

## GPCR Ligand Pose and Functional Class Prediction

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## SUPPLEMENTAL TABLES

Table S1. List of experimentally determined Class A GPCR structures used in fingerprint development.

PDBID	GPCR	Species	Publication Date	Activation State	Ligand Name
5V54[1]	5HT1B	Homo sapiens	2018-02-07	Inactive	CHEMBL428892
4IAQ[2]	5HT1B	Homo sapiens	2013-03-13	Inactive	dihydroergotamine
6G79[3]	5HT1B	Homo sapiens	2018-06-20	Active	donitriptan
4IAR[2]	5HT1B	Homo sapiens	2013-03-13	Inactive	ergotamine
6A93[4]	5HT2A	Homo sapiens	2019-02-13	Inactive	risperidone
6A94[4]	5HT2A	Homo sapiens	2019-02-13	Inactive	zotepine
6DS0[5]	5HT2B	Homo sapiens	2018-08-29	Intermediate	LY266097
5TVN[6]	5HT2B	Homo sapiens	2017-02-01	Intermediate	lysergide
4IB4[7]	5HT2B	Homo sapiens	2013-03-13	Intermediate	ergotamine
4NC3[8]	5HT2B	Homo sapiens	2013-12-18	Intermediate	ergotamine
5TUD[9]	5HT2B	Homo sapiens	2017-07-26	Active	ergotamine
6DRX[5]	5HT2B	Homo sapiens	2018-08-29	Intermediate	lisuride
6DRY[5]	5HT2B	Homo sapiens	2018-08-29	Intermediate	methylergonovine
6DRZ[5]	5HT2B	Homo sapiens	2018-08-29	Intermediate	methysergide
6BQG[10]	5HT2C	Homo sapiens	2018-02-14	Active	ergotamine
6BQH[10]	5HT2C	Homo sapiens	2018-02-14	Inactive	ritanserin
5UEN[11]	AA1R	Homo sapiens	2017-03-01	Inactive	DU172
5N2S[12]	AA1R	Homo sapiens	2017-07-26	Inactive	PSB36
6D9H[13]	AA1R	Homo sapiens	2018-06-20	Active	adenosine
5IU7[14]	AA2AR	Homo sapiens	2016-06-29	Inactive	2-(furan-2-yl)-5-N-[2-(4-phenylpiperidin-1-yl)ethyl]-1H-[1,2,4]triazolo[1,5-a][1,3,5]triazin-8-ium-5,7-diamine
5IUA[14]	AA2AR	Homo sapiens	2016-06-29	Inactive	2-(furan-2-yl)-5-N-[3-(4-phenylpiperazin-1-yl)propyl]-1H-[1,2,4]triazolo[1,5-a][1,3,5]triazin-8-ium-5,7-diamine
5UIG[15]	AA2AR	Homo sapiens	2017-02-08	Inactive	5-amino-N-[(2-methoxyphenyl)methyl]-2-(3-methylphenyl)-2h-1,2,3-triazole-4-carboximidamide
4UG2[16]	AA2AR	Homo sapiens	2015-04-08	Active	CGS 21680
4UHR[16]	AA2AR	Homo sapiens	2015-04-08	Active	CGS 21680
5OLV[17]	AA2AR	Homo sapiens	2018-01-17	Inactive	CHEMBL1671936
5IUB[14]	AA2AR	Homo sapiens	2016-06-29	Inactive	CHEMBL184061
3UZC[18]	AA2AR	Homo sapiens	2012-03-21	Inactive	CHEMBL2024114
5OLZ[17]	AA2AR	Homo sapiens	2018-01-17	Inactive	CHEMBL2024114
5OM1[17]	AA2AR	Homo sapiens	2018-01-17	Inactive	CHEMBL2024114
5OM4[17]	AA2AR	Homo sapiens	2018-01-17	Inactive	CHEMBL2024114
5IU8[14]	AA2AR	Homo sapiens	2016-06-29	Inactive	CHEMBL3934661
2YDV[19]	AA2AR	Homo sapiens	2011-05-18	Active	NECA
5G53[20]	AA2AR	Homo sapiens	2016-08-03	Active	NECA
6GDG[21]	AA2AR	Homo sapiens	2018-05-16	Active	NECA

5N2R[12]	AA2AR	Homo sapiens	2017-07-26	Inactive	PSB36
3QAK[22]	AA2AR	Homo sapiens	2011-03-09	Active	UK-432,097
5WF5[23]	AA2AR	Homo sapiens	2018-02-21	Active	UK-432,097
5WF6[23]	AA2AR	Homo sapiens	2018-02-21	Active	UK-432,097
3EML[24]	AA2AR	Homo sapiens	2008-10-14	Inactive	ZM-241385
3PWH[25]	AA2AR	Homo sapiens	2011-09-07	Inactive	ZM-241385
3VG9[26]	AA2AR	Homo sapiens	2012-02-01	Inactive	ZM-241385
3VGA[26]	AA2AR	Homo sapiens	2012-02-01	Inactive	ZM-241385
4E1Y[27]	AA2AR	Homo sapiens	2012-07-25	Inactive	ZM-241385
5IU4[14]	AA2AR	Homo sapiens	2016-06-29	Inactive	ZM-241385
5JTB[28]	AA2AR	Homo sapiens	2017-05-31	Inactive	ZM-241385
5K2A[29]	AA2AR	Homo sapiens	2016-09-21	Inactive	ZM-241385
5K2B[29]	AA2AR	Homo sapiens	2016-09-21	Inactive	ZM-241385
5K2C[29]	AA2AR	Homo sapiens	2016-09-21	Inactive	ZM-241385
5K2D[29]	AA2AR	Homo sapiens	2016-09-21	Inactive	ZM-241385
5NLX[30]	AA2AR	Homo sapiens	2017-09-27	Inactive	ZM-241385
5NM2[30]	AA2AR	Homo sapiens	2017-09-27	Inactive	ZM-241385
5NM4[30]	AA2AR	Homo sapiens	2017-09-27	Inactive	ZM-241385
5OLG[17]	AA2AR	Homo sapiens	2018-01-17	Inactive	ZM-241385
5UVI[31]	AA2AR	Homo sapiens	2017-05-24	Inactive	ZM-241385
5VRA[32]	AA2AR	Homo sapiens	2017-12-13	Inactive	ZM-241385
6AQF[33]	AA2AR	Homo sapiens	2018-01-10	Inactive	ZM-241385
2YDO[19]	AA2AR	Homo sapiens	2011-05-18	Active	adenosine
3RFM[25]	AA2AR	Homo sapiens	2011-09-07	Inactive	caffeine
5MZP[12]	AA2AR	Homo sapiens	2017-07-26	Inactive	caffeine
3UZA[18]	AA2AR	Homo sapiens	2012-03-21	Inactive	compound 4g [PMID: 22220592]
5MZJ[12]	AA2AR	Homo sapiens	2017-07-26	Inactive	theophylline
5OLO[17]	AA2AR	Homo sapiens	2018-01-17	Inactive	tozadenant
5OLH[17]	AA2AR	Homo sapiens	2018-01-17	Inactive	vipadenant
3REY[25]	AA2AR	Homo sapiens	2011-09-07	Inactive	xanthine amine congener
5CXV[34]	ACM1	Homo sapiens	2016-03-09	Inactive	0HK
6OIJ[35]	ACM1	Homo sapiens	2019-05-08	Active	iperoxo
5ZKB[36]	ACM2	Homo sapiens	2018-11-21	Inactive	AF-DX 384
3UON[37]	ACM2	Homo sapiens	2012-02-01	Inactive	CHEMBL558910
5ZK3[36]	ACM2	Homo sapiens	2018-11-21	Inactive	CHEMBL558910
5YC8[36]	ACM2	Homo sapiens	2018-11-21	Inactive	N-methyl scopolamine
5ZK8[36]	ACM2	Homo sapiens	2018-11-21	Inactive	N-methyl scopolamine
5ZKC[36]	ACM2	Homo sapiens	2018-11-21	Inactive	N-methyl scopolamine
4MQS[38]	ACM2	Homo sapiens	2013-11-27	Active	iperoxo
5ZHP[39]	ACM3	Rattus norvegicus	2018-11-28	Inactive	(1R,2R,4S,5S,7s)-7-([4-fluoro-2-(thiophen-2-yl)phenyl]carbamoyl)oxy)-9,9-dimethyl-3-oxa-9-azatricyclo[3.3.1.0~2,4~]nonan-9-ium
4U16[40]	ACM3	Rattus norvegicus	2014-11-26	Inactive	N-methyl scopolamine
4DAJ[41]	ACM3	Rattus norvegicus	2012-02-22	Inactive	tiotropium

4U14[40]	ACM3	Rattus norvegicus	2014-11-26	Inactive	tiotropium
4U15[40]	ACM3	Rattus norvegicus	2014-11-26	Inactive	tiotropium
5DSG[34]	ACM4	Homo sapiens	2016-03-16	Inactive	tiotropium
6OL9[42]	ACM5	Homo sapiens	2019-12-11	Inactive	tiotropium
2VT4[43]	ADRB1	Meleagris gallopavo	2008-06-24	Inactive	(S)-cyanopindolol
2YCY[44]	ADRB1	Meleagris gallopavo	2011-06-08	Inactive	(S)-cyanopindolol
4BVN[45]	ADRB1	Meleagris gallopavo	2014-04-02	Inactive	(S)-cyanopindolol
5F8U[46]	ADRB1	Meleagris gallopavo	2015-12-23	Inactive	(S)-cyanopindolol
6H7O[47]	ADRB1	Meleagris gallopavo	2018-10-17	Active	(S)-cyanopindolol
6H7N[47]	ADRB1	Meleagris gallopavo	2018-10-17	Active	(S)-xamoterol
5A8E[48]	ADRB1	Meleagris gallopavo	2015-09-30	Inactive	7-methylcyanopindolol
4AMI[49]	ADRB1	Meleagris gallopavo	2012-05-23	Inactive	bucindolol
2Y02[50]	ADRB1	Meleagris gallopavo	2011-01-12	Inactive	carmoterol
3ZPR[51]	ADRB1	Meleagris gallopavo	2013-04-03	Inactive	CHEMBL1559535
3ZPQ[51]	ADRB1	Meleagris gallopavo	2013-04-03	Inactive	CHEMBL200234
4AMJ[49]	ADRB1	Meleagris gallopavo	2012-05-23	Inactive	CHEMBL3799125
2YCW[44]	ADRB1	Meleagris gallopavo	2011-06-01	Inactive	carazolol
2Y00[50]	ADRB1	Meleagris gallopavo	2011-01-12	Inactive	dobutamine
2Y01[50]	ADRB1	Meleagris gallopavo	2011-03-30	Inactive	dobutamine
6H7L[47]	ADRB1	Meleagris gallopavo	2018-10-17	Active	dobutamine
2YCZ[44]	ADRB1	Meleagris gallopavo	2011-06-01	Inactive	iodocyanopindolol
2Y03[50]	ADRB1	Meleagris gallopavo	2011-01-12	Inactive	levisoprenaline
6H7J[47]	ADRB1	Meleagris gallopavo	2018-10-17	Active	levisoprenaline
6IBL[52]	ADRB1	Meleagris gallopavo	2019-01-09	Active	arformoterol
2Y04[50]	ADRB1	Meleagris gallopavo	2011-01-12	Inactive	levosalbutamol

