin receptor subtypes in rabbit saphenous vein. *J Cardiovasc Pharmacol* **26 Suppl 3**: S163-8 [PMID:8587352]
 38. Douglas SA and Ohlstein EH. (1997) Signal transduction mechanisms mediating the vascular actions of endothelin. *J Vasc Res* **34**: 152-64 [PMID:9226297]
 39. Elliott JD, Lago MA, Cousins RD, Gao A, Leber JD, Erhard KF, Nambi P, Elshourbagy NA, Kumar C and Lee JA *et al.*. (1994) 1,3-Diarylindan-2-carboxylic acids, potent and selective non-peptide endothelin receptor antagonists. *J Med Chem* **37**: 1553-7 [PMID:8201588]
 40. Elliott JD, Ohlstein EH, Peishoff CE, Ellens HM and Lago MA. (1998) Endothelin receptor antagonists. *Pharm Biotechnol* **11**: 113-29 [PMID:9760678]
 41. Elshourbagy NA, Adamou JE, Gagnon AW, Wu HL, Pullen M and Nambi P. (1996) Molecular characterization of a novel human endothelin receptor splice variant. *J Biol Chem* **271**: 25300-25307 [PMID:8810293]
 42. Elshourbagy NA, Korman DR, Wu HL, Sylvester DR, Lee JA, Nuthalaganti P, Bergsma DJ, Kumar CS and Nambi P. (1993) Molecular characterization and regulation of the human endothelin receptors. *J Biol Chem* **268**: 3873-9 [PMID:8440682]
 43. Fukuroda T, Fujikawa T, Ozaki S, Ishikawa K, Yano M and Nishikibe M. (1994) Clearance of circulating

- endothelin-1 by ETB receptors in rats. *Biochem Biophys Res Commun* **199**: 1461-5 [PMID:8147891]
44. Gardiner SM, Compton AM and Bennett T. (1989) Regional hemodynamic effects of endothelin-1 in conscious, unrestrained, Wistar rats. *J Cardiovasc Pharmacol* **13 Suppl 5**: S202-4 [PMID:2473311]
 45. Gardiner SM, Compton AM, Kemp PA and Bennett T. (1990) Regional and cardiac haemodynamic effects of NG-nitro-L-arginine methyl ester in conscious, Long Evans rats. *Br J Pharmacol* **101**: 625-31 [PMID:2076481]
 46. Gellai M, De Wolf R, Fletcher T and Nambi P. (1997) Contribution of endogenous endothelin-1 to the maintenance of vascular tone: role of nitric oxide. *Pharmacology* **55**: 299-308 [PMID:9413859]
 47. Griswold DE, Douglas SA, Martin LD, Davis TG, Davis L, Ao Z, Luttmann MA, Pullen M, Nambi P and Hay DW *et al.* (1999) Endothelin B receptor modulates inflammatory pain and cutaneous inflammation. *Mol Pharmacol* **56**: 807-12 [PMID:10496965]
 48. Harland SP, Kuc RE, Pickard JD and Davenport AP. (1995) Characterization of endothelin receptors in human brain cortex, gliomas, and meningiomas. *J Cardiovasc Pharmacol* **26 Suppl 3**: S408-11 [PMID:8587429]
 49. Hatae N, Aksentijevich N, Zemkova HW, Kretschmannova K, Tomic M and Stojilkovic SS. (2007) Cloning and functional identification of novel endothelin receptor type A isoforms in pituitary. *Mol Endocrinol* **21**: 1192-204 [PMID:17312275]
 50. Haynes WG and Webb DJ. (1994) Contribution of endogenous generation of endothelin-1 to basal vascular tone. *Lancet* **344**: 852-4 [PMID:7916401]
 51. Horstmeyer A, Cramer H, Sauer T, Müller-Esterl W and Schroeder C. (1996) Palmitoylation of endothelin receptor A. Differential modulation of signal transduction activity by post-translational modification. *J Biol Chem* **271**: 20811-9 [PMID:8702836]
 52. Hoshino T, Yamauchi R, Kikkawa K, Yabana H and Murata S. (1998) Pharmacological profile of T-0201, a highly potent and orally active endothelin receptor antagonist. *J Pharmacol Exp Ther* **286**: 643-9 [PMID:9694915]
