Table S6. G_s-mediated cAMP accumulation assay results of D5R.

Potency (pEC50) were extracted from a minimum of 3 independent assays in at least triplicate. pEC50 displayed values are mean ± SEM. Delta FOB for difference in either Fold of Basal (FOB) or Delta pEC50 when compared to wild-type receptor value. Average Emax and basal values were determined from "log(agonist) vs. response – Variable slope (four parameters) or log(inhibition) vs. response – Variable slope (four parameters)" function in Graphpad Prism 8.4 software (Graphpad Software Inc., San Diego, CA) and were divided by 10^3 for display, basal values are enclosed with parentheses in the table column. Color scheme is based on the effects of mutations on relative pEC50 and Fold of Basal (FOB) values with red for reduced potency/efficacy and blue for increased potency/efficacy when compared to wild-type values for each ligand. ND - not determined.

		D5-Dopamine					D5R-Rotigotine				
BW		**Emax (Basal)**	**FOB**	**ΔFOB**	**pEC50**	**ΔpEC50**	**Emax (Basal)**	**FOB**	**ΔFOB**	**pEC50**	**ΔpEC50**
	WT	18.2 ± 2.9 (1.8 ± 0.5)	13.2 ± 4.9	0	9.82 ± 0.08	0	17.5 ± 1.2 (1.7 ± 0.3)	11.8 ± 2.3	0	9.25 ± 0.12	0.00
2.61	K98A	29.5 ± 8.3 (1.3 ± 0.5)	24.9 ± 2.4	11.7	9.51 ± 0.02	-0.31	31.9 ± 0.1 (1.5 ± 0.1)	24.0 ± 2.6	10.8	9.29 ± 0.12	0.04
3.28	W116A	37.9 ± 8.9 (0.3 ± 0.1)	142.1 ± 5.9	128.9	7.02 ± 0.01	-2.8	24.0 ± 2.9 (0.3 ± 0.1)	97.3 ± 7.3	84.1	6.13 ± 0.11	-3.12
3.32	D120A	16.9 ± 5.2 (13.2 ± 4)	1.3 ± 0.1	-11.9	7.10 ± 1.19	-2.72	N.D.	N.D.	N.D.	N.D.	N.D.
3.33	I121A	30.2 ± 7.2 (0.2 ± 0.1)	131.9 ± 10.3	118.7	5.47 ± 0.13	-4.35	27.7 ± 4.1 (0.2 ± 0.1)	119.4 ± 13.0	106.2	5.48 ± 0.10	-3.77
3.36	S124A	36 ± 11.6 (0.7 ± 0.3)	61.2 ± 9.1	48	7.46 ± 0.14	-2.36	38.5 ± 9.2 (0.8 ± 0.3)	58.5 ± 7.1	45.3	7.39 ± 0.13	-1.86
3.37	T125A	18.8 ± 7.2 (1.2 ± 0.5)	15.8 ± 0.2	2.6	6.35 ± 0.10	-3.47	25.6 ± 5.1 (1.1 ± 0.3)	23.8 ± 1.7	10.6	8.43 ± 0.10	-0.82
3.40	I128A	18.6 ± 4.0 (0.1 ± 0.1)	124.6 ± 2.6	111.4	6.44 ± 0.10	-3.38	2.0 ± 0.5 (0.1 ± 0.1)	13.8 ± 2.0	0.6	6.75 ± 0.22	-2.50
ECL2	S219A	18.9 ± 5.0 (1.3 ± 0.3)	19.1 ± 8.0	5.9	9.87 ± 0.11	0.05	21.4 ± 3.4 (1.8 ± 0.4)	14.1 ± 4.6	0.9	9.49 ± 0.09	0.24
ECL2	L221A	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
5.42	S229A	22.4 ± 4.6 (2.0 ± 0.5)	15.3 ± 6.4	2.1	7.49 ± 0.11	-2.33	23.0 ± 4.0 (1.7 ± 0.6)	21.0 ± 6.4	7.8	6.37 ± 0.43	-2.88
5.43	S230A	35 ± 12.6 (0.2 ± 0.1)	178.6 ± 77.3	165.4	7.48 ± 0.14	-2.34	39.4 ± 9.2 (0.4 ± 0.1)	95.4 ± 12.5	82.2	7.37 ± 0.10	-1.88
5.46	S233A	33.5 ± 9.4 (2.4 ± 0.6)	18.8 ± 8.3	5.6	6.27 ± 0.14	-3.55	24.7 ± 5.2 (1.9 ± 0.6)	20.4 ± 6.9	7.2	9.84 ± 0.19	0.59
6.48	W309A	31.4 ± 10.1 (0.1 ± 0.1)	273.5 ± 27.0	260.3	5.73 ± 0.06	-4.09	7.0 ± 1.8 (0.1 ± 0.1)	55.1 ± 6.4	41.9	7.10 ± 0.11	-2.15
6.51	F312A	27.4 ± 7.4 (0.2 ± 0.1)	128.9 ± 13.9	115.7	6.16 ± 0.21	-3.66	29.6 ± 5.9 (0.2 ± 0.1)	164.7 ± 28.2	151.5	6.66 ± 0.15	-2.59
6.52	F313A	37.7 ± 16.6 (0.2 ± 0.1)	150.3 ± 22.4	137.1	6.64 ± 0.40	-3.18	42.0 ± 11.4 (0.2 ± 0.1)	161.2 ± 19.9	148.0	6.76 ± 0.21	-2.49
6.55	N316A	30.6 ± 15.2 (0.2 ± 0.1)	135.3 ± 21.0	122.1	6.72 ± 0.06	-3.1	34.1 ± 12.0 (0.1 ± 0.1)	247.6 ± 75.5	234.4	6.92 ± 0.06	-2.33
7.35	F341A	30.7 ± 9.5 (0.4 ± 0.1)	76.1 ± 0.4	62.9	7.96 ± 0.04	-1.86	34.1 ± 5.3 (0.4 ± 0.1)	86.9 ± 3.9	73.7	7.62 ± 0.08	-1.63
7.36	D342A	24.7 ± 8.2 (3.1 ± 0.3)	7.4 ± 1.8	-5.8	9.58 ± 0.18	-0.24	27.5 ± 7.3 (2.8 ± 0.5)	9.7 ± 2.3	-3.5	9.26 ± 0.25	0.01
7.39	V345A	20.4 ± 4.4 (3.8 ± 1.0)	5.5 ± 0.3	-7.7	9.78 ± 0.04	-0.04	20.4 ± 3.4 (3.8 ± 0.9)	5.6 ± 0.3	-7.6	9.91 ± 0.11	0.66
7.43	W349A	11.6 ± 3.3 (0.1 ± 0.1)	75.5 ± 13.9	62.3	6.92 ± 0.06	-2.9	1.6 ± 0.3 (0.2 ± 0.1)	9.2 ± 0.9	-4.0	6.17 ± 0.34	-3.08