6H7M[47]	ADRB1	Meleagris gallopavo	2018-10-17	Active	levosalbutamol
3P0G[53]	ADRB2	Homo sapiens	2011-01-19	Active	BI-167107
3SN6[54]	ADRB2	Homo sapiens	2011-07-20	Active	BI-167107
4LDE[55]	ADRB2	Homo sapiens	2013-09-25	Active	BI-167107
3NYA[56]	ADRB2	Homo sapiens	2010-08-11	Inactive	CHEMBL1160734
3NY8[56]	ADRB2	Homo sapiens	2010-08-11	Inactive	CHEMBL1233766
3NY9[56]	ADRB2	Homo sapiens	2010-08-11	Inactive	CHEMBL1233771
2RH1[57]	ADRB2	Homo sapiens	2007-10-30	Inactive	carazolol
4GBR[58]	ADRB2	Homo sapiens	2012-10-24	Inactive	carazolol
5D5A[59]	ADRB2	Homo sapiens	2016-01-13	Inactive	carazolol
5D5B[59]	ADRB2	Homo sapiens	2016-01-13	Inactive	carazolol
5D6L[60]	ADRB2	Homo sapiens	2016-08-17	Inactive	carazolol
5JQH[61]	ADRB2	Homo sapiens	2016-07-13	Inactive	carazolol
3PDS[62]	ADRB2	Homo sapiens	2011-01-12	Inactive	FAUC50
4QKX[63]	ADRB2	Homo sapiens	2014-07-23	Active	Q27453560
6MXT[64]	ADRB2	Homo sapiens	2018-11-14	Active	salmeterol
3D4S[65]	ADRB2	Homo sapiens	2008-06-17	Inactive	timolol
4LDL[55]	ADRB2	Homo sapiens	2013-09-25	Active	hydroxybenzylisoproterenol
4LDO[55]	ADRB2	Homo sapiens	2013-09-25	Active	(-)-adrenaline
5X7D[66]	ADRB2	Homo sapiens	2017-08-16	Inactive	carazolol
4ZUD[67]	AGTR1	Homo sapiens	2015-10-07	Inactive	olmesartan
4YAY[68]	AGTR1	Homo sapiens	2015-04-22	Inactive	ZD-7155
6DO1[69]	AGTR1	Homo sapiens	2019-01-30	Active	angiotensin-like peptide S118
5UNF[70]	AGTR2	Homo sapiens	2017-04-05	Active	compound 1 [PMID: 28379944]
5UNG[70]	AGTR2	Homo sapiens	2017-04-05	Active	compound 1 [PMID: 28379944]
5UNH[70]	AGTR2	Homo sapiens	2017-04-05	Active	compound 2 [PMID: 28379944]
6JOD[71]	AGTR2	Homo sapiens	2020-01-15	Active	angiotensin II
5XJM[72]	AGTR2	Homo sapiens	2018-07-11	Active	ile8-angiotensin II
6KNM[73]	APJ	Homo sapiens	2020-01-29	Inactive	JN241
5VBL [74]	APJ	Homo sapiens	2017-05-31	Inactive	AMG3054
5O9H[75]	C5AR1	Homo sapiens	2018-01-10	Inactive	NDT9513727
6C1Q[76]	C5AR1	Homo sapiens	2018-05-30	Inactive	NDT9513727
6C1R[76]	C5AR1	Homo sapiens	2018-05-30	Inactive	PMX53
6GPS[77]	CCR2	Homo sapiens	2019-01-02	Inactive	MK-0812
6GPX[77]	CCR2	Homo sapiens	2019-01-02	Inactive	MK-0812
5T1A [78]	CCR2	Homo sapiens	2016-12-14	Inactive	(3S)-1-((1S,2R,4R)-4-[methyl(propan-2-yl)amino]-2-propylcyclohexyl)-3-[[6-(trifluoromethyl)quinazolin-4-yl]amino]pyrrolidin-2-one
6AKY[79]	CCR5	Homo sapiens	2018-10-24	Inactive	CCR5 antagonist 34
6AKX[79]	CCR5	Homo sapiens	2018-10-24	Inactive	N-[(1S)-3-((3-exo)-3-[3-methyl-5-(propan-2-yl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]octan-8-yl)-1-(thiophen-2-yl)propyl]cyclopentanecarboxamide

4MBS[80]	CCR5	Homo sapiens	2013-09-11	Inactive	maraviroc
6MEO[81]	CCR5	Homo sapiens	2018-12-12	Inactive	GP120
6MET[81]	CCR5	Homo sapiens	2018-12-12	Inactive	GP120
5UIW[82]	CCR5	Homo sapiens	2017-06-28	Inactive	5P7-CCL5
6QZH[83]	CCR7	Homo sapiens	2019-09-04	Inactive	3-[[4-[[[(1~{R})-2,2-dimethyl-1-(5-methylfuran-2-yl)propyl]amino]-1,1-bis(oxidanylidene)-1,2,5-thiadiazol-3-yl]amino]-~{N},~{N},6-trimethyl-2-oxidanyl-benzamide
5LWE[84]	CCR9	Homo sapiens	2016-12-07	Inactive	vercimon
6RZ4[85]	CLTR1	Homo sapiens	2019-10-30	Intermediate	pranlukast
6RZ5[85]	CLTR1	Homo sapiens	2019-10-30	Intermediate	zafirlukast
6RZ8[85]	CLTR2	Homo sapiens	2019-12-11	Intermediate	ONO-2080365
6RZ6[85]	CLTR2	Homo sapiens	2019-12-11	Intermediate	ONO-2570366
6RZ7[85]	CLTR2	Homo sapiens	2019-12-11	Intermediate	ONO-2570366
6RZ9[85]	CLTR2	Homo sapiens	2019-12-11	Intermediate	ONO-2770372
5XRA[86]	CNR1	Homo sapiens	2017-07-12	Active	AM11542
5TGZ[87]	CNR1	Homo sapiens	2016-11-02	Inactive	AM6538
5XR8[86]	CNR1	Homo sapiens	2017-07-12	Active	AM841
6N4B[88]	CNR1	Homo sapiens	2019-01-30	Active	MDMB-fubinaca
5U09[89]	CNR1	Homo sapiens	2016-12-07	Inactive	taranabant
5ZTY[90]	CNR2	Homo sapiens	2019-01-30	Inactive	AM10257
6KPC[91]	CNR2	Homo sapiens	2020-02-12	Inactive	AM841
6KPF[91]	CNR2	Homo sapiens	2020-02-12	Active	AM841
6PT0[92]	CNR2	Homo sapiens	2020-02-12	Active	WIN55212-2
3ODU[93]	CXCR4	Homo sapiens	2010-10-27	Inactive	isothiourea-1t
3OE6[93]	CXCR4	Homo sapiens	2010-10-27	Inactive	isothiourea-1t
3OE8[93]	CXCR4	Homo sapiens	2010-10-27	Inactive	isothiourea-1t
3OE9[93]	CXCR4	Homo sapiens	2010-10-27	Inactive	isothiourea-1t
3OE0[93]	CXCR4	Homo sapiens	2010-10-27	Inactive	CVX15
4RWS[94]	CXCR4	Homo sapiens	2015-02-11	Inactive	vMIP-II
6LUQ[95]	DRD2	Homo sapiens	2020-03-04	Inactive	haloperidol
6CM4[96]	DRD2	Homo sapiens	2018-03-14	Inactive	risperidone
3PBL[97]	DRD3	Homo sapiens	2010-11-03	Inactive	eticlopride
5WIU[98]	DRD4	Homo sapiens	2017-10-18	Inactive	nemonapride
5WIV[98]	DRD4	Homo sapiens	2017-10-18	Inactive	nemonapride
6K1Q[99]	EDNRB	Homo sapiens	2019-07-17	Inactive	IRL 2500
5X93[100]	EDNRB	Homo sapiens	2017-08-16	Inactive	K-8794
5GLH[101]	EDNRB	Homo sapiens	2016-09-07	Inactive	endothelin
6IGK[102]	EDNRB	Homo sapiens	2018-11-21	Inactive	endothelin-3
6IGL[102]	EDNRB	Homo sapiens	2018-11-21	Inactive	IRL1620
6K1Q[103]	EDNRB	Homo sapiens	2019-07-17	Inactive	IRL2500
6LRY[104]	EDNRB	Homo sapiens	2020-02-12	Inactive	sarafotoxin S6b
5TZR[105]	FFAR1	Homo sapiens	2017-06-07	Intermediate	MK-8666
5TZY[105]	FFAR1	Homo sapiens	2017-06-07	Intermediate	MK-8666