 53. Hosoda K, Hammer RE, Richardson JA, Baynash AG, Cheung JC, Giaid A and Yanagisawa M. (1994) Targeted and natural (piebald-lethal) mutations of endothelin-B receptor gene produce megacolon associated with spotted coat color in mice. *Cell* **79**: 1267-76 [PMID:8001159]
 54. Hosoda K, Nakao K, Hiroshi-Arai, Suga S, Ogawa Y, Mukoyama M, Shirakami G, Saito Y, Nakanishi S and Imura H. (1991) Cloning and expression of human endothelin-1 receptor cDNA. *FEBS Lett* **287**: 23-6 [PMID:1652463]
 55. Iglarz M, Binkert C, Morrison K, Fischli W, Gatfield J, Treiber A, Weller T, Bolli MH, Boss C and Buchmann S *et al.* (2008) Pharmacology of macitentan, an orally active tissue-targeting dual endothelin receptor antagonist. *J Pharmacol Exp Ther* **327**: 736-45 [PMID:18780830]
 56. Ihara M, Noguchi K, Saeki T, Fukuroda T, Tsuchida S, Kimura S, Fukami T, Ishikawa K, Nishikibe M and Yano M. (1992) Biological profiles of highly potent novel endothelin antagonists selective for the ETA receptor. *Life Sci* **50**: 247-55 [PMID:1310132]
 57. Ihara M, Saeki T, Fukuroda T, Kimura S, Ozaki S, Patel AC and Yano MA. (1992) Novel radioligand [¹²⁵I]BQ-3020 selective for endothelin (ET_B) receptors. *Life Sci* **51**: PL47-PL52 [PMID:1321937]
 58. Ihara M, Yamanaka R, Ohwaki K, Ozaki S, Fukami T, Ishikawa K, Towers P and Yano M. (1995) [3H]BQ-123, a highly specific and reversible radioligand for the endothelin ETA receptor subtype. *Eur J Pharmacol* **274**: 1-6 [PMID:7768260]
 59. Inoue A, Yanagisawa M, Kimura S, Kasuya Y, Miyauchi T, Goto K and Masaki T. (1989) The human endothelin family: three structurally and pharmacologically distinct isopeptides predicted by three separate genes. *Proc Natl Acad Sci USA* **86**: 2863-7 [PMID:2649896]
 60. Ishikawa K, Ihara M, Noguchi K, Mase T, Mino N, Saeki T, Fukuroda T, Fukami T, Ozaki S and Nagase T *et al.* (1994) Biochemical and pharmacological profile of a potent and selective endothelin B-receptor antagonist, BQ-788. *Proc Natl Acad Sci USA* **91**: 4892-6 [PMID:8197152]
 61. Izume T, Miyauchi H, Shihoya W and Nureki O. (2020) Crystal structure of human endothelin ET_B receptor in complex with sarafotoxin S6b. *Biochem Biophys Res Commun* **528**: 383-388 [PMID:32001000]
 62. Jae HS, Winn M, von Geldern TW, Sorensen BK, Chiou WJ, Nguyen B, Marsh KC and Opgenorth TJ. (2001) Pyrrolidine-3-carboxylic acids as endothelin antagonists. 5. Highly selective, potent, and orally active ET(A) antagonists. *J Med Chem* **44**: 3978-84 [PMID:11689084]
 63. Ji Y, Duan J, Yuan Q, He X, Yang G, Zhu S, Wu K, Hu W, Gao T and Cheng X *et al.* (2023) Structural basis of peptide recognition and activation of endothelin receptors. *Nat Commun* **14**: 1268 [PMID:36882417]

64. Johnström P, Harris NG, Fryer TD, Barret O, Clark JC, Pickard JD and Davenport AP. (2002) (18)F-Endothelin-1, a positron emission tomography (PET) radioligand for the endothelin receptor system: radiosynthesis and in vivo imaging using microPET. *Clin Sci* **103 Suppl 48**: 4S-8S [PMID:12193043]
65. Karet FE, Kuc RE and Davenport AP. (1993) Novel ligands BQ123 and BQ3020 characterize endothelin receptor subtypes ETA and ETB in human kidney. *Kidney Int* **44**: 36-42 [PMID:8355464]
