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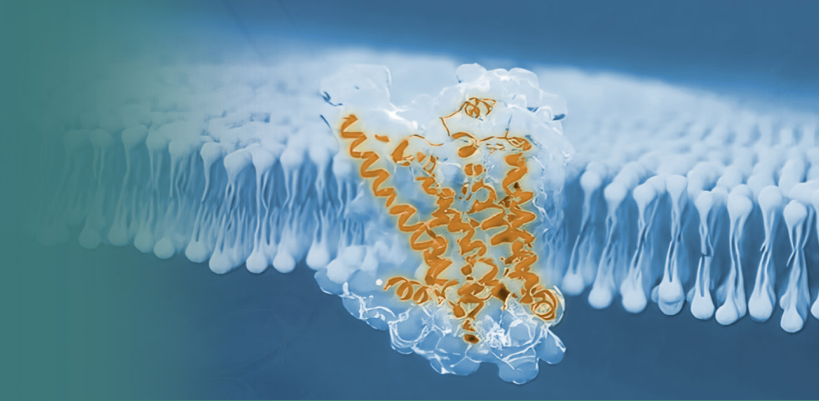

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GPCR Target	Reference
Multiple GPCRs	
Multiple	1. Tena-Campos M, Ramon E, Rivera D, Borroto-Escuela DO, Romero-Fernandez W, Fuxe K, Garriga P. (2014). G-protein-coupled receptors oligomerization: emerging signaling units and new opportunities for drug design. *Curr Protein Pept Sci.* 15(7):648-58 http://www.ncbi.nlm.nih.gov/pubmed/25175459 2. Bohn LM, McDonald PH. (2010). Seeking Ligand Bias: Assessing GPCR Coupling to Beta-Arrestins for Drug Discovery. *Drug Discov Today Technol.* 2010 Spring;7(1):e37-e42. http://www.ncbi.nlm.nih.gov/pubmed/21218149 3. Verkaar F, van Rosmalen JW, Blomenröhr M, van Koppen CJ, Blankesteijn WM, Smits JF and Zaman GJ.(2008). G protein-independent cell-based assays for drug discovery on seven-transmembrane receptors. *Biotechnol Annu Rev* 14:253-74. http://www.ncbi.nlm.nih.gov/pubmed/18606367
Multiple (ProLink Vector, Parental)	4. Yin H, Chu A, Li W, Wang B, Shelton F, Otero F, Nguyen DG, Caldwell JS and Chen YA. (2009). Lipid G protein-coupled receptor ligand identification using β-arrestin PathHunter assay. *J Biol Chem* 284(18):12328-38. http://www.ncbi.nlm.nih.gov/pubmed/19286662
S1P1, GCGR, CHRM5, HRH2, OPRD1, ADRB2	5. Bassoni DL, Raab WJ, Achacoso PL, Loh CY and Wehrman TS. (2012). Measurements of β-arrestin recruitment to activated seven transmembrane receptors using enzyme complementation. *Methods Mol Biol* 897:181-203. http://www.ncbi.nlm.nih.gov/pubmed/22674166
5-Hydroxytryptamine (Serotonin)	
5HT1A	6. Stroth N, Nisob M, Colabufob NA, Perroneb R, Svenningssona P, Lacivitab E, Leopoldo M, (2015). Arylpiperazine Agonists of the Serotonin 5-HT1A Receptor Preferentially Activate cAMP Signaling versus Recruitment of β-Arrestin-2. *Bioorganic & Medicinal Chemistry.* 762:221-228. http://www.ncbi.nlm.nih.gov/pubmed/26081758
5HT2A	7. Schmid CL, Streicher JM, Meltzer HY, Bohn LM. (2014). Clozapine acts as an agonist at serotonin 2A receptors to counter MK-801-induced behaviors through a βarrestin2-independent activation of Akt. *Neuropsychopharmacology.* 39(8):1902-13. http://www.ncbi.nlm.nih.gov/pubmed/24531562 8. Blough BE, Landavazo A, Decker AM, Partilla JS, Baumann MH, Rothman RB. (2014). Interaction of psychoactive tryptamines with biogenic amine transporters and serotonin receptor subtypes. *Psychopharmacology (Berl).* 231(21):4135-44. http://www.ncbi.nlm.nih.gov/pubmed/24800892
5HT2A, 5HT2C	9. Clarke WP, Chavera TA, Silva M, Sullivan LC, Berg KA. (2013). Signalling profile differences: paliperidone versus risperidone. *Br J Pharmacol* 170(3):532-45. http://www.ncbi.nlm.nih.gov/pubmed/23826915
5HT2B	10. Unett DJ, Gatlin J, Anthony TL, Buzard DJ, Chang S, Chen C, Chen X, Dang HTM, Frazer J, Le MK, Sadeque AJM, Xing C and Gaidarov I. (2013). Kinetics of 5-HT2B receptor signaling: profound agonist-dependent effects on signaling onset and duration. *J Pharmacol Exp Ther* 347(3):645-59. http://www.ncbi.nlm.nih.gov/pubmed/24049061

GPCR Target	Reference
Acetylcholine Receptors (Muscarinic)	
CHRM1	11. Digby GJ, Noetzel MJ, Bubser M, Utley TJ, Walker AG, Byun NE, Lebois EP, Xiang Z, Sheffler DJ, Cho HP, *et al.* (2012). Novel allosteric agonists of M1 muscarinic acetylcholine receptors induce brain region-specific responses that correspond with behavioral effects in animal models. *J Neurosci* 32(25):8532-44. http://www.ncbi.nlm.nih.gov/pubmed/22723693 12. Watt ML, Schober DA, Hitchcock S, Liu B, Chesterfield AK, McKinzie D and Felder CC. (2011). Pharmacological characterization of LY593093, an M1 muscarinic acetylcholine receptor-selective partial orthosteric agonist. *J Pharmacol Exp Ther* 338(2):622-632. http://www.ncbi.nlm.nih.gov/pubmed/21558436 13. Ma L, Seager MA, Wittmann M, Jacobson M, Bickel D, Burno M, Jones K, Graufelds VK, Xu G, Pearson M *et al.* (2009). Selective activation of the M1 muscarinic acetylcholine receptor achieved by allosteric potentiation. *Proc Natl Acad Sci USA* 106(37):15950-5. http://www.ncbi.nlm.nih.gov/pubmed/19717450
Acetylcholine Receptors (Muscarinic) ...continued	
CHRM3	14. Li H, Yu X, Liles C, Khan M, Vanderlinde-Wood M, Galloway A, Zillner C, Benbrook A, Reim S, Collier D, Hill MA, Raj SR, Okamoto LE, Cunningham MW, Aston CE, Kem DC. (2014). Autoimmune basis for postural tachycardia syndrome. *J Am Heart Assoc.* 26;3(1):e000755. http://www.ncbi.nlm.nih.gov/pubmed/24572257 15. Li H, Kem DC, Reim S, Khan M, Vanderlinde-Wood M, Zillner C, Collier D, Liles C, Hill MA, Cunningham MW, Aston CE and Yu X. (2012). Agonistic autoantibodies as vasodilators in orthostatic hypotension: a new mechanism. *Hypertension* 59(2):402-8. http://www.ncbi.nlm.nih.gov/pubmed/22215709 16. Poulin B, Butcher A, McWilliams P, Bourgognon JM, Pawlak R, Kong KC, Bottrill A, Mistry S, Wess J, Rosethorne EM, Charlton SJ and Tobin AB. (2010). The M3-muscarinic receptor regulates learning and memory in a receptor phosphorylation/arrestin-dependent manner. *Proc Natl Acad Sci U S A* 107(20):9440-5. http://www.ncbi.nlm.nih.gov/pubmed/20439723 17. Kong KC, Butcher AJ, McWilliams P, Jones D, Wess J, Hamdan FF, Werry T, Rosethorne EM, Charlton SJ, Munson SE, Cragg HA, Smart AD and Tobin AB. (2010). M3-muscarinic receptor promotes insulin release via receptor phosphorylation/arrestin-dependent activation of protein kinase D1. *Proc Natl Acad Sci USA* 107(49):21181-6. http://www.ncbi.nlm.nih.gov/pubmed/21078968
Adenosine Receptors	
ADORA1, 2, 3	18. Alnouri MW, Jepards S, Casari A, Schiedel AC, Hinz S, Müller CE. (2015). Selectivity is species-dependent: Characterization of standard agonists and antagonists at human, rat, and mouse adenosine receptors. *Purinergic Signal. [Epub ahead of print]* http://www.ncbi.nlm.nih.gov/pubmed/26126429
ADORA2B	19. Gao ZG, Balasubramanian R, Kiselev E, Wei Q, Jacobson KA. (2014). Probing biased/partial agonism at the G protein-coupled A(2B) adenosine receptor. *Biochem Pharmacol.* 90(3):297-306. http://www.ncbi.nlm.nih.gov/pubmed/24853985