5KW2 [106]	FFAR1	Homo sapiens	2018-05-02	Intermediate	(3~{S})-3-cyclopropyl-3-[2-[1-[2-[2,2-dimethylpropyl-(6-methylpyridin-2-yl)carbamoyl]-5-methoxy-phenyl]piperidin-4-yl]-1-benzofuran-6-yl]propanoic acid
4PHU[107]	FFAR1	Homo sapiens	2014-07-16	Intermediate	fasiglifam
6OMM[108]	FPR2	Homo sapiens	2020-02-26	Active	CHEMBL552527
6LW5[109]	FPR2	Homo sapiens	2020-03-25	Active	CHEMBL552527
6LI0[110]	GPR52	Homo sapiens	2020-02-26	Inactive	derivative 17
3RZE[111]	HRH1	Homo sapiens	2011-06-15	Inactive	doxepin
4Z36[112]	LPAR1	Homo sapiens	2015-06-03	Inactive	ONO-3080573
4Z34[112]	LPAR1	Homo sapiens	2015-06-03	Inactive	ONO-9780307
4Z35[112]	LPAR1	Homo sapiens	2015-06-03	Inactive	ONO-9910539
6ME4[113]	MTR1A	Homo sapiens	2019-04-24	Inactive	2-iodomelatonin
6ME3[113]	MTR1A	Homo sapiens	2019-04-24	Inactive	2-phenylmelatonin
6PS8[114]	MTR1A	Homo sapiens	2019-11-13	Inactive	2-phenylmelatonin
6ME5[113]	MTR1A	Homo sapiens	2019-04-24	Inactive	agomelatine
6ME2[113]	MTR1A	Homo sapiens	2019-04-24	Inactive	ramelteon
6ME6[113]	MTR1B	Homo sapiens	2019-04-24	Inactive	2-phenylmelatonin
6ME7[113]	MTR1B	Homo sapiens	2019-04-24	Inactive	2-phenylmelatonin
6ME8[113]	MTR1B	Homo sapiens	2019-04-24	Inactive	2-phenylmelatonin
6ME9[113]	MTR1B	Homo sapiens	2019-04-24	Inactive	ramelteon
6HLL[115]	NK1R	Homo sapiens	2019-01-16	Inactive	CP 99994
6E59[116]	NK1R	Homo sapiens	2018-12-12	Inactive	L760735
6HLO[115]	NK1R	Homo sapiens	2019-01-16	Inactive	aprepitant
6J20[117]	NK1R	Homo sapiens	2019-03-06	Inactive	aprepitant
6J21[117]	NK1R	Homo sapiens	2019-03-06	Inactive	aprepitant
6HLP[115]	NK1R	Homo sapiens	2019-01-16	Inactive	netupitant
5ZBH[118]	NPY1R	Homo sapiens	2018-04-25	Inactive	BMS-193885
5ZBQ[118]	NPY1R	Homo sapiens	2018-04-25	Inactive	CHEMBL3747822
3ZEV [119]	NTR1	Rattus norvegicus	2014-01-29	Inactive	neurotensin
4BUO [119]	NTR1	Rattus norvegicus	2014-01-29	Inactive	neurotensin
4BV0 [119]	NTR1	Rattus norvegicus	2014-01-29	Inactive	neurotensin
4BWB [119]	NTR1	Rattus norvegicus	2014-01-29	Inactive	neurotensin
4GRV [120]	NTR1	Rattus norvegicus	2012-10-17	Active	neurotensin 8-13
4XEE [121]	NTR1	Rattus norvegicus	2015-07-29	Active	neurotensin
4XES [121]	NTR1	Rattus norvegicus	2015-07-29	Active	neurotensin
5T04 [122]	NTR1	Rattus norvegicus	2016-12-21	Active	neurotensin
4EJ4[123]	OPRD	Mus musculus	2012-05-16	Inactive	naltrindole
4N6H[124]	OPRD	Homo sapiens	2013-12-25	Inactive	naltrindole
4RWD [125]	OPRD	Homo sapiens	2015-01-14	Inactive	(3S)-2-[(2S)-2-azanyl-3-(2,6-dimethyl-4-oxidanyl-phenyl)propanoyl]-N-[(2S)-1-[[[(2S)-1-azanyl-1-oxidanylidene-3-phenyl-propan-2-yl]amino]-1-oxidanylidene-3-phenyl-

4RWA [125]	OPRD	Homo sapiens	2015-01-14	Inactive	propan-2-yl]-3,4-dihydro-1H-isoquinoline-3-carboxamide (3S)-2-[(2S)-2-azanyl-3-(2,6-dimethyl-4-oxidanyl-phenyl)propanoyl]-N-[(2S)-1-[(2S)-1-azanyl-1-oxidanylidene-3-phenyl-propan-2-yl]amino]-1-oxidanylidene-3-phenyl-propan-2-yl]-3,4-dihydro-1H-isoquinoline-3-carboxamide
4DJH[126]	OPRK	Homo sapiens	2012-03-21	Inactive	JDtic
6B73[127]	OPRK	Homo sapiens	2018-01-17	Active	MP1104
5C1M[128]	OPRM	Mus musculus	2015-08-05	Active	BU72
4DKL[129]	OPRM	Mus musculus	2012-03-21	Inactive	methyl 4-[[[(4R,4aS,7R,7aR,12bS)-3-(cyclopropylmethyl)-4a,9-dihydroxy-1,2,4,5,6,7,7a,13-octahydro-4,12-methanobenzofuro[3,2-e]isoquinolin-7-yl]amino]-4-oxobutanoate
6DDE [130]	OPRM	Mus musculus	2018-06-13	Active	DAMGO
6DDF [130]	OPRM	Mus musculus	2018-06-13	Active	DAMGO
5DHG[131]	OPRX	Homo sapiens	2015-10-21	Inactive	CHEMBL1783826
5DHH[131]	OPRX	Homo sapiens	2015-10-21	Inactive	SB 612111
4EA3[132]	OPRX	Homo sapiens	2012-04-25	Inactive	compound 24 [PMID: 16451050]
2Z1Y [133]	OPSD	Todarodes pacificus	2008-05-06	Inactive	11-cis retinal
6TP4[134]	OX1R	Homo sapiens	2020-01-01	Inactive	ACT-462206
6TOS[134]	OX1R	Homo sapiens	2020-01-15	Inactive	CHEMBL2413522
6TQ4[134]	OX1R	Homo sapiens	2020-01-01	Inactive	CHEMBL4590386
6TQ6[134]	OX1R	Homo sapiens	2020-01-01	Inactive	CHEMBL4592653
6TQ7[134]	OX1R	Homo sapiens	2020-01-01	Inactive	SB-334867
6TQ9[134]	OX1R	Homo sapiens	2020-01-01	Inactive	SB-408124
4ZJC[135]	OX1R	Homo sapiens	2016-03-09	Inactive	SB-674042
6TP3[134]	OX1R	Homo sapiens	2020-01-01	Inactive	daridorexant
6TP6[134]	OX1R	Homo sapiens	2020-01-01	Inactive	filorexant
6TOT[134]	OX1R	Homo sapiens	2020-01-15	Inactive	lemborexant
4ZJ8[135]	OX1R	Homo sapiens	2016-03-09	Inactive	suvorexant
6TO7[134]	OX1R	Homo sapiens	2020-01-01	Inactive	suvorexant
5WQC[136]	OX2R	Homo sapiens	2017-11-29	Inactive	EMPA
5WS3[136]	OX2R	Homo sapiens	2017-12-13	Inactive	EMPA
6TPG[134]	OX2R	Homo sapiens	2020-01-01	Inactive	EMPA
6TPN[134]	OX2R	Homo sapiens	2020-01-01	Inactive	HTL6641
4S0V[137]	OX2R	Homo sapiens	2015-01-14	Inactive	suvorexant
6TPJ[134]	OX2R	Homo sapiens	2020-01-01	Inactive	suvorexant
5NDZ [138]	PAR2	Homo sapiens	2017-05-03	Intermediate	2-(6-bromanyl-1,3-benzodioxol-5-yl)-~{N}-(4-cyanophenyl)-1-[(1~{S})-1-cyclohexylethyl]benzimidazole-5-carboxamide



4XNW[139]	P2RY1	Homo sapiens	2015-04-01	Intermediate	MRS2500
4XNV[139]	P2RY1	Homo sapiens	2015-04-01	Intermediate	1-[2-(2-tert-butylphenoxy)pyridin-3-yl]-3-[4-(trifluoromethoxy)phenyl]urea
4PXZ[140]	P2Y12	Homo sapiens	2014-04-30	Intermediate	2-(methylsulfanyl)adenosine 5'-(trihydrogen diphosphate)
4PY0[140]	P2Y12	Homo sapiens	2014-04-30	Intermediate	2-(methylsulfanyl)adenosine 5'-(trihydrogen diphosphate)
4NTJ[141]	P2Y12	Homo sapiens	2014-03-26	Intermediate	AZD1283
3VW7[142]	PAR1	Homo sapiens	2012-12-12	Intermediate	vorapaxar
5NDD[143]	PAR2	Homo sapiens	2017-05-03	Intermediate	AZ8838
6D27[144]	PD2R2	Homo sapiens	2018-10-03	Inactive	CHEMBL179036
6D26[144]	PD2R2	Homo sapiens	2018-10-03	Inactive	fevipiprant
6M9T[145]	PE2R3	Homo sapiens	2018-12-05	Active	misoprostol-FA
6AK3[146]	PE2R3	Homo sapiens	2018-12-05	Active	prostaglandin E <sub>2</sub>
5YWY[147]	PE2R4	Homo sapiens	2018-12-05	Inactive	ONO-AE3-208
5YHL[147]	PE2R4	Homo sapiens	2018-12-05	Inactive	ONO-AE3-208-Br
5ZKQ[148]	PTAFR	Homo sapiens	2018-06-20	Intermediate	ABT-491
5ZKP[148]	PTAFR	Homo sapiens	2018-06-20	Other	foropafant
5X33[149]	Q9WTK1	Cavia porcellus	2018-01-03	Inactive	BIIL 260
3V2W[150]	S1PR1	Homo sapiens	2012-02-15	Inactive	W146
3V2Y[150]	S1PR1	Homo sapiens	2012-02-15	Inactive	W146
6RNK[151]	SUCR1	Rattus norvegicus	2019-08-14	Intermediate	NF-56-EJ40
6IIV[152]	TA2R	Homo sapiens	2018-12-19	Intermediate	daltroban
6IIU[152]	TA2R	Homo sapiens	2018-12-19	Intermediate	ramatroban
4XT3[153]	US28	Strain AD169	2015-03-04	Active	CX <sub>3</sub> CL1
4XT1[153]	US28	Strain AD169	2015-03-04	Active	CX <sub>3</sub> CL1
5WB2[154]	US38	Strain AD169	2018-06-13	Active	CX <sub>3</sub> CL1

Table S2. Cross-docking structure pairs used to test interaction fingerprints. Ligands docked in two different charge states due to ionizable groups with pKa values near 7 are noted with \*.

