

Supplementary Information for

β 2-adrenergic receptor regulates ER-mitochondria contacts

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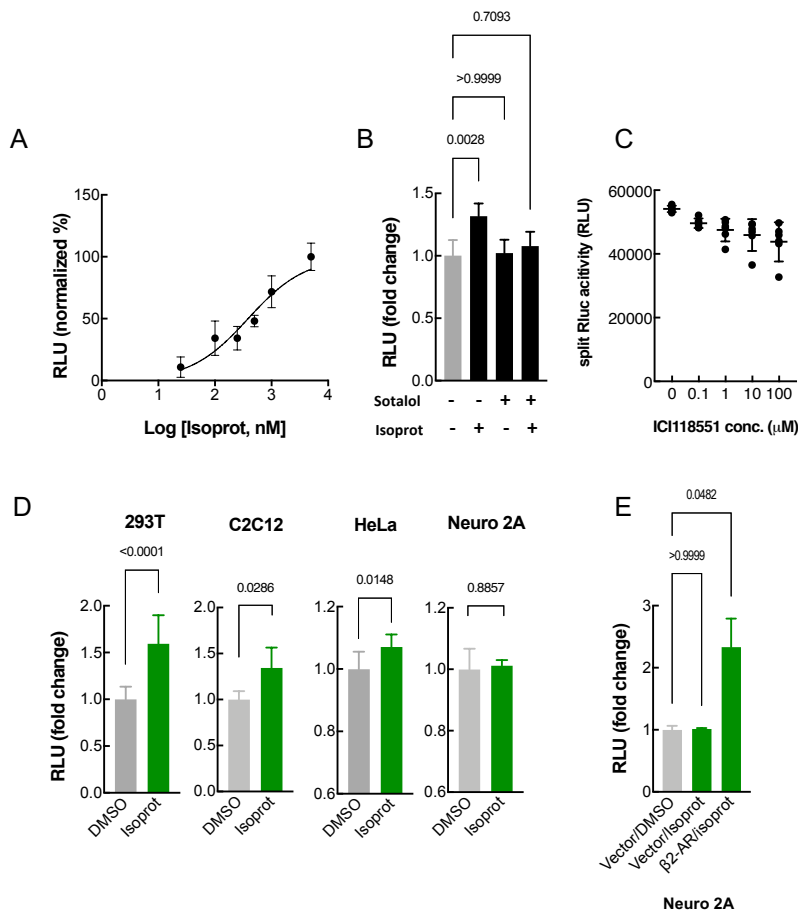


Figure S1. **A**, A concentration-responsive curve of isoproterenol (25, 100, 250, 500, 1000, 5000 nM) effect on split-Rluc activity ($n = 16$; nonlinear regression (non-linear fit, $EC_{50} = 385.4$ nM); Error bars: SEM). **B**, The effect of β -AR antagonist (sotalolol, 250 μ M) on isoproterenol (isoprot)-induced split-Rluc activity. $n = 6$; Kruskal-Wallis test with Dunn's multiple comparisons test. **C**, Split-Rluc activities (RLU, relative light unit) of HEK293T cells treated with different concentrations of ICI 118551 hydrochloride, an inverse β 2-AR agonist. **D**, Split-Rluc activities (fold change, normalized with the mean of DMSO) of HEK293T, HeLa, C2C12 or Neuro2a cells, treated with DMSO (control) or isoproterenol (1 μ M). $n = 15$ (293T), 4 (C2C12 and N2a), 8 (HeLa); Unpaired two-tailed t-test (for 293T); Mann-Whitney test (C2C12, HeLa, N2a). 293T data presented here are from the same set data used in Fig 2SA, just for easy comparison. **E**, Split Rluc activities of the Neuro2a cells transfected with vector or β 2-AR construct treated with DMSO or isoprot as indicated. All data in B, D,E: mean $\pm$ SD; data in C: median with interquartile range. p values (if ≤ 0.05 , significant) are indicated at the top of each graph.