ADORA3	20. Verzijl D and Ijzerman AP. (2011). Functional selectivity of adenosine receptor ligands. *Purinergic Signal* 7(2):171-92. http://www.ncbi.nlm.nih.gov/pubmed/21544511 21. Gao ZG, Verzijl D, Zweemer A, Ye K, Goblyos A, Ijzerman AP and Jacobson KA. (2011). Functionally biased modulation of A(3) adenosine receptor agonist efficacy and potency by imidazoquinolinamine allosteric enhancers. *Biochem Pharmacol* 82(6):658-68. http://www.ncbi.nlm.nih.gov/pubmed/21718691ov/pubmed/21544511 22. Gao ZG and Jacobson KA. (2008). Translocation of arrestin induced by human A(3) adenosine receptor ligands in an engineered cell line: comparison with G protein-dependent pathways. *Pharmacol Res* 57(4):303-11. http://www.ncbi.nlm.nih.gov/pubmed/18424164
Adrenoreceptors	
ADRA2C	23. Kurko D, Kapui Z, Nagy J, Lendvai B, Kolok S. (2014). Analysis of functional selectivity through G protein-dependent and -independent signaling pathways at the adrenergic α2C receptor. *Brain Res Bull.* 107: 89-10. http://www.ncbi.nlm.nih.gov/pubmed/25080296
ADRB1	24. Rastogi T, Leder C, Kümmerer K. (2015). Re-Designing of Existing Pharmaceuticals for Environmental Biodegradability: A tiered approach with β-Blocker Propranolol as an example. *Environ Sci Technol. [Epub ahead of print]* http://www.ncbi.nlm.nih.gov/pubmed/26291878
ADRB1 (Internalization)	25. Hutchings CJ, Cseke G, Osborne G, Woolard J, Zhukov A, Koglin M, Jazayeri A, Pandya-Pathak J, Langmead CJ, Hill SJ, Weir M, Marshall FH. (2014). Monoclonal anti-β1-adrenergic receptor antibodies activate G protein signaling in the absence of β-arrestin recruitment. *mAbs.* 6(1):246-61. http://www.ncbi.nlm.nih.gov/pubmed/24253107

GPCR Target	Reference
Adrenoreceptors ...continued	
ADRB2	26. Kopra K, Kainulainen M, Mikkonen P, Rozwandowicz-Jansen A, Hänninen P and Härmä H. (2013). Multiparametric homogeneous method for identification of ligand binding to G protein-coupled receptors: receptor-ligand binding and β-arrestin assay. *Analytical Chemistry* 85(4):2276-228. http://www.ncbi.nlm.nih.gov/pubmed/23330639 27. Weiss DR, Ahn S, Sassano MF, Kleist A, Zhu X, Strachan R, Roth BL, Lefkowitz RJ and Shoichet BK. (2013). Conformation guides molecular efficacy in docking screens of activated β-2 adrenergic G-protein coupled receptor. *ACS Chem Biol* 8(5):1018-26. http://www.ncbi.nlm.nih.gov/pubmed/23485065
ADRB2 (internalization)	28. Rosethorne EM, Bradley ME, Kent TC, Charlton SJ. (2015). Functional desensitization of the β2 adrenoceptor is not dependent on agonist efficacy. *Pharmacol Res Perspect.* 3(1):e00101. http://www.ncbi.nlm.nih.gov/pubmed/25692019
Angiotensin Receptors	
AGTR1	29. Dabul S, Bathgate-Siryk A, Valero TR, Jafferjee M, Sturchler E, McDonald P, Koch WJ, Lymperopoulos A. (2015). Suppression of adrenal βarrestin1-dependent aldosterone production by ARBs: head-to-head comparison. *Sci Reports* 5:8116. http://www.ncbi.nlm.nih.gov/pubmed/25631300 30. Li H, Kem DC, Zhang L, Huang B1, Liles C, Benbrook A, Gali H, Veitla V, Scherlag BJ, Cunningham MW, Yu X. (2015). Novel retro-inverso Peptide inhibitor reverses Angiotensin receptor autoantibody-induced hypertension in the rabbit. *Hypertension.* 65(4):793-9. http://www.ncbi.nlm.nih.gov/pubmed/25691619 31. Kim KS, Abraham D, Williams B, Violin JD, Mao L and Rockman HA. (2012). β-Arrestin-biased AT1R stimulation promotes cell survival during acute cardiac injury. Am *J Physiol Heart Circ Physiol* 303:H1001-10. http://www.ncbi.nlm.nih.gov/pubmed/22886417 32. Violin JD, DeWire SM, Yamashita D, Rominger DH, Nguyen L, Schiller K, Whalen EJ, Gowen M and Lark MW. (2010). Selectively engaging β-arrestins at the angiotensin II type 1 receptor reduces blood pressure and increases cardiac performance. *J Pharmacol Exp Ther* 335(3):572-579. http://www.ncbi.nlm.nih.gov/pubmed/20801892
Apelin Receptors	
AGTRL1	33. Siddiquee K, Hampton J, McAnally D, May L and Smith L. (2013). The apelin receptor inhibits the angiotensin II type 1 receptor via allosteric trans-inhibition. *Br J Pharmacol* 168(5):1104-17. http://www.ncbi.nlm.nih.gov/pubmed/22935142
AGTRL1 (Internalization)	34. Brame AL, Maguire JJ, Yang P, Dyson A, Torella R, Cheriyan J, Singer M, Glen RC, Wilkinson IB, Davenport AP (2015). Design, characterization, and first-in-human study of the vascular actions of a novel biased apelin receptor agonist. *Hypertension.* 65(4):834-40. http://www.ncbi.nlm.nih.gov/pubmed/25712721
Calcitonin Receptors	
CALCRL-RAMP1	35. Hay DL, Harris PWR, Kowalczyk R, Brimble MA, Rathbone DL, Barwell J, Conner AC and Poyner DR. (2014). Structure–activity relationships of the N-terminus of calcitonin gene-related peptide: key roles of alanine-5 and threonine-6 in receptor activation. *Br J Pharmacol* 171(2):415-26. http://www.ncbi.nlm.nih.gov/pubmed/24125506 36. Andreassen KV, Hjuler ST, Furness SG, Sexton PM, Christopoulos A, Nosjean O, Karsdal MA, Henriksen K. (2014) Prolonged calcitonin receptor signaling by salmon, but not human calcitonin, reveals ligand bias. *Plos One.* 9(3):e92042. http://www.ncbi.nlm.nih.gov/pubmed/24643196 37. Andreassen KV, Feigh M, Hjuler ST, Gydesen S, Henriksen JE, Beck-Nielsen H, Christiansen C, Karsdal MA, Henriksen K. (2014) A novel oral dual amylin and calcitonin receptor agonist (KBP-042) exerts antiobesity and antidiabetic effects in rats. *Am J Physiol Endocrinol Metab.* 307(1):E24-33. http://www.ncbi.nlm.nih.gov/pubmed/24801386
Cannabinoid Receptors	
CNR1	38. Priestley RS, Nickolls SA, Alexander SP, Kendall DA. (2014). A potential role for cannabinoid receptors in the therapeutic action of fenofibrate. *FASEB J.* 29(4):1446-55. http://www.ncbi.nlm.nih.gov/pubmed/25550466 39. Baillie GL, Horswill J, Anavi-Goffer S, Reggio PH, Abood ME, Bolognini D, McAllister S, Strange PG, Stephens GJ, Pertwee RG, *et al.* (2013). CB1 Receptor Allosteric Modulators Display both Agonist and Signaling Pathway Specificity. *Mol Pharmacol* 83(2):322-38. http://www.ncbi.nlm.nih.gov/pubmed/23160940 40. van der Lee MM, Blomenröhr M, van der Doelen AA, Wat JW, Smits N, Hanson BJ, van Koppen CJ and Zaman GJ. (2009). Pharmacological characterization of receptor redistribution and β-arrestin recruitment assays for the cannabinoid receptor 1. *J Biomol Screen* 14(7):811-23. http://www.ncbi.nlm.nih.gov/pubmed/19520790

GPCR Target	Reference
Cannabinoid Receptors ...continued	
CNR1, CNR2	41. Altomonte S, Baillie GL, Ross RA, Riley J, Zanda M (2014).The pentafluorosulfanyl group in cannabinoid receptor ligands: synthesis and comparison with trifluoromethyl and tert-butyl analogues. *RSC Advances* 39(4)20164-76. http://pubs.rsc.org/en/content/articlelanding/2014/ra/c4ra01212g 42. Dossou KS, Devkota KP, Kavanagh PV, Beutler JA, Egan JM and Moaddel R. (2013). Development and preliminary validation of a plate-based CB1/CB2 receptor functional assay. *Anal Biochem* 437(2):138-43. http://www.ncbi.nlm.nih.gov/pubmed/23481912 43. Yang R, Fredman G, Krishnamoorthy S, Agrawal N, Irimia D, Piomelli D and Serhan CN. (2011). Decoding functional metabolomics with docosahexaenoyl ethanolamide (DHEA) identifies novel bioactive signals. *J Biol Chem* 286(36):31532-41. http://pubs.rsc.org/en/content/articlelanding/2014/ra/c4ra01212g