Receptor	Protein PDB	Protein State	Ligand PDB	Ligand Function	Fingerprint(s)
AA1R	5N2S [12]	Inactive	6D9H [13]	Agonist	A, B
AA1R	6D9H [13]	Inactive	5N2S [12]	Agonist	A, B
AA1R	5N2S [12]	Inactive	5UEN [11]	Antagonist	Inactive
AA1R	5UEN [11]	Inactive	5N2S [12]	Agonist	Inactive
AA2AR	5WF5 [23]	Active	4UHR [16]	Agonist	A, B
AA2AR	4UHR [16]	Active	5WF5 [23]	Agonist	A, B
AA2AR	5WF5 [23]	Active	4UG2 [16]	Agonist	Active
AA2AR	4UG2 [16]	Active	5WF5* [23]	Agonist	Active
AA2AR	5IU4 [14]	Inactive	5MJZ [12]	Antagonist	Inactive
AA2AR	5MZJ [12]	Inactive	5IU4 [14]	Antagonist	Inactive
ADRB1	6IBL [52]	Active	4BVN [45]	Antagonist	A, B
ADRB1	4BVN [45]	Inactive	6IBL [52]	Agonist	A, B
ADRB1	6IBL [52]	Active	7JJO [155]	Agonist	Active
ADRB1	7JJO [155]	Active	6IBL [52]	Agonist	Active
ADRB1	4BVN [45]	Inactive	4AMJ [49]	Inverse Agonist	Inactive
ADRB1	4AMJ [49]	Inactive	4BVN [45]	Antagonist	Inactive
ADRB2	4LDE [55]	Active	5X7D [66]	Antagonist	A, B
ADRB2	5X7D [66]	Inactive	4LDE [55]	Agonist	A, B
ADRB2	4LDE [55]	Active	6MXT [64]	Agonist	Active
ADRB2	6MXT [64]	Active	4LDE [55]	Agonist	Active
CLTR1	6RZ5 [85]	Intermediate	6RZ4 [85]	Antagonist	Intermediate
CLTR1	6RZ4 [85]	Intermediate	6RZ5 [85]	Antagonist	Intermediate
CLTR1	6RZ7 [156]	Intermediate	6RZ8 [156]	Antagonist	Intermediate
CLTR1	6RZ8 [156]	Intermediate	6RZ7 [156]	Antagonist	Intermediate
CNR1	5XRA [86]	Active	5TGZ [87]	Antagonist	A, B
CNR1	5TGZ [87]	Inactive	5XRA [86]	Agonist	A, B
CNR1	5XRA [86]	Active	5U09 [89]	Inverse Agonist	A, B
CNR1	5U09 [89]	Inactive	5XRA [86]	Agonist	A, B
CNR1	5XRA [86]	Active	6N4B [88]	Agonist	Active
CNR1	6N4B [88]	Active	5XRA [86]	Agonist	Active
CNR1	5U09 [89]	Inactive	5TGZ [87]	Antagonist	A, B, Inactive
CNR1	5TGZ [87]	Inactive	5U09 [89]	Inverse Agonist	A, B, Inactive
MTR1A	6PS8 [114]	Inactive	6ME5 [113]	Agonist	Inactive
MTR1A	6ME5 [113]	Inactive	6PS8 [114]	Agonist	Inactive
MTR1B	6ME8 [113]	Inactive	6ME9 [113]	Agonist	Inactive
MTR1B	6ME9 [113]	Inactive	6ME8 [113]	Agonist	Inactive
OPRK	4DJH [126]	Inactive	6B73 [127]	Agonist	A, B
OPRK	6B73 [127]	Active	4DJH [126]	Antagonist	A, B
P2Y12	4PXZ [127]	Intermediate	4NTJ [141]	Antagonist	Intermediate
P2Y12	4NTJ [141]	Intermediate	4PXZ [140]	Agonist	Intermediate
5HT1B	4IAR [2]	Inactive	6G79 [3]	Agonist	A, B
5HT1B	6G79 [3]	Active	4IAR [2]	Agonist	A, B
5HT1B	4IAR [2]	Inactive	5V54 [1]	Antagonist	Inactive
5HT1B	5V54 [1]	Inactive	4IAR [2]	Agonist	Inactive
5HT2A	6A93 [4]	Inactive	6A94 [4]	Antagonist	Inactive
5HT2A	6A94 [4]	Inactive	6A93 [4]	Antagonist	Inactive
5HT2B	4IB4 [7]	Intermediate	6DRZ [5]	Antagonist	Intermediate
5HT2B	6DRZ [5]	Intermediate	4IB4 [7]	Agonist	Intermediate
5HT2B	6DRX [5]	Intermediate	6DS0 [5]	Antagonist	Intermediate

5HT2B	6DS0 [5]	Intermediate	6DRX [5]	Antagonist	Intermediate
5HT2B	6DRY [5]	Intermediate	5TVN [6]	Agonist	Intermediate
5HT2B	5TVN [6]	Intermediate	6DRY [5]	Agonist	Intermediate
5HT2B	6DRY [5]	Intermediate	6DS0 [5]	Antagonist	Intermediate
5HT2B	6DS0 [5]	Intermediate	6DRY [5]	Agonist	Intermediate
5HT2B	6DRX [5]	Intermediate	5TVN [6]	Agonist	Intermediate
5HT2B	5TVN [6]	Intermediate	6DRX [5]	Antagonist	Intermediate
5HT2C	6BQG [10]	Active	6BQH [10]	Inverse Agonist	A, B
5HT2C	6BQH [10]	Inactive	6BQG [10]	Agonist	A, B

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**Table S3.** Homology modeling targets and templates for GPCR comprising the external dataset used to validate the classifier.

Target Receptor	Template Receptor	CoINPocket Score <sup>c</sup>	Template PDBID	Template State	Loop Anchor 1 <sup>a</sup>	Loop Anchor 2
GPR31	SUCNR	1.19	6RNK	Intermediate	S153	G171
TAAR2	5HT1B	2.14	5V54	Inactive	F180	K207

<sup>a</sup>Anchor residues used for extracellular loop 2 modeling are numbered to match the numbering scheme present on GPCRdb.[157]

Table S4. List of experimentally determined Class A GPCR structures used in ligand prediction.

PDBID	GPCR	Species	Publication Date	Activation State	Ligand Name	Ligand Activity	Cross-docking PDBID <sup>a</sup>
7E2Y[158]	5HT1A	Homo sapiens	2021-04-14	Active	5-hydroxytryptamine	Agonist	7E2X
7E2Z[158]	5HT1A	Homo sapiens	2021-04-14	Active	aripiprazole	Agonist (partial)	7E2Y
5V54[1]	5HT1B	Homo sapiens	2018-02-07	Inactive	CHEMBL428892	Antagonist	7C61
4IAQ[2]	5HT1B	Homo sapiens	2013-03-13	Inactive	dihydroergotamine	Agonist	4IAR
6G79[3]	5HT1B	Homo sapiens	2018-06-20	Active	donitriptan	Agonist	4IAR
4IAR[2]	5HT1B	Homo sapiens	2013-03-13	Inactive	ergotamine	Agonist	4IAQ
7C61[159]	5HT1B	Homo sapiens	2020-07-29	Inactive	ergotamine	Antagonist	5V54
7E32[158]	5HT1D	Homo sapiens	2021-04-21	Active	5-hydroxytryptamine	Agonist	NA <sup>a</sup>
7E33[158]	5HT1E	Homo sapiens	2021-04-14	Active	BRL-54443	Agonist	NA
7EXD[160]	5HT1F	Homo sapiens	2021-08-04	Active	lasmiditan	Agonist	NA
6WHA[161]	5HT2A	Homo sapiens	2020-09-23	Active	25-CN-NBOH	Agonist	7WC8
6WH4[161]	5HT2A	Homo sapiens	2020-09-23	Inactive	CHEMBL428892	Inverse agonist	7WC8
6WGT[161]	5HT2A	Homo sapiens	2020-09-23	Inactive	lysergide	Agonist	7WC8
7VOE[162]	5HT2A	Homo sapiens	2021-12-22	Inactive	aripiprazole	Agonist (partial)	7VOD
7VOD[162]	5HT2A	Homo sapiens	2021-12-22	Inactive	cariprazine	Agonist (partial)	7VOE
6A93[4]	5HT2A	Homo sapiens	2019-02-13	Inactive	risperidone	Antagonist	6A94
6A94[4]	5HT2A	Homo sapiens	2019-02-13	Inactive	zotepine	Antagonist	6A93
6DS0[5]	5HT2B	Homo sapiens	2018-08-29	Intermediate	LY266097	Antagonist	6DRX
5TVN[6]	5HT2B	Homo sapiens	2017-02-01	Intermediate	lysergide	Agonist	4IB4
4IB4[7]	5HT2B	Homo sapiens	2013-03-13	Intermediate	ergotamine	Agonist	4NC3
4NC3[8]	5HT2B	Homo sapiens	2013-12-18	Intermediate	ergotamine	Agonist	4IB4
5TUD[9]	5HT2B	Homo sapiens	2017-07-26	Active	ergotamine	Agonist	4IB4
6DRX[5]	5HT2B	Homo sapiens	2018-08-29	Intermediate	lisuride	Antagonist	6DRZ
6DRY[5]	5HT2B	Homo sapiens	2018-08-29	Intermediate	methylergonovine	Agonist	4IB4
6DRZ[5]	5HT2B	Homo sapiens	2018-08-29	Intermediate	methysergide	Antagonist	6DRX
6BQG[10]	5HT2C	Homo sapiens	2018-02-14	Active	ergotamine	Agonist	6BQH
6BQH[10]	5HT2C	Homo sapiens	2018-02-14	Inactive	ritanserin	Inverse agonist	6BQG
5UEN[11]	AA1R	Homo sapiens	2017-03-01	Inactive	DU172	Antagonist	5N2S