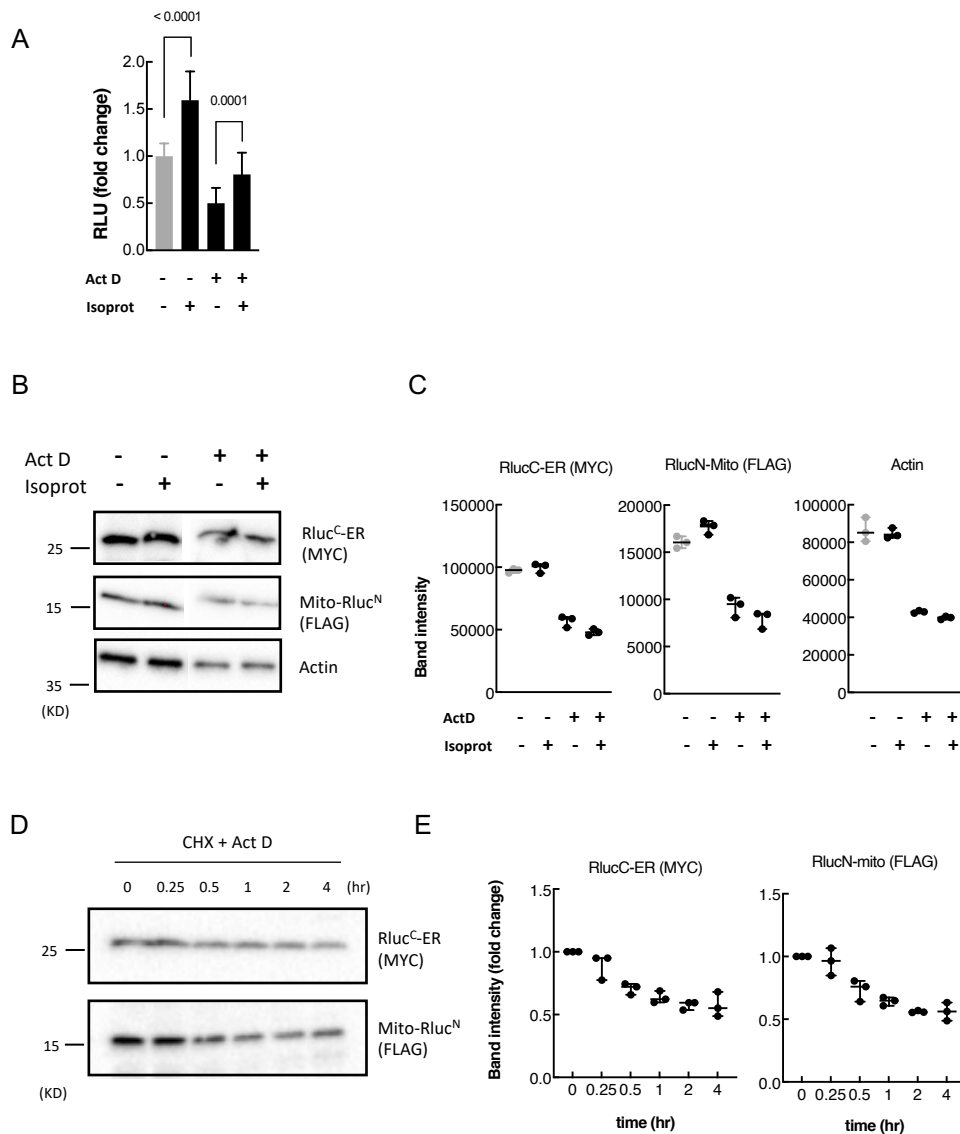


Figure S2. **A**, The effect of the transcription inhibitor actinomycin D (ActD, 0.8 μ M) on isoproterenol (1 μ M)-induced split-Rluc activity. One-way ANOVA with Sidak's multiple comparisons test ($n = 15$). **B**, The effect of Act D and isoproterenol on the expression level of split-Rluc fragments. Western blot analysis of split-Rluc fragments in HEK293T cells treated with indicated drugs, probed with MYC (for Rluc^C-ER), FLAG (for Mito-Rluc^N), or actin (loading control) antibody. Full-length blots are presented in Supplementary Figure 7. **C**, Quantification of Western blot analysis as shown in C. **D**, Western blot analysis of protein levels for split-Rluc fragments in HEK293T cells treated with Act D (0.8 μ M) and cycloheximide (protein translation inhibitor, 20 μ g/ml). Samples were taken at the time points indicated and probed with MYC or FLAG antibody. Full-length blots are presented in Supplementary Figure 8. **E**, Quantification of Western blot analysis as shown in D. Data in A: mean $\pm$ SD; data in C, E: median with interquartile range. p values (if ≤ 0.05 , significant) are indicated at the top of each graph.