CNR2	44. Mukhopadhyay P, Baggelaar M, Erdelyi K, Cao Z, Cinar R, Fezza F, Ignatowska-Jankowska B, Wilkerson J, van Gils N, Hansen T, Ruben M, Soethoudt M, Heitman L, Kunos G, Maccarrone M, Lichtman A, Pacher P, van der Stelt M. (2015). The novel, orally available and peripherally restricted selective cannabinoid CB2 -receptor agonist LEI-101 prevents cisplatin-induced nephrotoxicity. *Br J Pharmacol. [Epub ahead of print]* http://www.ncbi.nlm.nih.gov/pubmed/26398481 45. Chicca A, Gachet MS, Petrucci V, Schuehly W, Charles RP, Gertsch J. (2015). 4'-O-methylhonokiol increases levels of 2-arachidonoyl glycerol in mouse brain via selective inhibition of its COX-2-mediated oxygenation. *J Neuroinflammation* 12(1):89. http://www.ncbi.nlm.nih.gov/pubmed/25962384 46. McGuinness D, Malikzay A, Visconti R, Lin K, Bayne M, Monsma F and Lunn CA. (2009). Characterizing cannabinoid CB2 receptor ligands using DiscoveRx PathHunter β-arrestin assay. *J Biomol Screen* 14(1):49-58. http://www.ncbi.nlm.nih.gov/pubmed/19171920
Chemerin Receptors	
CMKLR1	47. Graham KL, Zhang JV, Lewén S, Burke TM, Dang T, Zoudilova M, Sobel RA, Butcher EC, Zabel BA. (2014). A novel CMKLR1 small molecule antagonist suppresses CNS autoimmune inflammatory disease. *PLoS One.* 9(12):e112925. http://www.ncbi.nlm.nih.gov/pubmed/25437209
Chemokine Receptors	
CCR1 (Internalization)	48. Gilchrist A, Gauntner TD, Fazzini A, Alley KM, Pyen DS, Ahn J, Ha SJ, Willett A, Sansom SE, Yarfi JL, Bachovchin KA, Mazzoni MR, Merritt JR. (2014). Identifying bias in CCR1 antagonists using radiolabelled binding, receptor internalization, β-arrestin translocation and chemotaxis assays. *Br J Pharmacol.* 171(22):5127-38. http://www.ncbi.nlm.nih.gov/pubmed/24990525
CCR1, CCR5	49. Rummel PC, Thiele S, Hansen LS, Petersen TP, Sparre-Ulrich AH, Ulven T and Rosenkilde MM. (2013). Extracellular disulfide bridges serve different purposes in two homologous chemokine receptors, CCR1 and CCR5. *Mol Pharm* 84(3):335-45 http://www.ncbi.nlm.nih.gov/pubmed/23765404
CCR4	50. Santulli-Marotto S, Fisher J, Petley T, Boakye K, Panavas T, Luongo J, Kavalkovich K, Rycyzyn M, Wu B, Gutshall L, Coelho A, Hogaboam CM and Ryan, M. (2013). Surrogate antibodies that specifically bind and neutralize CCL17 but not CCL22. *Monoclon Antib Immunodiagn Immunother* 32(3):162-71. http://www.ncbi.nlm.nih.gov/pubmed/23750473 51. Santulli-Marotto S, Boakye K, Lacy E, Wu S, Luongo J, Kavalkovich K, Coelh A, Hogaboam CM and Ryan M. (2013). Engagement of two distinct binding domains on CCL17 Is required for signaling through CCR4 and establishment of localized inflammatory conditions in the lung. *PLoS ONE* 8(12): e81465. http://www.ncbi.nlm.nih.gov/pubmed/24339934
CCR5	52. Steen A, Thiele S, Guo D, Hansen LS, Frimurer TM and Rosenkilde MM. (2013). Biased and constitutive signaling in the CC-chemokine receptor CCR5 by manipulating the interface between transmembrane helices 6 and 7. *J Biol Chem* 288(18):12511-21. http://www.ncbi.nlm.nih.gov/pubmed/23493400 53. Steen A, Sparre-Ulrich AH, Thiele S, Guo D, Frimurer TM, Rosenkilde MM. (2013). Gating Function of Isoleucine-116 in TM3 (position III:16/3.40) for the activity state of the CC-chemokine receptor 5 (CCR5). *Br J Pharmacol* 171(6):1566-79. http://www.ncbi.nlm.nih.gov/pubmed/24328926 54. White GE, McNeill E, Christou I, Channon KM and Greaves DR. (2011). Site-directed mutagenesis of the CC chemokine binding protein 35K-Fc reveals residues essential for activity and mutations that increase the potency of CC chemokine blockade. *Mol Pharmacol* 80(2):328-36. http://www.ncbi.nlm.nih.gov/pubmed/21586597
CCR9	55. Lee S., Eileen L. Heinrich EL, Li L, Lu J, Choi AH, Levy RA, Wagner JE, Yip MLR, Vaidehi N, Kim J,(2013). CCR9-mediated signaling through β-catenin and identification of a novel CCR9 antagonist. *Mo Oncology [Epub ahead of print]* http://www.ncbi.nlm.nih.gov/pubmed/26003048

GPCR Target	Reference
Chemokine Receptors	
CCR7, CCR9, PTHR1	56. Watts AO, Verkaar F, van der Lee MM, Timmerman CA, Kuijer M, van Offenbeek J, van Lith LH, Smit MJ, Leurs R, Zaman GJ and Vischer HF. (2013). β-Arrestin recruitment and G protein signaling by the atypical human chemokine decoy receptor CCX-CKR. *J Biol Chem* 288(10):7169-81. http://www.ncbi.nlm.nih.gov/pubmed/23341447
Chemokines (multiple)	57. Verkaar F, van Offenbeek J, van der Lee MM, van Lith LH, Watts AO, Rops AL, Aguilar DC, Ziarek JJ, van der Vlag J, Handel TM, Volkman BF, Proudfoot AE, Vischer HF, Zaman GJ, Smit MJ. (2014). Chemokine cooperativity is caused by competitive glycosaminoglycan binding. *J Immunol* 192(8):3908-14. http://www.ncbi.nlm.nih.gov/pubmed/24639348 58. Garin A, Johnson Z, Hermant A, Beltran F, Ratinaud Y, Michel A, Krohn S, Gaudet M, Carboni S, Ji H, Missotten M, Leger O, Power C and Proudfoot A. (2013). Chemokine receptor antagonist development. *Methods Mol Biol* 1013:67-92. http://www.ncbi.nlm.nih.gov/pubmed/23625494 59. Rajagopal S, Bassoni DL, Campbell JJ, Gerard NP, Gerard C and Wehrman TS. (2013). Biased agonism as a mechanism for differential signaling by chemokine receptors. *J Biol Chem* 288(49):35039-48. http://www.ncbi.nlm.nih.gov/pubmed/24145037
CXCR1, CXCR2	60. Maedaa DY, Pecka AM, Schulera AD, Quinnb MT, Kirpotinab LN, Wicombc WN, Autend RL, Gundlae R, Zebalaa JA (2015). Boronic acid-containing CXCR1/2 antagonists: Optimization of metabolic stability, in vivo evaluation, and a proposed receptor binding model. *Bioorg & Med Chem Let.* 25(11):2280-4. http://www.ncbi.nlm.nih.gov/pubmed/25933594
CXCR2	61. Heo J, Dogra P, Masi TJ, Pitt EA, de Kruijf P, Smit MJ, Sparer TE. (2015). Novel Human Cytomegalovirus Viral Chemokines, vCXCL-1s, Display Functional Selectivity for Neutrophil Signaling and Function. *J Immunol.* 195(1):227-36. http://www.ncbi.nlm.nih.gov/pubmed/25987741 62. Kashima K, Watanabe M, Sato Y, Hata J, Ishii N, Aoki Y. (2014).Inhibition of metastasis of rhabdomyosarcoma by a novel neutralizing antibody to CXC chemokine receptor-4. *Cancer Sci* 105(10):1343-50. http://www.ncbi.nlm.nih.gov/pubmed/25154453 63. de Kruijf P, van Heteren J, Lim HD, Conti PG, van der Lee MM, Bosch L, Ho KK, Auld D, Ohlmeyer M, Smit MJ, *et al.* (2009). Nonpeptidergic allosteric antagonists differentially bind to the CXCR2 chemokine receptor. *J Pharmacol Exp Ther* 329(2):783-90. http://www.ncbi.nlm.nih.gov/pubmed/19190236