5N2S[12]	AA1R	Homo sapiens	2017-07-26	Inactive	PSB36	Agonist	5UEN
6D9H[13]	AA1R	Homo sapiens	2018-06-20	Active	adenosine	Agonist	7LD3
7LD3[163]	AA1R	Homo sapiens	2021-09-08	Active	adenosine	Agonist	7LD4
7LD4[163]	AA1R	Homo sapiens	2021-09-08	Active	adenosine	Agonist	7LD3
5IU7[14]	AA2AR	Homo sapiens	2016-06-29	Inactive	2-(furan-2-yl)-5-N-[2-(4-phenylpiperidin-1-yl)ethyl]-1H-[1,2,4]triazolo[1,5-a][1,3,5]triazin-8-ium-5,7-diamine	Antagonist	5NM4
5IUA[14]	AA2AR	Homo sapiens	2016-06-29	Inactive	2-(furan-2-yl)-5-N-[3-(4-phenylpiperazin-1-yl)propyl]-1H-[1,2,4]triazolo[1,5-a][1,3,5]triazin-8-ium-5,7-diamine	Antagonist	5NM4
6ZDV[164]	AA2AR	Homo sapiens	2020-09-16	Inactive	2-methyl-3-(4-methylthiazol-2-yl)-4-oxo-6-propyl-4H-chromen-7-yl acetate	Antagonist	5NM4
5UIG[15]	AA2AR	Homo sapiens	2017-02-08	Inactive	5-amino-N-[(2-methoxyphenyl)methyl]-2-(3-methylphenyl)-2h-1,2,3-triazole-4-carboximidamide	Antagonist	5NM4
4UG2[16]	AA2AR	Homo sapiens	2015-04-08	Active	CGS 21680	Agonist	5WF5
4UHR[16]	AA2AR	Homo sapiens	2015-04-08	Active	CGS 21680	Agonist	5WF5
7ARO[165]	AA2AR	Homo sapiens	2021-04-07	Inactive	CHEMBL124345	Agonist (partial)	5NM4
5OLV[17]	AA2AR	Homo sapiens	2018-01-17	Inactive	CHEMBL1671936	Antagonist	5NM4
5IUB[14]	AA2AR	Homo sapiens	2016-06-29	Inactive	CHEMBL184061	Antagonist	5NM4
3UZC[18]	AA2AR	Homo sapiens	2012-03-21	Inactive	CHEMBL2024114	Antagonist	5NM4
5OLZ[17]	AA2AR	Homo sapiens	2018-01-17	Inactive	CHEMBL2024114	Antagonist	5NM4
5OM1[17]	AA2AR	Homo sapiens	2018-01-17	Inactive	CHEMBL2024114	Antagonist	5NM4
5OM4[17]	AA2AR	Homo sapiens	2018-01-17	Inactive	CHEMBL2024114	Antagonist	5NM4
6ZDR[164]	AA2AR	Homo sapiens	2020-09-16	Inactive	CHEMBL2030687	Antagonist	5NM4
5IU8[14]	AA2AR	Homo sapiens	2016-06-29	Inactive	CHEMBL3934661	Antagonist	5NM4
2YDV[19]	AA2AR	Homo sapiens	2011-05-18	Active	NECA	Agonist	5WF5
5G53[20]	AA2AR	Homo sapiens	2016-08-03	Active	NECA	Agonist	5WF5
6GDG[21]	AA2AR	Homo sapiens	2018-05-16	Active	NECA	Agonist	5WF5
5N2R[12]	AA2AR	Homo sapiens	2017-07-26	Inactive	PSB36	Antagonist	5NM4
3QAK[22]	AA2AR	Homo sapiens	2011-03-09	Active	UK-432,097	Agonist	5WF5
5WF5[23]	AA2AR	Homo sapiens	2018-02-21	Active	UK-432,097	Agonist	4UHR
5WF6[23]	AA2AR	Homo sapiens	2018-02-21	Active	UK-432,097	Agonist	5WF5
3EML[24]	AA2AR	Homo sapiens	2008-10-14	Inactive	ZM-241385	Antagonist	5NM4

3PWH[25]	AA2AR	Homo sapiens	2011-09-07	Inactive	ZM-241385	Antagonist	5NM4
3VG9[26]	AA2AR	Homo sapiens	2012-02-01	Inactive	ZM-241385	Antagonist	5NM4
3VGA[26]	AA2AR	Homo sapiens	2012-02-01	Inactive	ZM-241385	Antagonist	5NM4
4E1Y[27]	AA2AR	Homo sapiens	2012-07-25	Inactive	ZM-241385	Antagonist	5NM4
5IU4[14]	AA2AR	Homo sapiens	2016-06-29	Inactive	ZM-241385	Antagonist	5NM4
5JTB[28]	AA2AR	Homo sapiens	2017-05-31	Inactive	ZM-241385	Antagonist	5NM4
5K2A[29]	AA2AR	Homo sapiens	2016-09-21	Inactive	ZM-241385	Antagonist	5NM4
5K2B[29]	AA2AR	Homo sapiens	2016-09-21	Inactive	ZM-241385	Antagonist	5NM4
5K2C[29]	AA2AR	Homo sapiens	2016-09-21	Inactive	ZM-241385	Antagonist	5NM4
5K2D[29]	AA2AR	Homo sapiens	2016-09-21	Inactive	ZM-241385	Antagonist	5NM4
5NLX[30]	AA2AR	Homo sapiens	2017-09-27	Inactive	ZM-241385	Antagonist	5NM4
5NM2[30]	AA2AR	Homo sapiens	2017-09-27	Inactive	ZM-241385	Antagonist	5NM4
5NM4[30]	AA2AR	Homo sapiens	2017-09-27	Inactive	ZM-241385	Antagonist	5IU4
5OLG[17]	AA2AR	Homo sapiens	2018-01-17	Inactive	ZM-241385	Antagonist	5NM4
5UVI[31]	AA2AR	Homo sapiens	2017-05-24	Inactive	ZM-241385	Antagonist	5NM4
5VRA[32]	AA2AR	Homo sapiens	2017-12-13	Inactive	ZM-241385	Antagonist	5NM4
6AQF[33]	AA2AR	Homo sapiens	2018-01-10	Inactive	ZM-241385	Antagonist	5NM4
6JZH[166]	AA2AR	Homo sapiens	2019-10-30	Inactive	ZM-241385	Antagonist	5NM4
6LPJ[167]	AA2AR	Homo sapiens	2020-11-25	Inactive	ZM-241385	Antagonist	5NM4
6LPK[167]	AA2AR	Homo sapiens	2020-11-25	Inactive	ZM-241385	Antagonist	5NM4
6LPL[167]	AA2AR	Homo sapiens	2020-11-25	Inactive	ZM-241385	Antagonist	5NM4
6MH8[168]	AA2AR	Homo sapiens	2019-04-24	Inactive	ZM-241385	Antagonist	5NM4
6PS7[114]	AA2AR	Homo sapiens	2019-11-13	Inactive	ZM-241385	Antagonist	5NM4
6S0L[169]	AA2AR	Homo sapiens	2020-07-15	Inactive	ZM-241385	Antagonist	5NM4
6S0Q[169]	AA2AR	Homo sapiens	2020-07-15	Inactive	ZM-241385	Antagonist	5NM4
6WQA[170]	AA2AR	Homo sapiens	2020-11-18	Inactive	ZM-241385	Antagonist	5NM4
7RM5[171]	AA2AR	Homo sapiens	2021-09-08	Inactive	ZM-241385	Antagonist	5NM4
2YDO[19]	AA2AR	Homo sapiens	2011-05-18	Active	adenosine	Agonist	5WF5
3RFM[25]	AA2AR	Homo sapiens	2011-09-07	Inactive	caffeine	Antagonist	5NM4
5MZIP[12]	AA2AR	Homo sapiens	2017-07-26	Inactive	caffeine	Antagonist	5NM4
3UZA[18]	AA2AR	Homo sapiens	2012-03-21	Inactive	compound 4g [PMID: 22220592]	Antagonist	5NM4
6GT3[172]	AA2AR	Homo sapiens	2019-06-26	Inactive	imaradenant	Antagonist	5NM4
5MZJ[12]	AA2AR	Homo sapiens	2017-07-26	Inactive	theophylline	Antagonist	5NM4
5OLO[17]	AA2AR	Homo sapiens	2018-01-17	Inactive	tozadenant	Antagonist	5NM4

5OLH[17]	AA2AR	Homo sapiens	2018-01-17	Inactive	vipadenant	Antagonist	5NM4
3REY[25]	AA2AR	Homo sapiens	2011-09-07	Inactive	xanthine amine congener	Antagonist	5NM4
5CXV[34]	ACM1	Homo sapiens	2016-03-09	Inactive	0HK	Antagonist	6WJC
6ZG9[173]	ACM1	Homo sapiens	2021-10-06	Inactive	7-fluoro-5-methyl-3-[1-(oxan-4-yl)piperidin-4-yl]-1H-benzimidazol-2-one	Agonist	6ZfZ
6ZfZ[173]	ACM1	Homo sapiens	2021-10-06	Inactive	CHEMBL3354065	Agonist	6ZG4
6ZG4[173]	ACM1	Homo sapiens	2021-10-06	Inactive	ethyl (4S)-4-[4-[(1-methylcyclobutyl)carbamoyl]piperidin-1-yl]azepane-1-carboxylate	Agonist	6ZfZ
6OIJ[35]	ACM1	Homo sapiens	2019-05-08	Active	iperoxo	Agonist	6ZfZ
5ZKB[36]	ACM2	Homo sapiens	2018-11-21	Inactive	AF-DX 384	Antagonist	5ZKC
3UON[37]	ACM2	Homo sapiens	2012-02-01	Inactive	CHEMBL558910	Antagonist	5ZKC
5ZK3[36]	ACM2	Homo sapiens	2018-11-21	Inactive	CHEMBL558910	Antagonist	5ZKC
6U1N[174]	ACM2	Homo sapiens	2020-02-26	Active	LY2119620	Agonist	4MQS
5YC8[36]	ACM2	Homo sapiens	2018-11-21	Inactive	N-methyl scopolamine	Antagonist	5ZKC
5ZK8[36]	ACM2	Homo sapiens	2018-11-21	Inactive	N-methyl scopolamine	Antagonist	5ZKC
5ZKC[36]	ACM2	Homo sapiens	2018-11-21	Inactive	N-methyl scopolamine	Antagonist	5YC8
4MQS[38]	ACM2	Homo sapiens	2013-11-27	Active	iperoxo	Agonist	6OIK
5ZHP[39]	ACM3	Rattus norvegicus	2018-11-28	Inactive	(1R,2R,4S,5S,7s)-7-({[4-fluoro-2-(thiophen-2-yl)phenyl]carbamoyl}oxy)-9,9-dimethyl-3-oxa-9-azatricyclo[3.3.1.0~2,4~]nonan-9-ium	Antagonist	4U15
4U16[40]	ACM3	Rattus norvegicus	2014-11-26	Inactive	N-methyl scopolamine	Antagonist	4U15
4DAJ[41]	ACM3	Rattus norvegicus	2012-02-22	Inactive	tiotropium	Antagonist	4U15
4U14[40]	ACM3	Rattus norvegicus	2014-11-26	Inactive	tiotropium	Antagonist	4U15
5DSG[34]	ACM4	Homo sapiens	2016-03-16	Inactive	tiotropium	Antagonist	6KP6
6OL9[42]	ACM5	Homo sapiens	2019-12-11	Inactive	tiotropium	Inverse agonist	NA
6KUY[175]	ADRA2R	Homo sapiens	2019-12-04	Inactive	(2~{S})-4-fluoranyl-2-(1~{H}-imidazol-5-yl)-1-propan-2-yl-2,3-dihydroindole	Agonist (partial)	6KUX
6KUX[175]	ADRA2R	Homo sapiens	2019-12-04	Inactive	RSC	Antagonist	6KUY
6K41[176]	ADA2B	Homo sapiens	2020-04-15	Active	dexmedetomidine	Agonist	6K42
6K42[176]	ADA2B	Homo sapiens	2020-04-15	Active	dexmedetomidine	Agonist	6K41