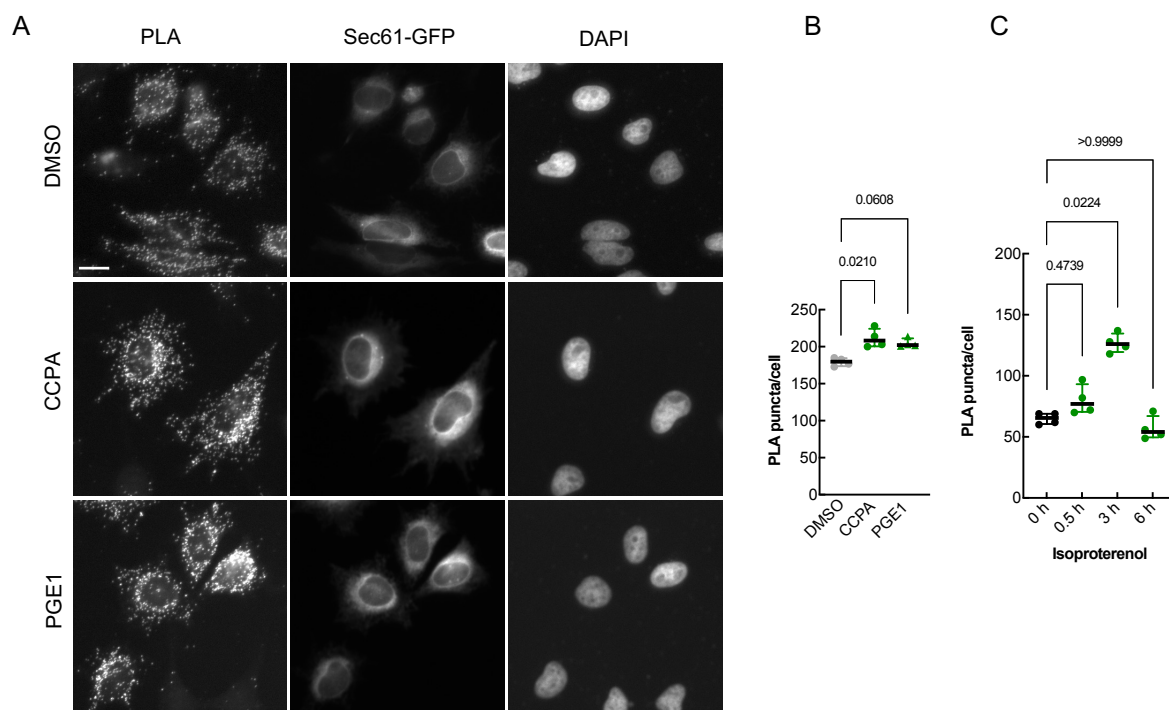


Figure S3. A, Representative images of proximity ligation assay (PLA) in HeLa cells treated with DMSO, CCPA, or PGE1 (1 μ M each). PLA fluorescent signal indicates a close apposition between ER and Mito. Sec61-GFP, to label ER; DAPI, nucleus. **B**, Quantifications of PLA signals as shown in A. Kruskal-Wallis test with Dunn's multiple comparisons test ($n = 4$ with 77-97 cells each). **C**, Quantification of PLA in HeLa cells treated with isoproterenol (1 μ M) for 0 (DMSO), 0.5, 3, or 6 hours ($n = 4$ with 71, 52, 48, 56 cells, respectively; Kruskal-Wallis test with Dunn's multiple comparison test). **C**, Representative images of TMRM (measuring mitochondrial membrane potential) fluorescent signal in HeLa cells treated with DMSO or CCPA (1 μ M each). p values (if ≤ 0.05 , significant) are indicated at the top of each graph. All data: median with interquartile range. Scale bars: 10 μ m