66. Karne S Jayawickreme CK and Lerner MR. (1993) Cloning and characterization of an endothelin-3 specific receptor (ETC receptor) from *Xenopus laevis* dermal melanophores. *J Biol Chem* **268**: 19126-19133 [PMID:8360195]
67. Kilpatrick SJ, Roberts JM, Lykins DL and Taylor RN. (1993) Characterization and ontogeny of endothelin receptors in human placenta. *Am J Physiol* **264**: E367-72 [PMID:8460684]
68. Kondo S, Morita T and Tashima Y. (1994) Endothelin receptor density in human hypertrophic and non-hypertrophic prostate tissue. *Tohoku J Exp Med* **172**: 381-4 [PMID:7524189]
69. Kowala MC, Murugesan N, Tellew J, Carlson K, Monshizadegan H, Ryan C, Gu Z, Kane B, Fadnis L and Baska RA *et al.*. (2004) Novel dual action AT1 and ETA receptor antagonists reduce blood pressure in experimental hypertension. *J Pharmacol Exp Ther* **309**: 275-84 [PMID:14718594]
70. Kuc RE, Karet FE and Davenport AP. (1995) Characterization of peptide and nonpeptide antagonists in human kidney. *J Cardiovasc Pharmacol* **26 Suppl 3**: S373-5 [PMID:8587419]
71. Kusumoto K, Kubo K, Kandori H, Kitayoshi T, Sato S, Wakimasu M, Watanabe T and Fujino M. (1994) Effects of a new endothelin antagonist, TAK-044, on post-ischemic acute renal failure in rats. *Life Sci* **55**: 301-10 [PMID:8028448]
72. Lin HY, Kaji EH, Winkel GK, Ives HE and Lodish HF. (1991) Cloning and functional expression of a vascular smooth muscle endothelin 1 receptor. *Proc Natl Acad Sci USA* **88**: 3185-9 [PMID:1849646]
73. Liu G, Henry Jr KJ, Szczepankiewicz BG, Winn M, Kozmina NS, Boyd SA, Wasicak J, von Geldern TW, Wu-Wong JR and Chiou WJ *et al.*. (1998) Pyrrolidine-3-carboxylic acids as endothelin antagonists. 3. Discovery of a potent, 2-nonyl, highly selective ETA antagonist (A-216546). *J Med Chem* **41**: 3261-75 [PMID:9703472]
74. MacCarthy PA, Grocott-Mason R, Prendergast BD and Shah AM. (2000) Contrasting inotropic effects of endogenous endothelin in the normal and failing human heart: studies with an intracoronary ET(A) receptor antagonist. *Circulation* **101**: 142-7 [PMID:10637200]
75. Maguire JJ and Davenport AP. (1995) ETA receptor-mediated constrictor responses to endothelin peptides in human blood vessels in vitro. *Br J Pharmacol* **115**: 191-7 [PMID:7647976]
76. Maguire JJ, Kuc RE and Davenport AP. (1997) Affinity and selectivity of PD156707, a novel nonpeptide endothelin antagonist, for human ET(A) and ET(B) receptors. *J Pharmacol Exp Ther* **280**: 1102-8 [PMID:9023329]
77. Maguire JJ, Kuc RE, Doherty AM and Davenport AP. (1995) Potency of PD155080, an orally active ETA receptor antagonist, determined for human endothelin receptors. *J Cardiovasc Pharmacol* **26 Suppl 3**: S362-4 [PMID:8587415]
78. Mihara S, Tozawa F, Itazaki K and Fujimoto M. (1998) Binding characterization of [3H]S-0139, an antagonist of the endothelin ET(A) receptor subtype. *Eur J Pharmacol* **342**: 319-24 [PMID:9548403]
79. Mizuguchi T, Nishiyama M, Moroi K, Tanaka H, Saito T, Masuda Y, Masaki T, de Wit D, Yanagisawa M and Kimura S. (1997) Analysis of two pharmacologically predicted endothelin B receptor subtypes by using the endothelin B receptor gene knockout mouse. *Br J Pharmacol* **120**: 1427-30 [PMID:9113361]