6KUW[177]	ADA2C	Homo sapiens	2019-12-04	Inactive	(8aR,12aS,13aR)-12-ethylsulfonyl-3-methoxy-5,6,8,8a,9,10,11,12a,13,13a-decahydroisoquinolino[2,1-g][1,6]naphthyridine	Antagonist	NA
7BTS[178]	ADRB1	Homo sapiens	2020-12-02	Active	(-)-adrenaline	Agonist	6H7N
2VT4[43]	ADRB1	Meleagris gallopavo	2008-06-24	Inactive	(S)-cyanopindolol	Antagonist	4BVN
2YCY[44]	ADRB1	Meleagris gallopavo	2011-06-08	Inactive	(S)-cyanopindolol	Antagonist	4BVN
4BVN[45]	ADRB1	Meleagris gallopavo	2014-04-02	Inactive	(S)-cyanopindolol	Antagonist	3ZPR
5F8U[46]	ADRB1	Meleagris gallopavo	2015-12-23	Inactive	(S)-cyanopindolol	Antagonist	4BVN
6H7O[47]	ADRB1	Meleagris gallopavo	2018-10-17	Active	(S)-cyanopindolol	Agonist	6H7N
6H7N[47]	ADRB1	Meleagris gallopavo	2018-10-17	Active	(S)-xamoterol	Agonist	7BU7
5A8E[48]	ADRB1	Meleagris gallopavo	2015-09-30	Inactive	7-methylcyanopindolol	Inverse agonist	4AMJ
7BU7[178]	ADRB1	Homo sapiens	2020-12-02	Active	BI-167107	Agonist	6H7N
4AMI[49]	ADRB1	Meleagris gallopavo	2012-05-23	Inactive	bucindolol	Agonist	2Y02
2Y02[50]	ADRB1	Meleagris gallopavo	2011-01-12	Inactive	carmoterol	Agonist	2Y03
3ZPR[51]	ADRB1	Meleagris gallopavo	2013-04-03	Inactive	CHEMBL1559535	Antagonist	4BVN
3ZPQ[51]	ADRB1	Meleagris gallopavo	2013-04-03	Inactive	CHEMBL200234	Antagonist	4BVN
4AMJ[49]	ADRB1	Meleagris gallopavo	2012-05-23	Inactive	CHEMBL3799125	Inverse agonist	5A8E
2YCW[44]	ADRB1	Meleagris gallopavo	2011-06-01	Inactive	carazolol	Antagonist	4BVN
7BVQ[178]	ADRB1	Homo sapiens	2020-12-02	Inactive	carazolol	Inverse agonist	4AMJ
2Y00[50]	ADRB1	Meleagris gallopavo	2011-01-12	Inactive	dobutamine	Agonist (partial)	2Y01

2Y01[50]	ADRB1	Meleagris gallopavo	2011-03-30	Inactive	dobutamine	Agonist (partial)	2Y00
6H7L[47]	ADRB1	Meleagris gallopavo	2018-10-17	Active	dobutamine	Agonist	6H7N
2YCZ[44]	ADRB1	Meleagris gallopavo	2011-06-01	Inactive	iodocyanopindolol	Antagonist	4BVN
2Y03[50]	ADRB1	Meleagris gallopavo	2011-01-12	Inactive	levisoprenaline	Agonist	2Y02
6H7J[47]	ADRB1	Meleagris gallopavo	2018-10-17	Active	levisoprenaline	Agonist	6H7N
7JJO[155]	ADRB1	Meleagris gallopavo	2020-09-02	Active	levisoprenaline	Agonist	6H7N
7BU6[178]	ADRB1	Homo sapiens	2020-12-02	Active	noradrenaline	Agonist	6H7N
6IBL[52]	ADRB1	Meleagris gallopavo	2019-01-09	Active	arformoterol	Agonist	6H7N
6TKO[52]	ADRB1	Meleagris gallopavo	2020-06-17	Active	arformoterol	Agonist	6H7N
2Y04[50]	ADRB1	Meleagris gallopavo	2011-01-12	Inactive	levosalbutamol	Agonist (partial)	2Y00
6H7M[47]	ADRB1	Meleagris gallopavo	2018-10-17	Active	levosalbutamol	Agonist	6H7N
3P0G[53]	ADRB2	Homo sapiens	2011-01-19	Active	BI-167107	Agonist	4LDE
3SN6[54]	ADRB2	Homo sapiens	2011-07-20	Active	BI-167107	Agonist	4LDE
4LDE[55]	ADRB2	Homo sapiens	2013-09-25	Active	BI-167107	Agonist	6MXT
6E67[179]	ADRB2	Homo sapiens	2019-06-05	Active	BI-167107	Agonist	4LDE
6NI3[180]	ADRB2	Homo sapiens	2019-11-20	Active	BI-167107	Agonist	4LDE
3NYA[56]	ADRB2	Homo sapiens	2010-08-11	Inactive	CHEMBL1160734	Antagonist	6PS2
6PRZ[114]	ADRB2	Homo sapiens	2019-11-13	Inactive	CHEMBL1160734	Antagonist	6PS2
6PS2[114]	ADRB2	Homo sapiens	2019-11-13	Inactive	CHEMBL1160734	Antagonist	6PS3
3NY8[56]	ADRB2	Homo sapiens	2010-08-11	Inactive	CHEMBL1233766	Inverse agonist	2RH1
6PS4[114]	ADRB2	Homo sapiens	2019-11-13	Inactive	CHEMBL1233766	Antagonist	6PS2
3NY9[56]	ADRB2	Homo sapiens	2010-08-11	Inactive	CHEMBL1233771	Inverse agonist	2RH1
6PS3[114]	ADRB2	Homo sapiens	2019-11-13	Inactive	CHEMBL3799125	Antagonist	6PS2
2RH1[57]	ADRB2	Homo sapiens	2007-10-30	Inactive	carazolol	Inverse agonist	5D5A

4GBR[58]	ADRB2	Homo sapiens	2012-10-24	Inactive	carazolol	Inverse agonist	2RH1
5D5A[59]	ADRB2	Homo sapiens	2016-01-13	Inactive	carazolol	Inverse agonist	2RH1
5D5B[59]	ADRB2	Homo sapiens	2016-01-13	Inactive	carazolol	Inverse agonist	2RH1
5D6L[60]	ADRB2	Homo sapiens	2016-08-17	Inactive	carazolol	Inverse agonist	2RH1
5JQH[61]	ADRB2	Homo sapiens	2016-07-13	Inactive	carazolol	Inverse agonist	2RH1
3PDS[62]	ADRB2	Homo sapiens	2011-01-12	Inactive	FAUC50	Agonist	6PS2
7DHR[181]	ADRB2	Homo sapiens	2020-12-16	Active	levisoprenaline	Agonist	4LDE
4QKX[63]	ADRB2	Homo sapiens	2014-07-23	Active	Q27453560	Agonist	4LDE
7BZ2[182]	ADRB2	Homo sapiens	2020-08-05	Active	arformoterol	Agonist	4LDE
6PS0[114]	ADRB2	Homo sapiens	2019-11-13	Inactive	carazolol	Antagonist	6PS2
7DHI[181]	ADRB2	Homo sapiens	2020-12-16	Active	levosalbutamol	Agonist	4LDE
6PS5[114]	ADRB2	Homo sapiens	2019-11-13	Inactive	propranolol	Antagonist	6PS2
6MXT[64]	ADRB2	Homo sapiens	2018-11-14	Active	salmeterol	Agonist	4LDE
3D4S[65]	ADRB2	Homo sapiens	2008-06-17	Inactive	timolol	Inverse agonist	2RH1
6PS1[114]	ADRB2	Homo sapiens	2019-11-13	Inactive	timolol	Antagonist	6PS2
6PS6[114]	ADRB2	Homo sapiens	2019-11-13	Inactive	timolol	Antagonist	6PS2
7DH5[183]	ADRB3	Canis lupus familiaris	2021-08-04	Active	mirabegron	Agonist	NA
4ZUD[67]	AGTR1	Homo sapiens	2015-10-07	Inactive	olmesartan	Inverse agonist	4YAY
4YAY[68]	AGTR1	Homo sapiens	2015-04-22	Inactive	ZD-7155	Antagonist	4ZUD
5UNF[70]	AGTR2	Homo sapiens	2017-04-05	Active	compound 1 [PMID: 28379944]	Antagonist	5UNG
5UNG[70]	AGTR2	Homo sapiens	2017-04-05	Active	compound 1 [PMID: 28379944]	Antagonist	5UNF
5UNH[70]	AGTR2	Homo sapiens	2017-04-05	Active	compound 2 [PMID: 28379944]	Antagonist	5UNF
5O9H[75]	C5AR1	Homo sapiens	2018-01-10	Inactive	NDT9513727	Antagonist	6C1R
7F8Y[184]	CCKAR	Homo sapiens	2021-10-13	Inactive	devazepide	Antagonist	7F8U
7F8U[184]	CCKAR	Homo sapiens	2021-10-13	Inactive	linitript	Antagonist	7F8Y
6GPS[77]	CCR2	Homo sapiens	2019-01-02	Inactive	MK-0812	Antagonist	6GPX
6GPX[77]	CCR2	Homo sapiens	2019-01-02	Inactive	MK-0812	Antagonist	6GPS
6AKY[79]	CCR5	Homo sapiens	2018-10-24	Inactive	CCR5 antagonist 34	Antagonist	5UIW
6AKX[79]	CCR5	Homo sapiens	2018-10-24	Inactive	N-[(1S)-3-((3-exo)-3-[3-methyl-5-(propan-2-yl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]octan-8-yl)-1-(thiophen-2-yl)propyl]cyclopentanecarboxamide	Antagonist	5UIW
4MBS[80]	CCR5	Homo sapiens	2013-09-11	Inactive	maraviroc	Antagonist	5UIW