CXCR3	64. Bernat V, Brox R, Heinrich MR, Auberson YP, Tschammer N. (2015) Ligand-Biased and Probe-Dependent Modulation of Chemokine Receptor CXCR3 Signaling by Negative Allosteric Modulators. *ChemMedChem.* 10(3):566-74. http://www.ncbi.nlm.nih.gov/pubmed/25233453 65. Bernat V, Admas TH, Brox R, Heinemann FW, Tschammer N. (2014). Boronic Acids as Probes for Investigation of Allosteric Modulation of the Chemokine Receptor CXCR3. *ACS Chem Biol.* 9(11):2664-77. http://www.ncbi.nlm.nih.gov/pubmed/25233453 66. Scholten DJ, Canals M, Wijtmans M, de Munnik S, Nguyen P, Verzijl D, de Esch IJ, Vischer HF, Smit MJ and Leurs R. (2012). Pharmacological characterization of a small-molecule agonist for the chemokine receptor CXCR3. *Br J Pharmacol* 166(3):898-911. http://www.ncbi.nlm.nih.gov/pubmed/21883151
CXCR4	67. Castaldo C, Benicchi T, Otrocka M, Mori E, Pilli E, Ferruzzi P, Valensin S, Diamanti D, Fecke W, Varrone M, Porcari V. (2014) CXCR4 Antagonists: A Screening Strategy for Identification of Functionally Selective Ligands. *J Biomol Screen.* 19(6):859-869. http://www.ncbi.nlm.nih.gov/pubmed/24632660
CXCR4, CXCR7	68. Segers VF, Revin V, Wu W, Qiu H, Yan Z, Lee RT and Sandrasagra A.(2011). Protease-resistant stromal cell-derived factor-1 for the treatment of experimental peripheral artery disease. *Circulation* 123(12):1306-15. http://www.ncbi.nlm.nih.gov/pubmed/21403096
CXCR7	69. Zabel BA, Wang Y, Lewen S, Berahovich RD, Penfold ME, Zhang P, Powers J, Summers BC, Miao Z, Zhao B, Jalili A, Janowska-Wieczorek A, Jaen JC and Schall TJ. (2009). Elucidation of CXCR7-mediated signaling events and inhibition of CXCR4-mediated tumor cell transendothelial migration by CXCR7 ligands. *J Immunol* 183(5):3204-11. http://www.ncbi.nlm.nih.gov/pubmed/19641136
CXCR7 (Internalization)	70. Liu S, Alomran R, Chernikova SB, Lartey F, Stafford J, Jang T, Merchant M, Zboralski D, Zollner S, Kruschinski A, Klussmann S, Recht L, and Brown MJ. (2014). Blockade of SDF-1 after irradiation inhibits tumor recurrences of autochthonous brain tumors in rats. *Neuro-Oncol* 16(1): 21–8. http://www.ncbi.nlm.nih.gov/pubmed/24335554

GPCR Target	Reference
Class A Orphan Receptors	
Orphans	71. Southern C, Cook JM, Neetoo-Isseljee Z, Taylor DL, Kettleborough CA, Merritt A, Bassoni DL, Raab WJ, Quinn E, Wehrman TS, Davenport AP, Brown AJ, Green A, Wigglesworth MJ and Rees S. (2013). Screening β-arrestin recruitment for the identification of natural ligands for orphan G-protein-coupled receptors. *J Biomol Screen* 18(5):599-609. http://www.ncbi.nlm.nih.gov/pubmed/23396314
GPR3	72. Ye C, Zhang Z, Wang Z, Hua Q, Zhang R, Xie X.. (2014).Identification of a novel small-molecule agonist for human G protein-coupled receptor 3. *J Pharmacol Exp Ther.* 349(3):437-43.
GPR18	73. Chiang N, Dalli J, Colas RA, Serhan CN. (2015) Identification of resolvin D2 receptor mediating resolution of infections and organ protection. *J Exp Med. [Epub ahead of print]* http://www.ncbi.nlm.nih.gov/pubmed/24633425
GPR18	74. Console-Bram L, Brailoiu E, Brailoiu GC, Sharir H, Abood ME. (2014). Activation of GPR18 by cannabinoid compounds: a tale of biased agonism. *Br J Pharmacol.* 171(16):3908-17. http://www.ncbi.nlm.nih.gov/pubmed/24762058
GPR18, GPR55	75. Rempel V, Atzler K, Behrenswerth A, Karcz T, Schoeder C, Hinz S, Kaleta M, Thimm D, Kiec-Kononowiczb K, Müller CE (2014). Bicyclic imidazole-4-one derivatives: a new class of antagonists for the orphan G protein-coupled receptors GPR18 and GPR55. *MedChemComm* 5, 632-49. http://pubs.rsc.org/en/content/articlelanding/2014/md/c3md00394a 76. Fuchs A, Rempel V and Muller CE. (2013). The natural product magnolol as a lead structure for the development of potent cannabinoid receptor agonists. *PLoS One* 8(10): e77739. http://www.ncbi.nlm.nih.gov/pubmed/24204944
GPR32	77. Krishnamoorthy S, Recchiuti A, Chiang N, Fredman G and Serhan CN. (2012). Resolvin D1 receptor stereoselectivity and regulation of inflammation and proresolving microRNAs. *Am J Pathol* 180(5):2018-27. http://www.ncbi.nlm.nih.gov/pubmed/22449948 78. Krishnamoorthy S, Recchiuti A, Chiang N, Yacoubian S, Lee CH, Yang R, Petasis NA and Serhan CN. (2010). Resolvin D1 binds human phagocytes with evidence for proresolving receptors. *Proc Natl Acad Sci USA* 107(4):1660-5. http://www.ncbi.nlm.nih.gov/pubmed/20080636
GPR35	79. MacKenzie AE, Caltabiano G, Kent TC, Jenkins L, McCallum JE, Hudson BD, Nicklin SA, Fawcett L, Lane R, Charlton SJ and Milligan G. (2014). The antiallergic mast cell stabilizers lodoxamide and bufrolin as the first high and equipotent agonists of human and rat GPR35. *Mol Pharmacol* 85(1):91-104. http://www.ncbi.nlm.nih.gov/pubmed/24113750 80. Neetoo-Isseljee Z, MacKenzie AE, Southern C, Jerman J, McIver EC, Harries N, Taylor DL and Milligan G. (2013). High-throughput identification and characterization of novel, species-selective GPR35 agonists. *J Pharmacol* 344(3): 568-78. http://www.ncbi.nlm.nih.gov/pubmed/23262279 81. Jenkins L, Alvarez-Curto E, Campbell K, de Munnik S, Canals M, Schlyer S and Milligan G. (2011). Agonist activation of the G protein-coupled receptor GPR35 involves transmembrane domain III and is transduced via Gα(1)(3) and β-arrestin-2. *Br J Pharmacol* 162(3):733-48. http://www.ncbi.nlm.nih.gov/pubmed/20958291
GPR35, GPR55	82. Shore DM, Reggio PH. (2015). The Therapeutic Potential of Orphan GPCRs, GPR35 and GPR55. *Front Pharmacol* (review article) 6:69. http://www.ncbi.nlm.nih.gov/pubmed/25926795 83. Funke M, Thimm D, Schiedel AC and Müller CE. (2013). 8-benzamidochromen-4-one-2-carboxylic acids - potent and selective agonists for the orphan G protein-coupled receptor GPR35. *J Med Chem* 56(12):5182-97. http://www.ncbi.nlm.nih.gov/pubmed/25926795