80. Molenaar P, Kuc RE and Davenport AP. (1992) Characterization of two new ETB selective radioligands, [125I]-BQ3020 and [125I]-[Ala1,3,11,15]ET-1 in human heart. *Br J Pharmacol* **107**: 637-9 [PMID:1472961]
81. Moravec CS, Reynolds EE, Stewart RW and Bond M. (1989) Endothelin is a positive inotropic agent in human and rat heart in vitro. *Biochem Biophys Res Commun* **159**: 14-8 [PMID:2647079]
82. Morphy R and Rankovic Z. (2005) Designed multiple ligands. An emerging drug discovery paradigm. *J Med Chem* **48**: 6523-43 [PMID:16220969]
83. Morris CD, Rose A, Curwen J, Hughes AM, Wilson DJ and Webb DJ. (2005) Specific inhibition of the endothelin A receptor with ZD4054: clinical and pre-clinical evidence. *Br J Cancer* **92**: 2148-52 [PMID:15956965]
84. Nagase T, Aoki T, Oka T, Fukuchi Y and Ouchi Y. (1997) ET-1-induced bronchoconstriction is mediated via ETB receptor in mice. *J Appl Physiol* **83**: 46-51 [PMID:9216943]
85. Nagiri C, Shihoya W, Inoue A, Kadji FMN, Aoki J and Nureki O. (2019) Crystal structure of human endothelin ET_B receptor in complex with peptide inverse agonist IRL2500. *Commun Biol* **2**: 236

[PMID:31263780]

86. Nakamuta M, Takayanagi R, Sakai Y, Sakamoto S, Hagiwara H, Mizuno T, Saito Y, Hirose S, Yamamoto M and Nawata H. (1991) Cloning and sequence analysis of a cDNA encoding human non-selective type of endothelin receptor. *Biochem Biophys Res Commun* **177**: 34-39 [PMID:1710450]
87. Nambi P, Pullen M and Spielman W. (1994) Species differences in the binding characteristics of [125I]IRL-1620, a potent agonist specific for endothelin-B receptors. *J Pharmacol Exp Ther* **268**: 202-7 [PMID:8301559]
88. O'Donnell SR and Kay CS. (1995) Effects of endothelin receptor selective antagonists, BQ-123 and BQ-788, on IRL 1620 and endothelin-1 responses of airway and vascular preparations from rats. *Pulm Pharmacol* **8**: 11-9 [PMID:8535094]
89. Ogawa Y, Nakao K, Arai H, Nakagawa O, Hosoda K, Suga S, Nakanishi S and Imura H. (1991) Molecular cloning of a non-isopeptide-selective human endothelin receptor. *Biochem Biophys Res Commun* **178**: 248-55 [PMID:1648908]
90. Ohlstein EH, Beck Jr GR, Douglas SA, Nambi P, Lago MA, Gleason JG, Ruffolo Jr RR, Feuerstein G and Elliott JD. (1994) Nonpeptide endothelin receptor antagonists. II. Pharmacological characterization of SB 209670. *J Pharmacol Exp Ther* **271**: 762-8 [PMID:7965794]
91. Ohlstein EH, Nambi P, Hay DW, Gellai M, Brooks DP, Luengo J, Xiang JN and Elliott JD. (1998) Nonpeptide endothelin receptor antagonists. XI. Pharmacological characterization of SB 234551, a high-affinity and selective nonpeptide ETA receptor antagonist. *J Pharmacol Exp Ther* **286**: 650-6 [PMID:9694916]
92. Ohlstein EH, Nambi P, Lago A, Hay DW, Beck G, Fong KL, Eddy EP, Smith P, Ellens H and Elliott JD. (1996) Nonpeptide endothelin receptor antagonists. VI: Pharmacological characterization of SB 217242, a potent and highly bioavailable endothelin receptor antagonist. *J Pharmacol Exp Ther* **276**: 609-15 [PMID:8632328]
93. Okazaki Y, Furuno M, Kasukawa T, Adachi J, Bono H, Kondo S, Nikaido I, Osato N, Saito R and Suzuki H *et al.*. (2002) Analysis of the mouse transcriptome based on functional annotation of 60,770 full-length cDNAs. *Nature* **420**: 563-73 [PMID:12466851]