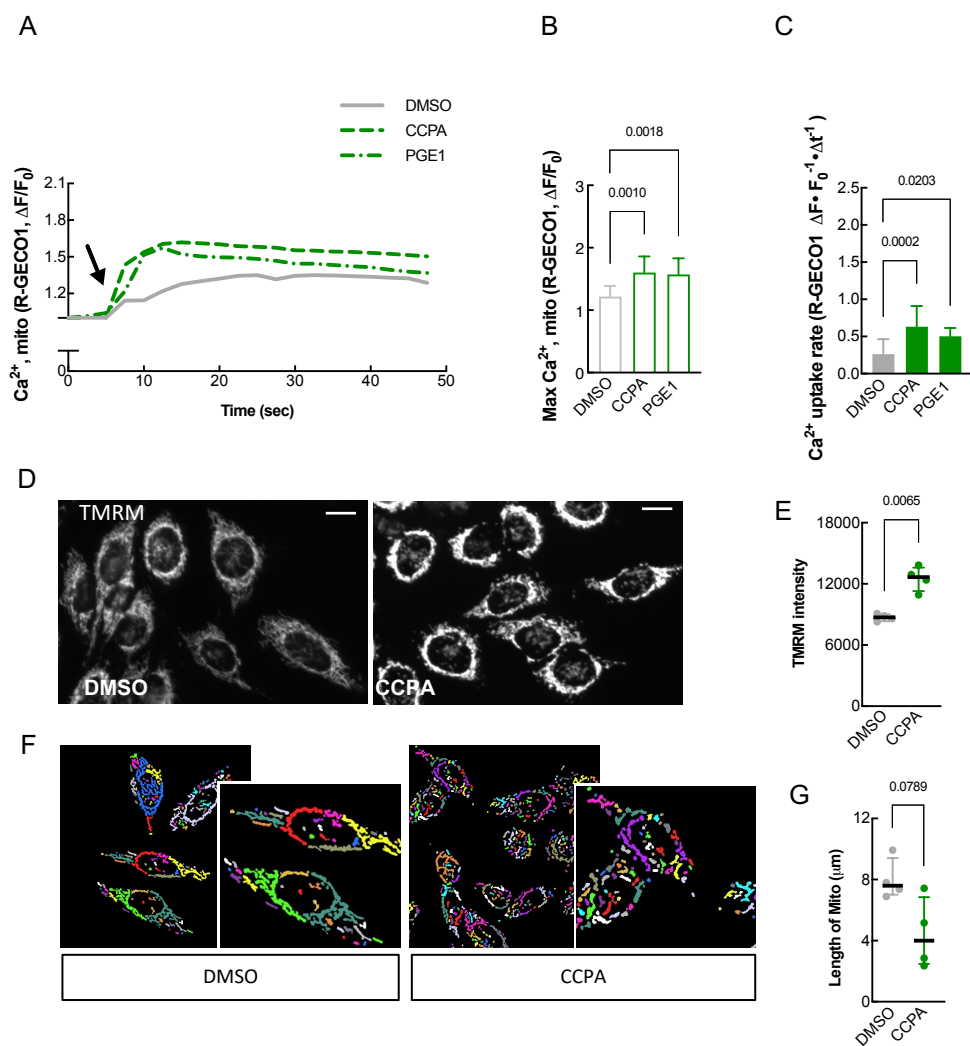


Figure S4. **A**, Mito Ca²⁺ uptake in response to histamine (100 μM). Mito-R-GECO1 fluorescent intensity change averaged over multiple cells (HeLa) is plotted every 2.5 sec in DMSO-, CCPA-, or PGE1- treated HeLa cells. Arrow: histamine addition. **B**, Maximum peak of Mito Ca²⁺ uptake (as in A). One-way ANOVA with Dunn's multiple comparisons test ($n = 10, 13, 15$ for DMSO, CCPA, PGE1). **C**, Mito Ca²⁺ uptake rate (as in A; 7.5 to 12.5 sec). Kruskal-Wallis test with Dunn's multiple comparisons test ($n = 12$, DMSO; 15, CCPA and PGE1). A-C are from the sister experiments shown in Fig 2A-C. **D**, Representative images of TMRM signal (for Mito membrane potential) (HeLa cells). **E**, Quantification of TMRM intensity as in E. Unpaired two-tailed t -test with Welch's correction ($n = 4$ with 52 cells each). **F**, Representative images of Mito (converted in Image Analyst MKII software) used for length comparison (HeLa cells, 1 μM drug). **G**, Quantification of Mito length as in F. Mann Whitney test ($n = 4$ with 278 (DMSO) or 425-445 (CCPA) Mito for each experiment). Each drug: used at 1 μM final conc. Data in B, C: mean $\pm$ SD; data in E, G: median with interquartile range. Scale bars: 10 μm .