6RZ4[85]	CLTR1	Homo sapiens	2019-10-30	Intermediate	pranlukast	Antagonist	6RZ5
6RZ5[85]	CLTR1	Homo sapiens	2019-10-30	Intermediate	zafirlukast	Antagonist	6RZ4
6RZ8 [156]	CLTR2	Homo sapiens	2019-12-11	Intermediate	ONO-2080365	Antagonist	6RZ6
6RZ6[85]	CLTR2	Homo sapiens	2019-12-11	Intermediate	ONO-2570366	Antagonist	6RZ7
6RZ7 [156]	CLTR2	Homo sapiens	2019-12-11	Intermediate	ONO-2570366	Antagonist	6RZ6
6RZ9 [156]	CLTR2	Homo sapiens	2019-12-11	Intermediate	ONO-2770372	Antagonist	6RZ6
5XRA[86]	CNR1	Homo sapiens	2017-07-12	Active	AM11542	Agonist	5XR8
5TGZ[87]	CNR1	Homo sapiens	2016-11-02	Inactive	AM6538	Antagonist	5U09
5XR8[86]	CNR1	Homo sapiens	2017-07-12	Active	AM841	Agonist	5XRA
6KPG[91]	CNR1	Homo sapiens	2020-02-12	Active	AM841	Agonist	5XRA
7V3Z[185]	CNR1	Homo sapiens	2021-11-24	Active	CP55940	Agonist	5XRA
6N4B[88]	CNR1	Homo sapiens	2019-01-30	Active	MDMB-fubinaca	Agonist	5XRA
5U09[89]	CNR1	Homo sapiens	2016-12-07	Inactive	taranabant	Inverse agonist	5TGZ
5ZTY[90]	CNR2	Homo sapiens	2019-01-30	Inactive	AM10257	Antagonist	6KPC
6KPC[91]	CNR2	Homo sapiens	2020-02-12	Inactive	AM841	Agonist	5ZTY
6KPF[91]	CNR2	Homo sapiens	2020-02-12	Active	AM841	Agonist	6PT0
6PT0[92]	CNR2	Homo sapiens	2020-02-12	Active	WIN55212-2	Agonist	6KPF
3ODU[93]	CXCR4	Homo sapiens	2010-10-27	Inactive	isothiourea-1t	Antagonist	3OE0
3OE6[93]	CXCR4	Homo sapiens	2010-10-27	Inactive	isothiourea-1t	Antagonist	3ODU
3OE8[93]	CXCR4	Homo sapiens	2010-10-27	Inactive	isothiourea-1t	Antagonist	3ODU
3OE9[93]	CXCR4	Homo sapiens	2010-10-27	Inactive	isothiourea-1t	Antagonist	3ODU
7JVP[186]	DRD1	Homo sapiens	2021-02-24	Active	39YLC3L0ZU	Agonist	7JVQ
7CKX[187]	DRD1	Homo sapiens	2021-03-03	Active	A77636	Agonist	7JVP
7JV5[186]	DRD1	Homo sapiens	2021-02-24	Active	CHEMBL1160787	Agonist	7JVP
7CRH[187]	DRD1	Homo sapiens	2021-03-03	Active	CHEMBL1416789	Agonist	7JVP
7CKY[187]	DRD1	Homo sapiens	2021-03-03	Active	CHEMBL3697578	Agonist	7JVP
7JOZ[188]	DRD1	Homo sapiens	2021-04-14	Active	CHEMBL4453318	Agonist	7JVP
7JVQ[186]	DRD1	Homo sapiens	2021-02-24	Active	apomorphine	Agonist	7JVP
7CKW[187]	DRD1	Homo sapiens	2021-03-03	Active	fenoldopam	Agonist	7JVP
6VMS[189]	DRD2	Homo sapiens	2020-06-17	Active	bromocriptine	Agonist	7JVR
7JVR[186]	DRD2	Homo sapiens	2021-02-24	Active	bromocriptine	Agonist	6VMS
6LUQ[95]	DRD2	Homo sapiens	2020-03-04	Inactive	haloperidol	Antagonist	7DFP
6CM4[96]	DRD2	Homo sapiens	2018-03-14	Inactive	risperidone	Inverse agonist	6LUQ
7DFP[190]	DRD2	Homo sapiens	2020-12-30	Inactive	spiperone	Antagonist	6LUQ

7CMV[191]	DRD3	Homo sapiens	2021-03-10	Active	CHEMBL70565	Agonist	7CMU
3PBL[97]	DRD3	Homo sapiens	2010-11-03	Inactive	eticlopride	Antagonist	7CMV
7CMU[191]	DRD3	Homo sapiens	2021-03-10	Active	pramipexole	Agonist	7CMV
6IQL[192]	DRD4	Mus musculus	2019-12-04	Inactive	L745870	Antagonist	5WIU
5WIU[98]	DRD4	Homo sapiens	2017-10-18	Inactive	nemonapride	Antagonist	5WIV
5WIV[98]	DRD4	Homo sapiens	2017-10-18	Inactive	nemonapride	Antagonist	5WIU
6K1Q[99]	EDNRB	Homo sapiens	2019-07-17	Inactive	IRL 2500	Inverse agonist	6IGK
5X93[100]	EDNRB	Homo sapiens	2017-08-16	Inactive	K-8794	Antagonist	6IGK
5TZR[105]	FFAR1	Homo sapiens	2017-06-07	Intermediate	MK-8666	Agonist	4PHU
4PHU[107]	FFAR1	Homo sapiens	2014-07-16	Intermediate	fasiglifam	Agonist	5TZR
6KO5[193]	GHSR	Homo sapiens	2020-08-12	Inactive	CHEMBL1956994	Antagonist	7F83
7NA8[194]	GHSR	Homo sapiens	2021-12-15	Active	ibutamoren	Agonist	7NA7
7BR3[195]	GNRHR	Homo sapiens	2020-10-07	Inactive	elagolix	Antagonist	NA
7VUG[196]	GP139	Homo sapiens	2021-12-29	Active	JNJ-63533054	Agonist	7VUH
7VUH[196]	GP139	Homo sapiens	2021-12-29	Active	JNJ-63533054	Agonist	7VUG
7VUI[196]	GP139	Homo sapiens	2021-12-29	Active	JNJ-63533054	Agonist	7VUG
7VUJ[196]	GP139	Homo sapiens	2021-12-29	Active	JNJ-63533054	Agonist	7VUG
7CFM[197]	GPBAR	Homo sapiens	2020-09-09	Active	CHEMBL2331646	Agonist	7CFN
6LI0[110]	GPR52	Homo sapiens	2020-02-26	Inactive	derivative 17	Agonist	6LI2
3RZE[111]	HRH1	Homo sapiens	2011-06-15	Inactive	doxepin	Antagonist	7DFL
7DFL[198]	HRH1	Homo sapiens	2021-03-31	Active	histamine	Agonist	3RZE
4Z36[112]	LPAR1	Homo sapiens	2015-06-03	Inactive	ONO-3080573	Antagonist	4Z35
4Z34[112]	LPAR1	Homo sapiens	2015-06-03	Inactive	ONO-9780307	Antagonist	4Z35
4Z35[112]	LPAR1	Homo sapiens	2015-06-03	Inactive	ONO-9910539	Antagonist	4Z36
7K15[199]	LT4R1	Homo sapiens	2021-02-17	Inactive	N-(tert-butylsulfonyl)-4-fluoro-2-((3S,4R)-4-hydroxy-3-[(pyridin-2-yl)methyl]-3,4-dihydro-2H-1-benzopyran-7-yl}benzamide	Antagonist	7VKT
7F58[200]	MC4R	Homo sapiens	2021-11-03	Active	(3R)-N-[(2R)-3-(4-chlorophenyl)-1-[4-cyclohexyl-4-(1,2,4-triazol-1-ylmethyl) piperidin-1-yl]-1-oxidanylidene-propan-2-yl]-1,2,3,4-tetrahydroisoquinoline-3-carboxamide	Agonist	7PIU
7S8N[201]	MRGX2	Homo sapiens	2021-11-17	Active	(R)-ZINC-3573	Agonist	7S8L
7S8O[201]	MRGX2	Homo sapiens	2021-11-17	Active	(R)-ZINC-3573	Agonist	7S8L
7VDH[201]	MRGX2	Homo sapiens	2021-12-01	Active	compound 48/80	Agonist	7S8L

7VV6[201]	MRGX2	Homo sapiens	2021-12-01	Active	compound 48/80	Agonist	7S8L
7S8P[201]	MRGX4	Homo sapiens	2021-11-17	Active	N-[(1R,3R,5S,7R)-3,5-dimethyltricyclo[3.3.1.1~3,7~]decane-1-carbonyl]-D-phenylalanine	Agonist	NA
6ME4[113]	MTR1A	Homo sapiens	2019-04-24	Inactive	2-iodomelatonin	Agonist	6ME2
6ME3[113]	MTR1A	Homo sapiens	2019-04-24	Inactive	2-phenylmelatonin	Agonist	6ME2
6PS8[114]	MTR1A	Homo sapiens	2019-11-13	Inactive	2-phenylmelatonin	Agonist	6ME2
6ME5[113]	MTR1A	Homo sapiens	2019-04-24	Inactive	agomelatine	Agonist	6ME2
6ME2[113]	MTR1A	Homo sapiens	2019-04-24	Inactive	ramelteon	Agonist	6ME3
7DB6[202]	MTR1A	Homo sapiens	2021-08-18	Active	ramelteon	Agonist	7VGY
6ME6[113]	MTR1B	Homo sapiens	2019-04-24	Inactive	2-phenylmelatonin	Agonist	6ME8
6ME7[113]	MTR1B	Homo sapiens	2019-04-24	Inactive	2-phenylmelatonin	Agonist	6ME6
6ME8[113]	MTR1B	Homo sapiens	2019-04-24	Inactive	2-phenylmelatonin	Agonist	6ME6
6ME9[113]	MTR1B	Homo sapiens	2019-04-24	Inactive	ramelteon	Agonist	6ME6
6HLL[115]	NK1R	Homo sapiens	2019-01-16	Inactive	CP 99994	Antagonist	6HLP
6E59[116]	NK1R	Homo sapiens	2018-12-12	Inactive	L760735	Antagonist	6HLP
6HLO[115]	NK1R	Homo sapiens	2019-01-16	Inactive	aprepitant	Antagonist	6HLP
6J20[117]	NK1R	Homo sapiens	2019-03-06	Inactive	aprepitant	Antagonist	6HLP
6J21[117]	NK1R	Homo sapiens	2019-03-06	Inactive	aprepitant	Antagonist	6HLP
6HLP[115]	NK1R	Homo sapiens	2019-01-16	Inactive	netupitant	Antagonist	6HLO
5ZBH[118]	NPY1R	Homo sapiens	2018-04-25	Inactive	BMS-193885	Antagonist	5ZBQ
5ZBQ[118]	NPY1R	Homo sapiens	2018-04-25	Inactive	CHEMBL3747822	Antagonist	5ZBH
7DDZ[203]	NPY2R	Homo sapiens	2021-01-27	Inactive	CHEMBL1823578	Antagonist	NA
6Z8N[204]	NTR1	Rattus norvegicus	2021-02-10	Intermediate	(2~{S})-4-methyl-2-[(1-quinolin-8-ylsulfonylindol-3-yl)carbonylamino] pentanoic acid	Agonist	6Z4V
6ZA8[204]	NTR1	Rattus norvegicus	2021-02-10	Intermediate	CHEMBL508044	Agonist (partial)	6Z4V
6Z4Q[204]	NTR1	Rattus norvegicus	2021-02-10	Inactive	SR142948A	Inverse agonist	6ZIN
6Z4S[204]	NTR1	Rattus norvegicus	2021-02-10	Inactive	meclinetant	Inverse agonist	6ZIN
6ZIN[204]	NTR1	Rattus norvegicus	2021-02-10	Inactive	meclinetant	Inverse agonist	6Z4S
6PT3[205]	OPRD	Homo sapiens	2019-12-11	Active	DPI-287	Agonist	6PT2