GPR55	84. Kargl J, Brown AJ, Andersen L, Dorn G, Schicho R, Waldhoer M and Heinemann A. (2013). A selective antagonist reveals a potential role of G protein-coupled receptor 55 in platelet and endothelial cell function. *J Pharmacol Exp Ther* 346(1):54-66. http://www.ncbi.nlm.nih.gov/pubmed/23639801 85. Rempel V, Volz N, Gläser F, Nieger M, Bräse S and Müller CE. (2013). Antagonists for the orphan G-protein-coupled receptor GPR55 based on a coumarin scaffold. *J Med Chem* 56(11):4798-810. http://www.ncbi.nlm.nih.gov/pubmed/23679955 86. Yamashita A, Oka S, Tanikawa T, Hayashi Y, Nemoto-Sasaki Y, Sugiura T. (2013). The actions and metabolism of lysophosphatidylinositol, an endogenous agonist for GPR55. *Prostaglandins Other Lipid Mediat* 107:103-16. http://www.ncbi.nlm.nih.gov/pubmed/23714700
GPR101	87. Cho-Clark M, Larco DO, Semsarzadeh NN, Vasta F, Mani SK, Wu TJ. (2014). GnRH-(1-5) Transactivates EGFR in Ishikawa Human Endometrial Cells via an Orphan G Protein-Coupled Receptor. *Mol Endocrinol* 28(1):80-98. http://www.ncbi.nlm.nih.gov/pubmed/24264576
GPR132	88. Shehata MA, Christensen HB, Isberg V, Pedersen D, Bender A, Bräuner-Osborne H and Gloriam D. (2015) Identification of the first surrogate agonists for the G protein-coupled receptor GPR132. *RSC Advances. [Epub ahead of print]* http://pubs.rsc.org/en/content/articlelanding/2015/ra/c5ra04804d#!divAbstract

GPCR Target	Reference
Class A Orphan Receptors ...continued	
Orphan Panel, GPR173	89. Larco DO, Cho-Clark M, Mani SK and Wu TJ. (2013). The metabolite GnRH-(1-5) inhibits the migration of immortalized GnRH neurons. *Endocrinology* 154(2):783-95. http://www.ncbi.nlm.nih.gov/pubmed/23321696
GPR183 (EBI2)	90. Gessier F, Preuss I, Yin H, Rosenkilde MM, Laurent S, Endres R, Chen YA, Marsilje TH, Seuwen K, Nguyen DG, Sailer AW (2014). Identification and characterization of small molecule modulators of the Epstein-Barr virus-induced gene 2 (EBI2) receptor. *J Med Chem.* 57(8):3358-68. http://www.ncbi.nlm.nih.gov/pubmed/24678947 91. Benned-Jensen T, Norn C, Laurent S, Madsen CM, Larsen HM, Arfelt KN, Wolf RM, Frimurer T, Sailer AW, Rosenkilde MM. (2012). Molecular characterization of oxysterol binding to the Epstein-Barr virus-induced gene 2 (GPR183). *J Biol Chem* 287(42):35470-83. http://www.ncbi.nlm.nih.gov/pubmed/22875855 92. Benned-Jensen T, Madsen CM, Arfelt KN, Smethurts C, Blanchard A, Jepras R, Rosenkilde MM. (2013). Small molecule antagonism of oxysterol-induced Epstein-Barr virus induced gene 2 (EBI2) activation. *FEBS Open Bio.* 19;3:156-60. http://www.ncbi.nlm.nih.gov/pubmed/23772388
Complement Peptide (Anaphylotoxin)	
C5L2	93. Van Lith LH, Oosterom J, Van Elsas A and Zaman GJ. (2009). C5a-stimulated recruitment of β-Arrestin2 to the nonsignaling 7-transmembrane decoy receptor C5L2. *J Biomol Screen* 14(9):1067-75. http://www.ncbi.nlm.nih.gov/pubmed/19641221
Dopamine Receptors	
DRD1 (Internalization)	94. Conroy JL, Free RB, Sibley DR. (2015) Identification of G Protein-Biased Agonists That Fail To Recruit β–Arrestin or Promote Internalization of the D1 Dopamine Receptor. *ACS Chem Neurosci.* 6(4):681-92. http://www.ncbi.nlm.nih.gov/pubmed/25660762 95. Lee SM, Kant A, Blake D, Murthy V, Boyd K, Wyrick SJ, Mailman RB. (2014) SKF-83959 is not a highly-biased functionally selective D1 dopamine receptor ligand with activity at phospholipase C. *Neuropharmacology.* 86:145-54 http://www.ncbi.nlm.nih.gov/pubmed/24929112
DRD2	96. Kozuka C, Sunagawa S, Ueda R, Higa M, Ohshiro Y, Tanaka H, Shimizu-Okabe C, Takayama C, Matsushita M, Tsutsui M, Ishiuchi S, Nakata M, Yada T, Miyazaki JI, Oyadomari S, Shimabukuro M, Masuzaki H. (2015) A novel insulinotropic mechanism of whole grain-derived γ-oryzanol via the suppression of local dopamine D2 receptor signaling in mouse islet.. *Br J Pharmacol. [Epub ahead of print]* http://www.ncbi.nlm.nih.gov/pubmed/26140534 97. Brust TF, Hayes MP, Roman DL, Burris KD, Watts VJ.(2015) Bias analyses of preclinical and clinical D2 dopamine ligands: studies with immediate and complex signaling pathways. *J Pharmacol Exp Ther.* 352(3):480-93 http://www.ncbi.nlm.nih.gov/pubmed/25539635 98. Dix AV, Conroy JL, George Rosenker KM, Sibley DR, Appella DH.(2015) PNA-Based Multivalent Scaffolds Activate the Dopamine D2 Receptor. *ACS Med. Chem.* Lett 6(4):425-9. http://www.ncbi.nlm.nih.gov/pubmed/25893044 99. Free RB, Chun LS, Moritz AE, Miller BN, Doyle TB, Conroy JL, Padron A, Meade JA, Xiao J, Hu X, Dulcey AE, Han Y, Duan L, Titus S, Bryant-Genevier M, Barnaeva E, Ferrer M, Javitch JA, Beuming T, Shi L, Southall NT, Marugan JJ, Sibley DR (2014). Discovery and characterization of a G protein-biased agonist that inhibits β-arrestin recruitment to the D2 dopamine receptor. *Mol Pharmacol.* 2014 86(1):96-105. http://www.ncbi.nlm.nih.gov/pubmed/24755247 100. Allen JA, Yost JM, Setola V, Chen X, Sassano MF, Chen M, Peterson S, Yadav PN, Huang XP, Feng B, Jensen NH, Che X, Bai X, Frye SV, Wetsel WC, Caron MG, Javitch JA, Roth BL, Jin J. (2011). Discovery of β-arrestin-biased dopamine D2 ligands for probing signal transduction pathways essential for antipsychotic efficacy. Proc *Natl Acad Sci USA* 108(45):18488-93. http://www.ncbi.nlm.nih.gov/pubmed/22025698

GPCR Target	Reference
Dopamine Receptors ...continued	
DRD2, DRD3	101. van Wieringen JP, Michel MC, Janssen HM, Janssen AG, Elsinga PH, Booij J. (2014). Agonist signalling properties of radiotracers used for imaging of dopamine D2/3 receptors. *EJNMMI Research* 4:53 http://www.ncbi.nlm.nih.gov/pubmed/25977878 102. Xiao J, Free RB, Barnaeva E, Conroy J, Doyle T, Bryant-Genevier M, Taylor MK, Southall N, Hu X, Ferrer M, Titus S, Zheng W, Sibley DR, Marugan JJ. (2014). Discovery, optimization, and characterization of a novel series of dopamine D2 versus D3 receptor selective antagonists. *Probe Reports from the NIH Molecular Libraries Program [Internet].* http://www.ncbi.nlm.nih.gov/pubmed/24260782 103. Ananthan S, Saini SK, Zhou G, Hobrath JV, Padmalayam I, Zhai L, Bostwick JR, Antonio T, Reith ME, McDowell S, Cho E, McAleer L, Taylor M, Luedtke RR. (2014). Design, synthesis, and structure-activity relationship studies of a series of [4-(4-carboxamidobutyl)]-1-arylpiperazines: insights into structural features contributing to dopamine D3 versus D2 receptor subtype selectivity. *J Med Chem* 16(75):7042-60. http://www.ncbi.nlm.nih.gov/pubmed/25126833 104. Meade JA, Free RB, Miller NR, Chun LS, Doyle TB, Moritz AE, Conroy JL, Watts VJ, Sibley DR. (2014). (-)-Stepholidine is a potent pan-dopamine receptor antagonist of both G protein- and β-arrestin-mediated signaling. *Psychopharmacology.* 232(5):917-30. http://www.ncbi.nlm.nih.gov/pubmed/25231919 105. Hiller C, Kling RC, Heinemann FW, Meyer K, Hübner H, Gmeiner, P. (2013). Functionally selective dopamine D2/D3 receptor agonists comprising an enyne moiety. *J Med Chem* 56(12):5130-41. http://www.ncbi.nlm.nih.gov/pubmed/23730937