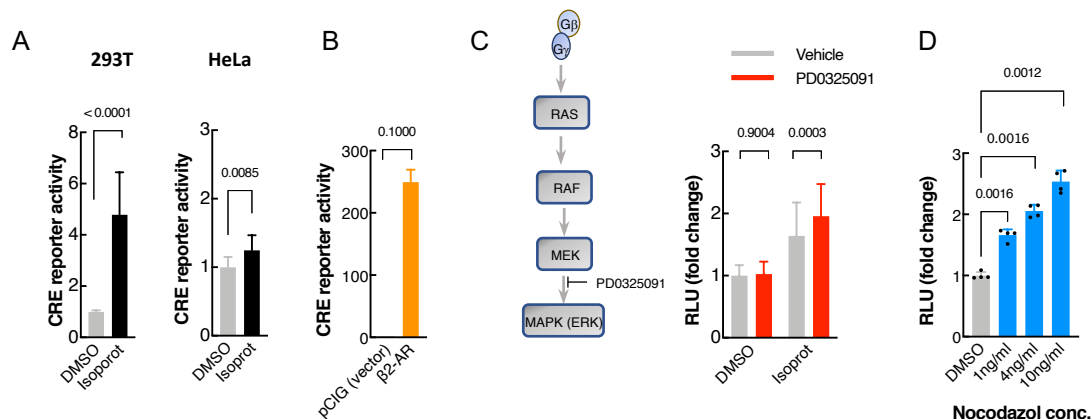


Figure S5. **A**, cAMP response element (CRE) reporter gene assay in HEK293T (A) or HeLa (B) cells treated with DMSO or isoproterenol (isoprot, 1 μ M). $n = 9$; Two-tailed unpaired t -test. **B**, cAMP response element (CRE) reporter gene activity in HEK293T cells transfected with pCIG (vector expressing GFP) or β 2-AR expression construct. $n = 3$; Mann Whitney test. **C**, (Left) Simplified schematic depicting G β γ downstream pathway leading to activation of MAPK. PD0325091 is a chemical inhibitor of MAPK. (Right) Split-Rluc activities (RLU, normalized to the mean of DMSO/Vehicle treated) of the HEK293T cells treated with vehicle or PD0325091 (1 μ M, MAPK inhibitor), in the presence of DMSO or isoproterenol (1 μ M). $n = 20$. 2-way ANOVA with Sidak's multiple comparisons test. **D**, Split-Rluc activities (RLU, normalized to the mean of DMSO) of the HEK293T cells treated with DMSO or indicated concentrations of nocodazole. $n = 4$. 1-way ANOVA with Dunnett's multiple comparisons test. p values (if ≤ 0.05 , significant) are indicated at the top of each graph. All data: mean $\pm$ SD.