94. Opgenorth TJ, Adler AL, Calzadilla SV, Chiou WJ, Dayton BD, Dixon DB, Gehrke LJ, Hernandez L, Magnuson SR and Marsh KC *et al.*. (1996) Pharmacological characterization of A-127722: an orally active and highly potent ETA-selective receptor antagonist. *J Pharmacol Exp Ther* **276**: 473-81 [PMID:8632312]
95. Panek RL, Major TC, Hingorani GP, Doherty AM, Taylor DG and Rapundalo ST. (1992) Endothelin and structurally related analogs distinguish between endothelin receptor subtypes. *Biochem Biophys Res Commun* **183**: 566-71 [PMID:1312833]
96. Peter MG and Davenport AP. (1995) Selectivity of [125I]-PD151242 for human, rat and porcine endothelin ETA receptors in the heart. *Br J Pharmacol* **114**: 297-302 [PMID:7881728]
97. Pierre LN and Davenport AP. (1999) Blockade and reversal of endothelin-induced constriction in pial arteries from human brain. *Stroke* **30**: 638-43 [PMID:10066864]
98. Pollock DM and Highsmith RF. (1998) Endothelin receptors and signalling mechanisms. Springer: 1-224 [ISBN: 3540559701]
99. Puffenberger EG, Hosoda K, Washington SS, Nakao K, deWit D, Yanagisawa M and Chakravart A. (1994) A missense mutation of the endothelin-B receptor gene in multigenic Hirschsprung's disease. *Cell* **79**: 1257-66 [PMID:8001158]
100. Ranjan AK and Gulati A. (2022) Sovateltide Mediated Endothelin B Receptors Agonism and Curbing Neurological Disorders. *Int J Mol Sci* **23** [PMID:35328566]
101. Reynolds EE, Hwang O, Flynn MA, Welch KM, Cody WL, Steinbaugh B, He JX, Chung FZ and Doherty AM. (1995) Pharmacological differences between rat and human endothelin B receptors. *Biochem Biophys Res Commun* **209**: 506-12 [PMID:7733918]
102. Riechers H, Albrecht HP, Amberg W, Baumann E, Bernard H, Böhm HJ, Klinge D, Kling A, Müller S and Raschack M *et al.*. (1996) Discovery and optimization of a novel class of orally active nonpeptidic endothelin-A receptor antagonists. *J Med Chem* **39**: 2123-8 [PMID:8667356]
103. Roux S, Breu V, Giller T, Neidhart W, Ramuz H, Coassolo P, Clozel JP and Clozel M. (1997) Ro 61-1790, a new hydrosoluble endothelin antagonist: general pharmacology and effects on experimental cerebral vasospasm. *J Pharmacol Exp Ther* **283**: 1110-8 [PMID:9399983]
104. Russell A and Watts S. (2000) Vascular reactivity of isolated thoracic aorta of the C57BL/6J mouse. *J*

- Pharmacol Exp Ther* **294**: 598-604 [PMID:10900237]
105. Russell FD and Davenport AP. (1996) Characterization of the binding of endothelin ET_B selective ligands in human and rat heart. *Br J Pharmacol* **119**: 631-6 [PMID:8904635]
 106. Saeki T, Ihara M, Fukuroda T, Yamagiwa M and Yano M. (1991) [Ala^{1,3,11,15}] endothelin-1 analogs with ET_B agonistic activity. *Biochem Biophys Res Commun* **179**: 286-292 [PMID:1652952]
 107. Saito Y, Mizuno T, Itakura M, Suzuki Y, Ito T, Hagiwara H and Hirose S. (1991) Primary structure of bovine endothelin ET_B receptor and identification of signal peptidase and metal proteinase cleavage sites. *J Biol Chem* **266**: 23433-7 [PMID:1660473]
 108. Sakamoto A, Yanagisawa M, Sakurai T, Takuwa Y, Yanagisawa H and Masaki T. (1991) Cloning and functional expression of human cDNA for the ET_B endothelin receptor. *Biochem Biophys Res Commun* **178**: 656-63 [PMID:1713452]