DRD3	106. Chen J, Levant B, Jiang C, Keck TM, Newman AH, Wang S. (2014). Tranylcypromine substituted cis-hydroxycyclobutylnaphthamides as potent and selective dopamine D_3 receptor antagonists. *J Med Chem.* 57(11):4962-8. http://www.ncbi.nlm.nih.gov/pubmed/24848155 107. Furman CA, Roof RA, Moritz AE, Miller BN, Doyle TB, Free RB, Banala AK, Paul NM, Kumar V, Sibley CD, Newman AH, Sibley DR. (2014). Investigation of the binding and functional properties of extended length D3 dopamine receptor-selective antagonists. *Eur Neuropsychopharmacol. [Epub ahead of print]* http://www.ncbi.nlm.nih.gov/pubmed/25583363 108. Banala AK, Levy BA, Khatri SS, Furman CA, Roof, RA, Mishra Y, Griffin SA, Sibley DR, Luedtke RR, and Newman AH. (2011). N-(3-fluoro-4-(4-(2-methoxy or 2,3-dichlorophenyl)piperazine-1-yl)butyl)arylcarboxamides as selective dopamine D3 receptor ligands: critical role of the carboxamide linker for D3 receptor selectivity. *J Med Chem* 54(10):3581-94. http://www.ncbi.nlm.nih.gov/pubmed/21495689
Endothelin Receptors	
EDNRA, EDNRB	109. Maguire JJ, Kuc RE, Pell VR, Green A, Brown M, Kumar S, Wehrman T, Quinn E and Davenport AP. (2012). Comparison of human ET(A) and ET(B) receptor signalling via G-protein and β-arrestin pathways. *Life Sci* 91(13-14):544-9. http://www.ncbi.nlm.nih.gov/pubmed/22480514
Follicle Stimulating Hormone Receptors (Glycoprotein Hormone Receptors)	
FSHR	110. Jiang X, Fischer D, Chen X, McKenna SD, Liu H, Sriraman V, Yu HN, Goutopoulos A, Arkinstall S, He X. (2014). AEvidence for Follicle-stimulating Hormone Receptor as a Functional Trimer. *J Biol Chem.* 289(20):14273-82. http://www.ncbi.nlm.nih.gov/pubmed/24692546
Formylpeptide Receptors	
FPR1	111. Forsman H, Onnheim K, Andreasson E and Dahlgren C. (2011). What formyl peptide receptors, if any, are triggered by compound 43 and lipoxin A4? *Scand J Immunol* 74(3):227-34. http://www.ncbi.nlm.nih.gov/pubmed/21535079
FPR1, FPR2	112. Cilibrizzi A, Schepetkin IA, Bartolucci G, Crocetti L, Dal Piaz V, Giovannoni MP, Graziano A, Kirpotina LN, Quinn MT and Vergelli C. (2012). Synthesis, enantioresolution, and activity profile of chiral 6-methyl-2,4-disubstituted pyridazin-3(2H)-ones as potent N-formyl peptide receptor agonists. *Bioorg Med Chem* 20(12):3781-92. http://www.ncbi.nlm.nih.gov/pubmed/22607879
FPR2/ALX	113. Dalli J, Consalvo AP, Ray V, Di Filippo C, D'Amico M, Mehta N and Perretti M. (2013). Proresolving and tissue-protective actions of annexin A1-based cleavage-resistant peptides are mediated by formyl peptide receptor 2/lipoxin A4 receptor. *J Immunol* 190(12):6478-87. http://www.ncbi.nlm.nih.gov/pubmed/23686496
Ghrelin Receptors	
GHSR	114. Bhattacharya SK, Andrews K, Beveridge R, Cameron KO, Chen C, Dunn M, Fernando D, Gao H, Hepworth D, Jackson VM, Khot V, Kong J, Kosa RE, Lapham K, Loria PM, Londregan AT, McClure KF, Orr ST, Patel J, Rose C, Saenz J, Stock IA, Storer G, VanVolkenburg M, Vrieze D, Wang G, Xiao J, Zhang Y. (2014). Discovery of PF-5190457, a Potent, Selective, and Orally Bioavailable Ghrelin Receptor Inverse Agonist Clinical Candidate. *ACS Med Chem Lett.* 5(5):474-9. http://www.ncbi.nlm.nih.gov/pubmed/24900864

GPCR Target	Reference
Glucagon Receptors	
GLP1R	115. Nakane A, Gotoh Y, Ichihara J, Nagata H. (2015). New Screening Strategy and Analysis for Identification of Allosteric Modulators for GLP-1 Receptor Using GLP-1(9-36)amide. *Anal Biochem [Epub ahead of print]* http://www.ncbi.nlm.nih.gov/pubmed/26341912 116. Al-Sabah S, Al-Fulaij M, Shaaban G, Ahmed HA, Mann RJ, Donnelly D, Bünemann M, Krasel C. (2014). The GIP receptor displays higher basal activity than the GLP-1 receptor but does not recruit GRK2 or arrestin3 effectively. *PLoS ONE* 9(9):e106890. http://www.ncbi.nlm.nih.gov/pubmed/25191754 117. Heard KR, Wu W, Li Y, Zhao P, Woznica I, Lai JH, Beinborn M, Sanford DG, Dimare MT, Chiluwal AK, Peters DE, Whicher D, Sudmeier JL, Bachovchin WW. (2013). A General Method for Making Peptide Therapeutics Resistant to Serine Protease Degradation: Application to Dipeptidyl Peptidase IV Substrates. *J Med Chem* 56(21):8339-51. http://www.ncbi.nlm.nih.gov/pubmed/24044354
GLP1R (Internalization)	118. Morris LC, Nance KD, Gentry PR, Days EL, Weaver CD, Niswender CM, Thompson AD, Jones CK, Locuson CW, Morrison RD, Daniels JS, Niswender KD, Lindsley CW. (2014). Discovery of (S)-2-cyclopentyl-N-((1-isopropylpyrrolidin2-yl)-9-methyl-1-oxo-2,9-dihydro-1H-pyrrido[3,4-b]indole-4-carboxamide (VU0453379): a novel, CNS penetrant glucagon-like peptide 1 receptor (GLP-1R) positive allosteric modulator (PAM). *J Med Chem.* 57(23):10192-7. http://www.ncbi.nlm.nih.gov/pubmed/25423411
Histamine Receptors	
HRH4	119. Nijmeijer S, Vischer HF, Sirci F, Schultes S, Engelhardt H, de Graaf C, Rosethorne EM, Charlton SJ and Leurs R. (2013). Detailed analysis of biased histamine H4 receptor signalling by JNJ 7777120 analogues. *Br J Pharmacol* 170(1):78-88. http://www.ncbi.nlm.nih.gov/pubmed/23351115 120. Rosethorne EM and Charlton SJ. (2011). Agonist-biased signaling at the histamine H4 receptor: JNJ7777120 recruits β-arrestin without activating G proteins. *Mol Pharmacol* 79(4):749-57. http://www.ncbi.nlm.nih.gov/pubmed/21134907
Lysophospholipid Receptors	
S1P1 (EDG1)	121. Taylor SJ, Demont EH, Gray J, Deeks N, Patel A, Nguyen D, Taylor M, Hood S, Watson R, Bit RA, McClure F, Ashall H, Witherington J (2015). Navigating CYP1A induction and arylhydrocarbon receptor agonism in drug discovery. A case history with S1P1 agonists. *J Med Chem [Epub ahead of print]* http://www.ncbi.nlm.nih.gov/pubmed/26393276 122. Gatfield J, Monnier L, Studer R, Bolli MH, Steiner B, Nayler O (2014). Sphingosine-1-phosphate (S1P) displays sustained S1P1 receptor agonism and signaling through S1P lyase-dependent receptor recycling. *Cell Signal.