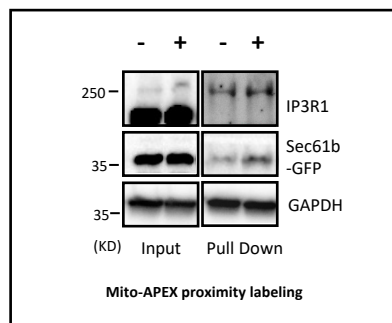
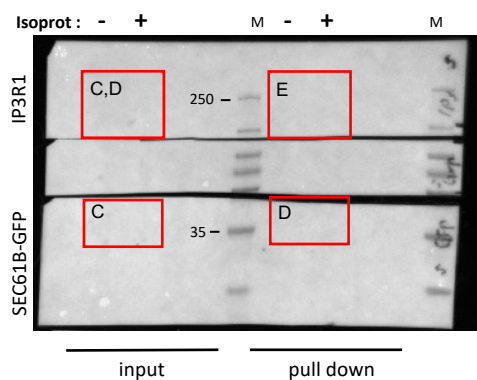
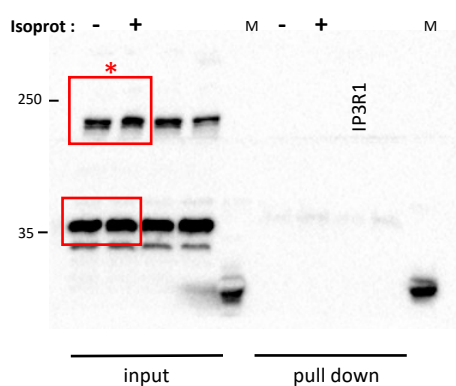
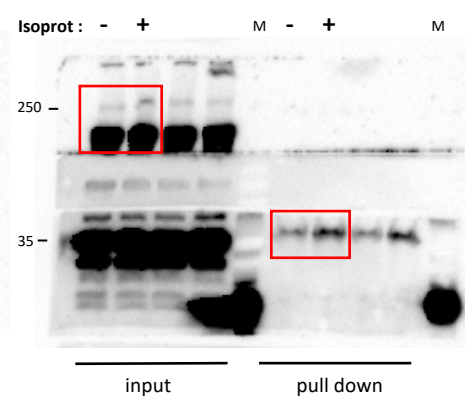
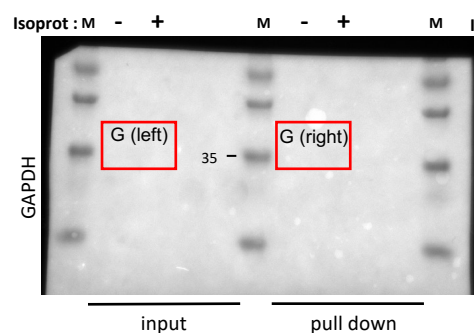
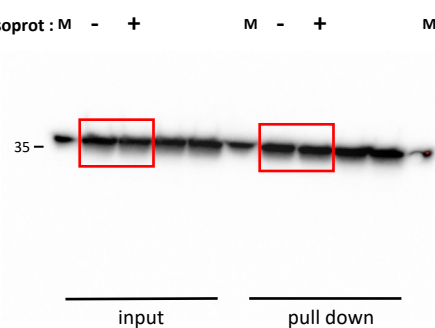
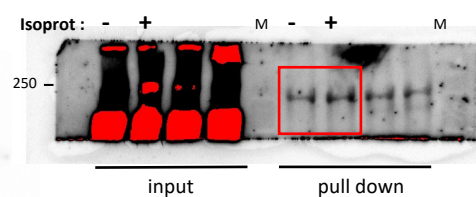
A**B****C Exposure 1****D Exposure 2****F****G****E Exposure 3**

Figure S6. A, Cropped images of the Western blot data presented in Fig. 2G. **B**, Uncropped image of the original blot cut into 3 different pieces used for IP3R or Sec61bGFP detection in A. Each red box labeled with C, D, E indicates each corresponding boxed area in C, D, and E. **C-E**, Uncropped images of the developed blots probed for IP3R1- or GFP (Sec61bGFP). * in C indicates the corresponding cropped area in D but with a shorter exposure. Blot in E is with enhanced development (Red highlighted bands: overexposed ones). **F**, Image of the original blot used for GAPDH detection in A. Red boxes labeled with G left or G right indicates the corresponding areas shown in G. **G**, Uncropped images of the developed Western blot probed for GAPDH. M: molecular weight size marker (numbers are in kD).