 109. Sakurai T, Yanagisawa M, Takuwa Y, Miyazaki H, Kimura S, Goto K and Masaki T. (1990) Cloning of a cDNA encoding a non-isopeptide-selective subtype of the endothelin receptor. *Nature* **348**: 732-5 [PMID:2175397]
 110. Schneider MP, Boesen EI and Pollock DM. (2007) Contrasting actions of endothelin ET(A) and ET(B) receptors in cardiovascular disease. *Annu Rev Pharmacol Toxicol* **47**: 731-59 [PMID:17002597]
 111. Shihoya W, Izume T, Inoue A, Yamashita K, Kadji FMN, Hirata K, Aoki J, Nishizawa T and Nureki O. (2018) Crystal structures of human ET_B receptor provide mechanistic insight into receptor activation and partial activation. *Nat Commun* **9**: 4711 [PMID:30413709]
 112. Shihoya W, Nishizawa T, Okuta A, Tani K, Dohmae N, Fujiyoshi Y, Nureki O and Doi T. (2016) Activation mechanism of endothelin ET_B receptor by endothelin-1. *Nature* **537**: 363-368 [PMID:27595334]
 113. Shihoya W, Nishizawa T, Yamashita K, Inoue A, Hirata K, Kadji FMN, Okuta A, Tani K, Aoki J and Fujiyoshi Y *et al.* (2017) X-ray structures of endothelin ET_B receptor bound to clinical antagonist bosentan and its analog. *Nat Struct Mol Biol* **24**: 758-764 [PMID:28805809]
 114. Shyamala V, Moulthrop TH, Stratton Thomas J and Tekamp Olson P. (1994) Two distinct human endothelin B receptors generated by alternative splicing from a single gene. *Cell Mol Biol Res* **40**: 285-296 [PMID:7866430]
 115. Simonson MS. (2001) Cell signalling by endothelin peptides. *Handb Exp Pharmacol* **152**: 115-140
 116. Stein PD, Hunt JT, Floyd DM, Moreland S, Dickinson KE, Mitchell C, Liu EC, Webb ML, Murugesan N and Dickey J *et al.* (1994) The discovery of sulfonamide endothelin antagonists and the development of the orally active ETA antagonist 5-(dimethylamino)-N-(3,4-dimethyl-5-isoxazolyl)-1-naphthalenesulfonamide. *J Med Chem* **37**: 329-31 [PMID:8308857]
 117. Strachan FE, Spratt JC, Wilkinson IB, Johnston NR, Gray GA and Webb DJ. (1999) Systemic blockade of the endothelin-B receptor increases peripheral vascular resistance in healthy men. *Hypertension* **33**: 581-5 [PMID:9931169]
 118. Takai M, Umemura I, Yamasaki K, Watakabe T, Fujitani Y, Oda K, Urade Y, Inui T, Yamamura T and Okada T. (1992) A potent and specific agonist, Suc-[Glu⁹,Ala^{11,15}]-endothelin-1(8-21), IRL 1620, for the ET_B receptor. *Biochem Biophys Res Commun* **184**: 953-9 [PMID:1315540]
 119. Takigawa M, Sakurai T, Kasuya Y, Abe Y, Masaki T and Goto K. (1995) Molecular identification of guanine-nucleotide-binding regulatory proteins which couple to endothelin receptors. *Eur J Biochem* **228**: 102-8 [PMID:7882989]
 120. Tanaka H, Moroi K, Iwai J, Takahashi H, Ohnuma N, Hori S, Takimoto M, Nishiyama M, Masaki T and Yanagisawa M *et al.* (1998) Novel mutations of the endothelin B receptor gene in patients with Hirschsprung's disease and their characterization. *J Biol Chem* **273**: 11378-83 [PMID:9556633]
 121. Tanaka T, Tsukuda E, Nozawa M, Nonaka H, Ohno T, Kase H, Yamada K and Matsuda Y. (1994) RES-701-1, a novel, potent, endothelin type B receptor-selective antagonist of microbial origin. *Mol Pharmacol* **45**: 724-30 [PMID:8183252]
 122. Uhlig S, von Bethmann AN, Featherstone RL and Wendel A. (1995) Pharmacologic characterization of endothelin receptor responses in the isolated perfused rat lung. *Am J Respir Crit Care Med* **152**: 1449-60 [PMID:7582276]