* 26(7):1576-88. http://www.ncbi.nlm.nih.gov/pubmed/24704119 123. Purschke WG, Hoehlig K, Buchner K, Zboralski D, Schwoebel F, Vater A, Klussmann S (2014). Identification and characterization of a mirror-image oligonucleotide that binds and neutralizes sphingosine 1-phosphate, a central mediator of angiogenesis. *Biochem J* 462(1):153-62. http://www.ncbi.nlm.nih.gov/pubmed/24832383 124. Lundstrom K. (2013). Present and future approaches to screening of G-protein-coupled receptors. *Future Med Chem* 5(5): 523-38. http://www.ncbi.nlm.nih.gov/pubmed/23573971 125. Xu H, McElvain M, Fiorino M, Henkle B, Sherman L, Xu Y, Tominey E, Kelley K, Adlam M, Bürli R, Siu J, Wong M and Cee VJ. (2013). Predictability of peripheral lymphocyte reduction of novel S1P1 agonist by *in vitro* GPCR signaling, *J Biomol Screen* 18(9):997-1007. http://www.ncbi.nlm.nih.gov/pubmed/23686102 126. Taylor S, Gray JR, Willis R, Deeks N, Haynes A, Campbell C, Gaskin P, Leavens K, Demont E, Dowell S, Cryan J, Morse M, Patel A, Garden H and Witherington J.(2012). The utility of pharmacokinetic-pharmacodynamic modeling in the discovery and optimization of selective S1P(1) agonists. *Xenobiotica* 42(7):671-86. http://www.ncbi.nlm.nih.gov/pubmed/22225501 127. Sanders MP, Roumen L, van der Horst E, Lane JR, Vischer HF, van Offenbeek J, de Vries H, Verhoeven S, Chow KY, Verkaar F, Beukers MW, McGuire R, Leurs R, Ijzerman AP, de Vlieg J, de Esch IJ, Zaman GJ, Klomp JP, Bender A and de Graaf C. (2012). A prospective cross-screening study on G-protein-coupled receptors: lessons learned in virtual compound library design. *J Med Chem* 55(11):5311-25. http://www.ncbi.nlm.nih.gov/pubmed/22563707 128. van Der Lee MM, Bras M, van Koppen CJ and Zaman GJ.(2008). β-Arrestin recruitment assay for the identification of agonists of the sphingosine 1-phosphate receptor EDG1. *J Biomol Screen* 13(10):986-98. http://www.ncbi.nlm.nih.gov/pubmed/19036707

GPCR Target	Reference
Lysophospholipid Receptors ...continued	
S1P1 (EDG1) (ProLink Vector)	129. Sykes DA, Riddy DM, Stamp C, Bradley ME, McGuiness N, Sattikar A, Guerini D, Rodrigues I, Glaenzel A, Dowling MR, Mullershausen F, Charlton SJ. (2014). Investigating the molecular mechanisms through which FTY720-P causes persistent S1P1 receptor internalization. *Br J Pharmacol.* 171(21):4797-807. http://www.ncbi.nlm.nih.gov/pubmed/24641481
S1P3 (EDG3)	130. Riddy D, Stamp C, Sykes D, Charlton S and Dowling M. (2012). Reassessment of the pharmacology of sphingosine-1-phosphate S1P(3) receptor ligands using the DiscoveRx PathHunter and Ca(2+) release functional assays. *Br J Pharmacol* 167(4):868-80. http://www.ncbi.nlm.nih.gov/pubmed/22577868
Melanin-concentrating Hormone Receptors	
MCHR1	131. Sakurai T, Ogawa K, Ishihara Y, Kasai S, Nakayama M. (2014). The MCH(1) receptor, an anti-obesity target, is allosterically inhibited by 8-methylquinoline derivatives possessing subnanomolar binding and long residence times. *Br J Pharmacol.* 171(5):1287-98. http://www.ncbi.nlm.nih.gov/pubmed/24670150
Melanocortin Receptors	
MC1R	132. Nix MA, Kaelin CB, Ta T, Weis A, Morton GJ, Barsh GS, Millhauser GL. (2013). Molecular and functional analysis of human b-defensin 3 action at melanocortin receptors. *Chem Biol* 20(6):784–95. http://www.ncbi.nlm.nih.gov/pubmed/23790489 133. Benned-Jensen T, Mokrosinski J, and Rosenkilde MM. (2011). The E92K melanocortin 1 receptor mutant induces cAMP production and arrestin recruitment but not ERK activity indicating biased constitutive signaling. *PLoS One* 6, e24644. http://www.ncbi.nlm.nih.gov/pubmed/21931793
MC4R	134. Ghamari-Langroudi M, Digby GJ, Sebag JA, Millhauser GL, Palomino R, Matthews R, Gillyard T, Panaro BL, Tough IR, Cox HM, Denton JS, Cone RD. (2015). G-protein-independent coupling of MC4R to Kir7.1 in hypothalamic neurons. *Nature.* 520(7545):94-8. http://www.ncbi.nlm.nih.gov/pubmed/25600267
Neurotensin Receptors	
NTS1	135. Hershberger PM, Hedrick MP, Peddibhotla S, Mangravita-Novo A, Gosalia P, Li Y, Gray W, Vicchiarelli M, Smith LH, Chung TD, Thomas JB, Caron MG, Pinkerton AB, Barak LS, Roth GP. (2014) Imidazole-derived agonists for the neurotensin 1 receptor. *Bioorg Med Chem Lett.* 24(1):262-7. http://www.ncbi.nlm.nih.gov/pubmed/24332089
Opioid Receptors	
OPRD1	136. Burford NT, Livingston K, Canals M, Ryan M, Budenholzer L, Han Y, Shang Y, Herbst JJ, O'Connell J, Banks M, Zhang L, Filizola M, Bassoni D, Wehrman TS, Christopoulos A, Traynor JR, Gerritz SW, Alt A. (2015). Discovery, Synthesis and Molecular Pharmacology of Selective Positive Allosteric Modulators of the δ-Opioid Receptor. *J Med Chem.* 58(10):4220-9. http://www.ncbi.nlm.nih.gov/pubmed/25901762
OPRD1, OPRK1, OPRM1	137. Hughes FM, Jr., Shaner BE, Brower JO, Woods RJ and Dix TA. (2013). Development of a peptide-derived orally-active kappa-opioid receptor agonist targeting peripheral pain. *Open Med Chem J* 2013(7):16-22. http://www.ncbi.nlm.nih.gov/pubmed/24222801

GPCR Target	Reference
Opioid Receptors ...continued	
OPRK1	138. Stahl EL, Zhou L, Ehlert FJ, Bohn LM. (2015). A Novel Method for Analyzing Extremely Biased Agonism at G Protein-Coupled Receptors. *Mol Pharmacol.* 87(5):866-77. http://www.ncbi.nlm.nih.gov/pubmed/25680753 139. Robinson, JD., and McDonald, PH. (2015). The orexin 1 receptor modulates kappa opioid receptor function via a JNK-dependent mechanism. *Cellular Signaling.* 27(7):1449-56. http://www.ncbi.nlm.nih.gov/pubmed/25857454 140. Frankowski KJ, Slauson SR, Lovell KM, Phillips AM, Streicher JM, Zhou L, Whipple DA, Schoenen FJ, Prisinzano TE, Bohn LM, Aubé J. (2014). Potency enhancement of the κ-opioid receptor antagonist probe ML140 through sulfonamide constraint utilizing a tetrahydroisoquinoline motif. *Bioorg Med Chem* S0968-0896(14)00881-5. http://www.ncbi.nlm.nih.gov/pubmed/25593096 141. Schmid CL, Streicher JM, Groer CE, Munro TA, Zhou L and Bohn LM. (2013). Functional selectivity of 6'-guanidinonaltrindole (6'-GNTI) at kappa opioid receptors in striatal neurons. *J Biol Chem* 288(31):22387-98. http://www.ncbi.nlm.nih.gov/pubmed/23775075 142. Beguin C, Potuzak J, Xu W, Liu-Chen, LY, Streicher, JM, Groer, CE, Bohn, LM, Carlezon, WA, Jr., and Cohen, B.M. (2012). Differential signaling properties at the kappa opioid receptor of 12-epi-salvinorin A and its analogues. *Bioorg Med Chem Lett* 22(2):1023-6. http://www.ncbi.nlm.nih.gov/pubmed/22204910 143. Roberts LR, Brady K, Brown A, Davey D, Feng L, Huang H, Liu D, Malet L, McMurray G, Phelan A, Saunders K and Bhat A. (2012). Kappa agonist CovX-Bodies. *Bioorg Med Chem Lett* 22(12):4173-8. http://www.ncbi.nlm.nih.gov/pubmed/22583618 144. Hedrick MP, Gosalia P, Frankowski K, Shi S, Prisinzano TE, Schoenen F, Aube J, Su Y, Vasile S, Sergienko E, *et al.* (2010). Selective KOP receptor antagonists: Probe 1. Probe Reports from the NIH Molecular Libraries Program *[Internet*]. Bethesda (MD): *National Center for Biotechnology Information 2010 Feb 28 [updated 2010 Oct 4].* http://www.ncbi.nlm.nih.gov/books/NBK50689/