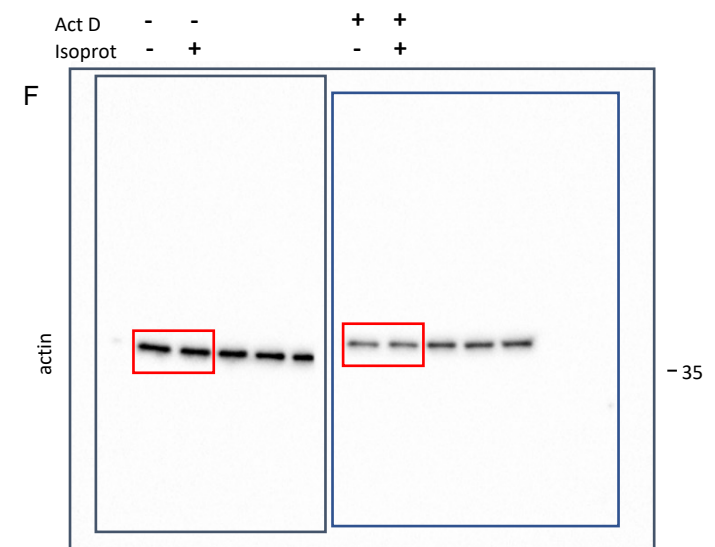
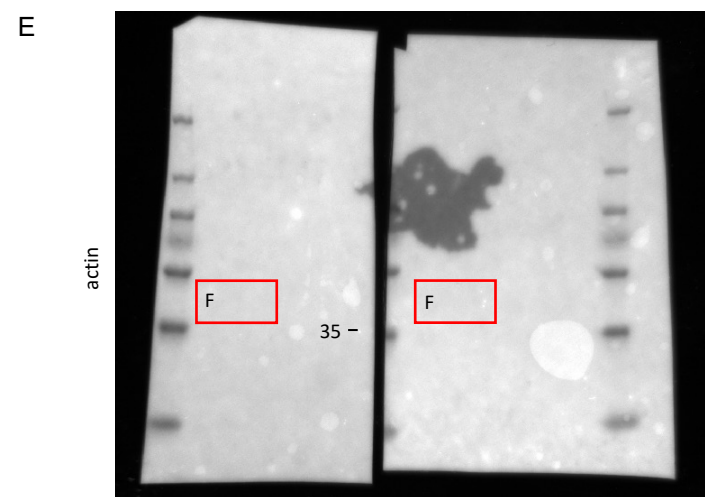
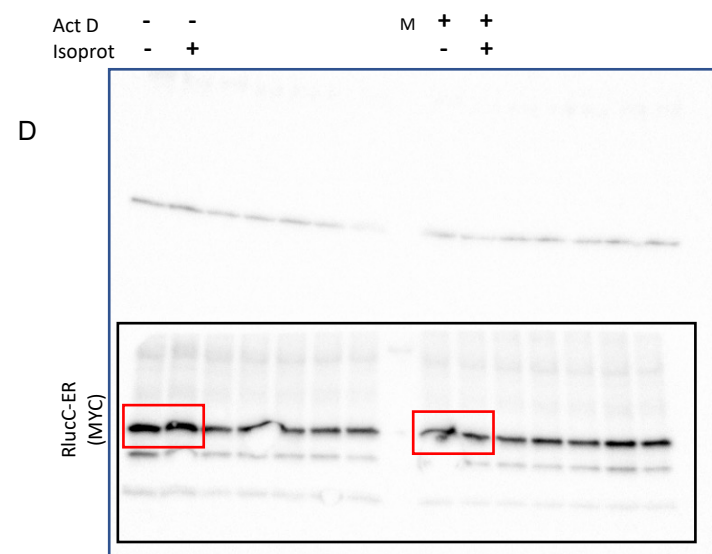
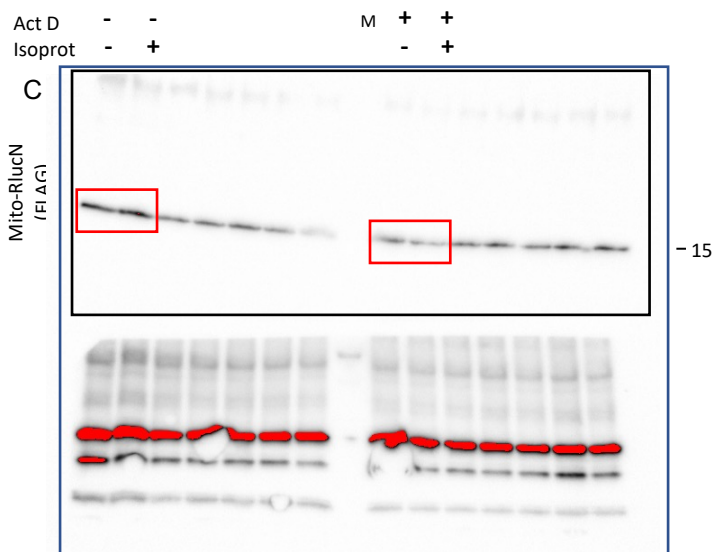
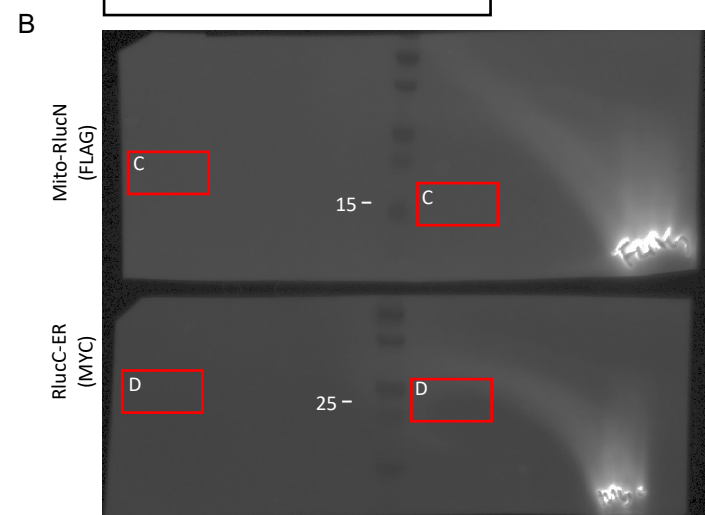
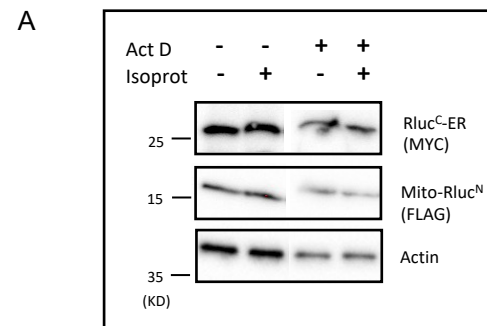