 123. von Geldern TW, Tasker AS, Sorensen BK, Winn M, Szczepankiewicz BG, Dixon DB, Chiou WJ, Wang L, Wessale JL and Adler A *et al.* (1999) Pyrrolidine-3-carboxylic acids as endothelin antagonists. 4. Side chain conformational restriction leads to ET(B) selectivity. *J Med Chem* **42**: 3668-78 [PMID:10479298]
 124. Warner TD, Allcock GH, Mickley EJ, Corder R and Vane JR. (1993) Comparative studies with the

- endothelin receptor antagonists BQ-123 and PD 142893 indicate at least three endothelin receptors. *J Cardiovasc Pharmacol* **22 Suppl 8**: S117-20 [PMID:7509920]
125. Warner TD, de Nucci G and Vane JR. (1989) Rat endothelin is a vasodilator in the isolated perfused mesentery of the rat. *Eur J Pharmacol* **159**: 325-6 [PMID:2646137]
 126. Watakabe T, Urade Y, Takai M, Umemura I and Okada T. (1992) A reversible radioligand specific for the ETB receptor: [125I]Tyr13-Suc-[Glu9,Ala11,15]-endothelin-1(8- 21), [125I]IRL 1620. *Biochem Biophys Res Commun* **185**: 867-73 [PMID:1320877]
 127. Watanabe T, Awane Y, Ikeda S, Fujiwara S, Kubo K, Kikuchi T, Kusumoto K, Wakimasu M and Fujino M. (1995) Pharmacology of a non-selective ETA and ETB receptor antagonist, TAK-044 and the inhibition of myocardial infarct size in rats. *Br J Pharmacol* **114**: 949-54 [PMID:7780649]
 128. Williams Jr DL, Jones KL, Pettibone DJ, Lis EV and Clineschmidt BV. (1991) Sarafotoxin S6c: an agonist which distinguishes between endothelin receptor subtypes. *Biochem Biophys Res Commun* **175**: 556-61 [PMID:1850245]
 129. Williams Jr DL, Murphy KL, Nolan NA, O'Brien JA, Pettibone DJ, Kivlighn SD, Krause SM, Lis Jr EV, Zingaro GJ and Gabel RA *et al.* (1995) Pharmacology of L-754,142, a highly potent, orally active, nonpeptidyl endothelin antagonist. *J Pharmacol Exp Ther* **275**: 1518-26 [PMID:8531124]
 130. Williams RJ. (1988) Self-assembling surfaces. *Nature* **332**: 393 [PMID:3352739]
 131. Winn M, von Geldern TW, Opgenorth TJ, Jae HS, Tasker AS, Boyd SA, Kester JA, Mantei RA, Bal R and Sorensen BK *et al.* (1996) 2,4-Diarylpyrrolidine-3-carboxylic acids—potent ETA selective endothelin receptor antagonists. 1. Discovery of A-127722. *J Med Chem* **39**: 1039-48 [PMID:8676339]
 132. Wu C, Chan MF, Stavros F, Raju B, Okun I, Mong S, Keller KM, Brock T, Kogan TP and Dixon RA. (1997) Discovery of TBC11251, a potent, long acting, orally active endothelin receptor-A selective antagonist. *J Med Chem* **40**: 1690-7 [PMID:9171878]
 133. Wu C, Decker ER, Holland GW, Brown PM, Stavros FD, Brock TA and Dixon RA. (2001) Nonpeptide endothelin antagonists in clinical development. *Drugs Today* **37**: 441-453 [PMID:12750762]
 134. Yamaji T, Fukuhara T and Kinoshita M. (1993) Increased capillary permeability to albumin in diabetic rat myocardium. *Circ Res* **72**: 947-57 [PMID:8477528]
 135. Yanagisawa H, Hammer RE, Richardson JA, Williams SC, Clouthier DE and Yanagisawa M. (1998) Role of Endothelin-1/Endothelin-A receptor-mediated signaling pathway in the aortic arch patterning in mice. *J Clin Invest* **102**: 22-33 [PMID:9649553]
 136. Zhang YF, Jeffery S, Burchill SA, Berry PA, Kaski JC and Carter ND. (1998) Truncated human endothelin receptor A produced by alternative splicing and its expression in melanoma. *Br J Cancer* **78**: 1141-6 [PMID:9820169]