OPRK1, OPRM1	145. Zhou L, Lovell KM, Frankowski KJ, Slauson SR, Phillips AM, Streicher JM, Stahl EL, Schmid CL, Hodder P, Madoux F, Cameron MD, Prisinzano TE, Aube J and Bohn LM. (2013). Development of functionally selective, small molecule agonists at kappa opioid receptors. *J Biol Chem* 288(51):36703-16. http://www.ncbi.nlm.nih.gov/pubmed/24187130
OPRM1	146. Bisignano P, Burford NT, Shang Y, Marlow B, Livingston K, Fenton AM, Rockwell K, Budenholzer L, Traynor JR, Gerritz SW, Alt A, Filizola M. (2015). Ligand-Based Discovery of a New Scaffold for Allosteric Modulation of the mu-Opioid Receptor. *J Chem Inf Model [Epub ahead of print]* http://www.ncbi.nlm.nih.gov/pubmed/26347990 147. Burford NT, Traynor JR and Alt A. (2015). Positive allosteric modulators of the μ-opioid receptor: a novel approach for future pain medications. *Br J Pharmacol.* 172(2):277-86. (review paper) http://www.ncbi.nlm.nih.gov/pubmed/24460691 148. Bird MF, Vardanyan RS, Hruby VJ, Calò G, Guerrini R, Salvadori S, Trapella C, McDonald J, Rowbotham DJ, Lambert D (2015). Development and characterisation of novel fentanyl-delta opioid receptor antagonist based bivalent ligands. *Br J Anaesth.* 114(4):646-56. http://www.ncbi.nlm.nih.gov/pubmed/25680364 149. Burford NT, Clark MJ, Wehrman TS, Gerritz SW, Banks M, O'Connell J, Traynor JR and Alt A. (2013). Discovery of positive allosteric modulators and silent allosteric modulators of the μ-opioid receptor. *Proc Natl Acad Sci USA* 110(26):10830-5. http://www.ncbi.nlm.nih.gov/pubmed/23754417 150. Chen XT, Pitis P, Liu G, Yuan C, Gotchev D, Cowan CL, Rominger DH, Koblish M, Dewire SM, Crombie AL, Violin JD, Yamashita DS. (2013). Structure-Activity Relationships and Discovery of a G Protein Biased μ Opioid Receptor Ligand, [(3-Methoxythiophen-2-yl)methyl]({2-[(9R)-9-(pyridin-2-yl)-6-oxaspiro-[4.5]decan-9-yl]ethyl})amine (TRV130), for the Treatment of Acute Severe Pain. *J Med Chem* 56(20):8019-31. http://www.ncbi.nlm.nih.gov/pubmed/24063433 151. Nickolls SA, Humphreys S, Clark M and McMurray G. (2013). Co-expression of GRK2 reveals a novel conformational state of the m-opioid receptor. *PLoS ONE* 8(12): e83691. http://www.ncbi.nlm.nih.gov/pubmed/24376730 152. Nickolls SA, Waterfield A, Williams RE and Kinloch RA. (2011). Understanding the effect of different assay formats on agonist parameters: a study using the m-opioid receptor. *J Biomol Screen* 16(7):706-16. http://www.ncbi.nlm.nih.gov/pubmed/21550962

GPCR Target	Reference
Opioid Receptors ...continued	
OPRM1 (Internalization)	153. DeWire SM, Yamashita DS, Rominger DH, Liu G, Cowan CL, Graczyk TM, Chen XT, Pitis PM, Gotchev D, Yuan C, Koblish M, Lark MW and Violin JD. (2013). A G protein-biased ligand at the μ-opioid receptor is potently analgesic with reduced gastrointestinal and respiratory dysfunction compared with morphine. *J Pharmacol Exp Ther* 344(3):708-17. http://www.ncbi.nlm.nih.gov/pubmed/20647394 154. McPherson J, Rivero G, Baptist M, Llorente J, Al-Sabah S, Krasel C, Dewey WL, Bailey CP, Rosethorne EM, Charlton SJ et al. (2010). m-opioid receptors: correlation of agonist efficacy for signalling with ability to activate internalization. *Mol Pharmacol* 78(4):756-66. http://www.ncbi.nlm.nih.gov/pubmed/20647394
OPRM1, OPRD1	155. Burford NT, Wehrman T, Bassoni D, O'Connell J, Banks M, Zhang L, Alt A. (2014). Identification of Selective Agonists and Positive Allosteric Modulators for μ- and δ-Opioid Receptors from a Single High-Throughput Screen. *J Biomol Screen.* 19(9):1255-65. http://www.ncbi.nlm.nih.gov/pubmed/25047277 156. Fujita W, Gomes I, Dove LS, Prohaska D, McIntyre G, Devi LA. (2014). Molecular characterization of eluxadoline as a potential ligand targeting mu-delta opioid receptor heteromers. *Biochem Pharmacol* 92(3):448-56. http://www.ncbi.nlm.nih.gov/pubmed/25261794
P2Y (Purinergic Receptor)	
P2YR12	157. Foster HR, Fuerst E, Lee TH, Cousins DJ and Woszczek G. (2013). Characterisation of P2Y(12) receptor responsiveness to cysteinyl leukotrienes. *PLoS One* 8:e58305. http://www.ncbi.nlm.nih.gov/pubmed/23472176 158. Fredman G, Van Dyke TE and Serhan CN. (2010). Resolvin E1 regulates adenosine diphosphate activation of human platelets. *Arterioscler Thromb Vasc Biol* 30(10):2005-13. http://www.ncbi.nlm.nih.gov/pubmed/20702811
Parathyroid Hormone Receptors	
PTHR1	159. Cupp ME, Song B, Kibler P, Raghavender US, Nayak SK, Thomsen W, Galande AK. (2013). Investigating hydrophobic ligand-receptor interactions in parathyroid hormone receptor using peptide probes. *J Pept Sci* 19(6):337-44. 160. Bivi N, Lezcano V, Romanello M, Bellido T, Plotkin LI. (2011). Connexin43 interacts with βarrestin: a pre-requisite for osteoblast survival induced by parathyroid hormone. *J Cell Biochem* 112(10):2920-30. http://www.ncbi.nlm.nih.gov/pubmed/21630325
PTHR1 (Internalization)	161. Cupp ME, Nayak SK, Adem AS and Thomsen WJ. (2013). Parathyroid hormone (PTH) and PTH-related peptide domains contributing to activation of different PTH receptor-mediated signaling pathways. *J Pharmacol Exp Ther* 345(3):404-18. http://www.ncbi.nlm.nih.gov/pubmed/23516330
Somatostatin Receptors	
SSTR2	162. Zhao X, Jones A, Olson KR, Peng K, Wehrman T, Park A, Mallari R, Nebalasca D, Young SW and Xiao SH. (2008). A homogeneous enzyme fragment complementation-based β-arrestin translocation assay for high-throughput screening of G-protein-coupled receptors. *J Biomol Screen* 13(8):737-47. http://www.ncbi.nlm.nih.gov/pubmed/18660457
Thrombin (Coagulation Factor II Receptor), Proteinase-activate	
PAR1	163. Hawes BE, Zhai Y, Hesk D, Wirth M, Wei H, Chintala M, Seiffert D. (2015). In vitro pharmacological characterization of vorapaxar, a novel platelet thrombin receptor antagonist. *Eur J Pharmacol. [Epub ahead of print]* http://www.ncbi.nlm.nih.gov/pubmed/26022529
Thyrotropin (Glycoprotein Hormone) Receptors	
TSHR	164. Boutin A, Eliseeva E, Gershengorn MC, Neumann S. (2014). β-Arrestin-1 mediates thyrotropin-enhanced osteoblast differentiation. *FASEB J.* 28(8):3446-55. http://www.ncbi.nlm.nih.gov/pubmed/26022529
VIP & PACAP Receptors	
VPAC2	165. Chu A, Caldwell JS, and Chen YA. (2010). Identification and characterization of a small molecule antagonist of human VPAC(2) receptor. *Mol Pharmacol* 77(1):95-101. http://www.ncbi.nlm.nih.gov/pubmed/19854890