4EJ4[123]	OPRD	Mus musculus	2012-05-16	Inactive	naltrindole	Antagonist	4N6H
4N6H[124]	OPRD	Homo sapiens	2013-12-25	Inactive	naltrindole	Antagonist	4RWD
4DJH[126]	OPRK	Homo sapiens	2012-03-21	Inactive	JDtic	Antagonist	6VI4
6VI4[206]	OPRK	Homo sapiens	2020-03-18	Inactive	JDtic	Antagonist	4DJH
6B73[127]	OPRK	Homo sapiens	2018-01-17	Active	MP1104	Agonist	4DJH
5C1M[128]	OPRM	Mus musculus	2015-08-05	Active	BU72	Agonist	7SBF
4DKL[129]	OPRM	Mus musculus	2012-03-21	Inactive	methyl 4-[[[(4R,4aS,7R,7aR,12bS)-3-(cyclopropylmethyl)-4a,9-dihydroxy-1,2,4,5,6,7,7a,13-octahydro-4,12-methanobenzofuro[3,2-e]isoquinolin-7-yl]amino]-4-oxobutanoate	Antagonist	5C1M
5DHG[131]	OPRX	Homo sapiens	2015-10-21	Inactive	CHEMBL1783826	Antagonist	5DHH
5DHH[131]	OPRX	Homo sapiens	2015-10-21	Inactive	SB 612111	Antagonist	5DHG
4EA3[132]	OPRX	Homo sapiens	2012-04-25	Inactive	compound 24 [PMID: 16451050]	Antagonist	5DHG
6TP4[134]	OX1R	Homo sapiens	2020-01-01	Inactive	ACT-462206	Antagonist	6TOD
6TOS[134]	OX1R	Homo sapiens	2020-01-15	Inactive	CHEMBL2413522	Antagonist	6TOD
6TQ4[134]	OX1R	Homo sapiens	2020-01-01	Inactive	CHEMBL4590386	Antagonist	6TOD
6TQ6[134]	OX1R	Homo sapiens	2020-01-01	Inactive	CHEMBL4592653	Antagonist	6TOD
6TOD[134]	OX1R	Homo sapiens	2020-01-01	Inactive	EMPA: N-ethyl-2-[(6-methoxypyridin-3-yl)-(2-methylphenyl)sulfonyl-amino]-N-(pyridin-3-ylmethyl)ethanamide	Antagonist	6TOS
6V9S[207]	OX1R	Homo sapiens	2020-07-15	Inactive	JH112	Antagonist	6TOD
6TQ7[134]	OX1R	Homo sapiens	2020-01-01	Inactive	SB-334867	Antagonist	6TOD
6TQ9[134]	OX1R	Homo sapiens	2020-01-01	Inactive	SB-408124	Antagonist	6TOD
4ZJC[135]	OX1R	Homo sapiens	2016-03-09	Inactive	SB-674042	Antagonist	6TOD
6TP3[134]	OX1R	Homo sapiens	2020-01-01	Inactive	daridorexant	Antagonist	6TOD
6TP6[134]	OX1R	Homo sapiens	2020-01-01	Inactive	filorexant	Antagonist	6TOD
6TOT[134]	OX1R	Homo sapiens	2020-01-15	Inactive	lemborexant	Antagonist	6TOD
4ZJ8[135]	OX1R	Homo sapiens	2016-03-09	Inactive	suvorexant	Antagonist	6TOD
6TO7[134]	OX1R	Homo sapiens	2020-01-01	Inactive	suvorexant	Antagonist	6TOD
5WQC[136]	OX2R	Homo sapiens	2017-11-29	Inactive	EMPA	Antagonist	5WS3
5WS3[136]	OX2R	Homo sapiens	2017-12-13	Inactive	EMPA	Antagonist	5WQC
6TPG[134]	OX2R	Homo sapiens	2020-01-01	Inactive	EMPA	Antagonist	5WQC
6TPN[134]	OX2R	Homo sapiens	2020-01-01	Inactive	HTL6641	Antagonist	5WQC

7L1V[208]	OX2R	Homo sapiens	2021-02-10	Active	compound 1 [PMID: 33547286]	Agonist	7L1U
4S0V[137]	OX2R	Homo sapiens	2015-01-14	Inactive	suvorexant	Antagonist	5WQC
6TPJ[134]	OX2R	Homo sapiens	2020-01-01	Inactive	suvorexant	Antagonist	5WQC
6TPK[209]	OXYR	Homo sapiens	2020-08-05	Inactive	retosiban	Antagonist	7RYC
4XNW[139]	P2RY1	Homo sapiens	2015-04-01	Intermediate	MRS2500	Antagonist	4XNV
4PXZ[140]	P2Y12	Homo sapiens	2014-04-30	Intermediate	2-(methylsulfanyl)adenosine 5'-(trihydrogen diphosphate)	Agonist	4NTJ
4PY0[140]	P2Y12	Homo sapiens	2014-04-30	Intermediate	2-(methylsulfanyl)adenosine 5'-(trihydrogen diphosphate)	Agonist (partial)	4PXZ
4NTJ[141]	P2Y12	Homo sapiens	2014-03-26	Intermediate	AZD1283	Antagonist	4PXZ
3VW7[142]	PAR1	Homo sapiens	2012-12-12	Intermediate	vorapaxar	Antagonist	7TD0
5NDD[143]	PAR2	Homo sapiens	2017-05-03	Intermediate	AZ8838	Antagonist	5NDZ
7M8W[210]	PD2R2	Homo sapiens	2021-08-25	Inactive	15(R)-15-methyl-prostaglandin D <sub>2</sub>	Antagonist	6D27
6D27[144]	PD2R2	Homo sapiens	2018-10-03	Inactive	CHEMBL179036	Antagonist	7M8W
6D26[144]	PD2R2	Homo sapiens	2018-10-03	Inactive	fevipiprant	Antagonist	7M8W
7CX2[211]	PE2R2	Homo sapiens	2021-05-05	Active	prostaglandin E <sub>2</sub>	Agonist	7CX3
7CX4[211]	PE2R2	Homo sapiens	2021-05-05	Active	evatanepag	Agonist	7CX3
7CX3[211]	PE2R2	Homo sapiens	2021-05-05	Active	taprenepag	Agonist	7CX2
6M9T[145]	PE2R3	Homo sapiens	2018-12-05	Active	misoprostol-FA	Agonist	6AK3
6AK3[146]	PE2R3	Homo sapiens	2018-12-05	Active	prostaglandin E <sub>2</sub>	Agonist	6M9T
5YWY[147]	PE2R4	Homo sapiens	2018-12-05	Inactive	ONO-AE3-208	Antagonist	5YHL
5YHL[147]	PE2R4	Homo sapiens	2018-12-05	Inactive	ONO-AE3-208-Br	Antagonist	5YWY
7D7M[212]	PE2R4	Homo sapiens	2020-11-18	Active	prostaglandin E <sub>2</sub>	Agonist	5YWY
5ZKQ[148]	PTAFR	Homo sapiens	2018-06-20	Intermediate	ABT-491	Inverse agonist	5ZKP
5ZKP[148]	PTAFR	Homo sapiens	2018-06-20	Other	foropafant	Antagonist	5ZKQ
5X33[149]	Q9WTK1	Cavia porcellus	2018-01-03	Inactive	BIIL 260	Antagonist	NA
7EO2[213]	S1PR1	Homo sapiens	2022-01-05	Active	(S)-FTY720-phosphate	Agonist	7TD4
3V2W[150]	S1PR1	Homo sapiens	2012-02-15	Inactive	W146	Antagonist	3V2Y
3V2Y[150]	S1PR1	Homo sapiens	2012-02-15	Inactive	W146	Antagonist	3V2W
7EO4[213]	S1PR1	Homo sapiens	2022-01-05	Active	siponimod	Agonist	7TD4
7WF7[213]	S1PR1	Homo sapiens	2022-01-05	Active	sphingosine 1-phosphate	Agonist	7TD4
7EW2[214]	S1PR3	Homo sapiens	2021-09-29	Active	(S)-FTY720-phosphate	Agonist	7EW3
7EW4[214]	S1PR3	Homo sapiens	2021-09-29	Active	CYM-5541	Agonist	7EW2
7EW3[214]	S1PR3	Homo sapiens	2021-09-29	Active	sphingosine 1-phosphate	Agonist	7EW2



7C4S[215]	S1PR3	Homo sapiens	2021-06-09	Active	sphingosine 1-phosphate	Agonist	7EW2
7EW1[216]	S1PR5	Homo sapiens	2021-09-29	Active	siponimod	Agonist	NA
6Z10[217]	SUCR1	Rattus norvegicus	2020-09-16	Intermediate	CHEMBL4751488	Antagonist	6RNK
6RNK[151]	SUCR1	Rattus norvegicus	2019-08-14	Intermediate	NF-56-EJ40	Antagonist	6Z10
6IIV[152]	TA2R	Homo sapiens	2018-12-19	Intermediate	daltroban	Antagonist	6IIU
6IIU[152]	TA2R	Homo sapiens	2018-12-19	Intermediate	ramatroban	Antagonist	6IIV

<sup>a</sup>Entries marked “NA” represent cases where a suitable structure for cross-docking was not available.

Table S5. Counts of active and inactive ligands docked into DUD-E experimentally determined structures and homology models.

Receptor	Inactive Ligands		Active Ligands			
	Number of Ligands <sup>a</sup>	Number of Ligands in Subset <sup>b</sup>	Number of IUPHAR[218] Ligands <sup>c</sup>	Number of Ligands in Subset <sup>b</sup>	Subset Agonists	Subset Antagonists
AA2AR	104	25	90	18	9	9
ADRB1	52	25	41	18	9	9
ADRB2	108	25	46	18	9	9
CXCR4	16	15	8	8	0	8
DRD3	5	5	57	18	9	9
Total	285	95	242	80	36	44

<sup>a</sup>Number of ligands docked into each target's experimentally determined structure retrieved from DUD-E.

<sup>b</sup>Number of ligands docked into each target's set of 3 loop-refined homology models.

<sup>c</sup>Number of active ligands retrieved from IUPHAR Guide to Pharmacology[218] per target.

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