Figure S7. A, Western blot data (cropped images) presented in Fig. S2B. **B,** Uncropped image of the original blots used for FLAG (top, for Mito-Rluc^N) and MYC (bottom, for Rluc^C-ER) detection shown in A. Red boxes labeled with C and D indicate the corresponding areas in C and D. **C, D,** Uncropped images of the developed blots probed for FLAG (C, for Mito-Rluc^N) or MYC (D, for Rluc^C-ER). B and C are the same blots with different exposure time. **E,** Uncropped image of the original blots used for actin detection shown in A. Red boxes labeled with F indicate the corresponding areas in F. **F,** Uncropped image of the developed blots probed for actin. Of note, the blots were blocked with 1% skim milk. M: molecular weight size marker (numbers are in kD). Red boxes indicate the cropped areas used in A (also Fig S2B).

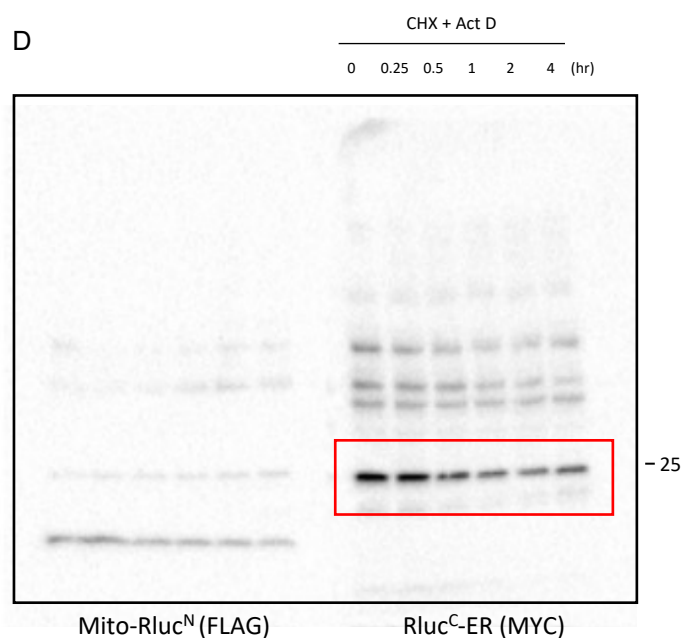
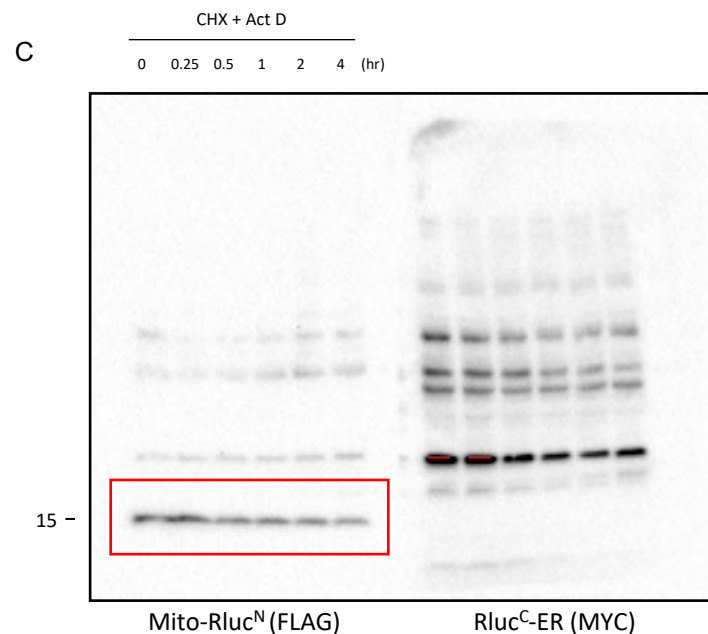
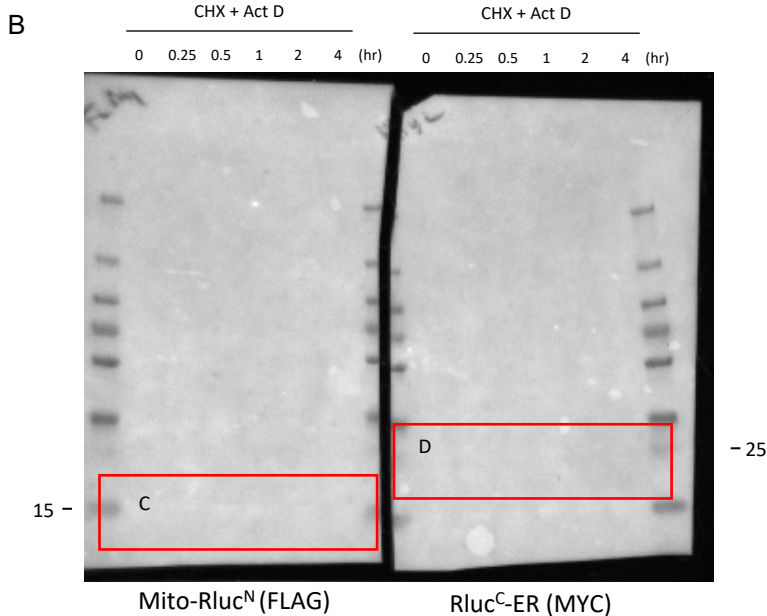
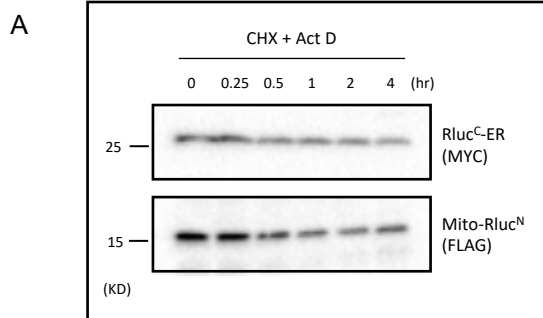


Figure S8. A, Western blot data (cropped) presented in Fig. S2C. **B**, Uncropped image of the original blots used for FLAG (left, for Mito-Rluc^N) and MYC (right, for Rluc^C-ER) detection shown in A. Red boxes labeled with C and D indicate the corresponding boxed areas in C and D. **C-D**, Uncropped images of the developed blots probed for FLAG (C, for Mito-Rluc^N) and for MYC (D, for Rluc^C-ER). C and D: the same blot with a different exposure time. Of note, blots were blocked with 1% BSA. M: molecular weight size marker (numbers are in kD). Red boxes indicate the cropped areas used in A (also Fig S2C).

Table S1. Potential hits from the initial screen

NCC_STRUC_ID	Drug Name	Target Pathway	Target GPCR	Target AR	Agonist/ Antagonist	sRluc activity
CPD000471620	Formoterol	GPCR	Adrenergic Rc	beta-2	agonist	81826.7
CPD000466295	Salmeterol	GPCR	Adrenergic Rc	beta-2	agonist	81826.7
CPD000058267	Isoproterenol	GPCR	Adrenergic Rc	beta	agonist	81826.7
CPD000857209	Epinephrine	GPCR	Adrenergic Rc	alpha, beta	agonist	81826.7
CPD000058335	Triamcinolone (76-25-	Glucocorticoid Rc				81826.7
CPD000058729	Duvadilan	GPCR	Adrenergic Rc	beta	agonist	45628.9
CPD001453712	Metaproterenol	GPCR	Adrenergic Rc	beta	agonist	45628.9
CPD000058329	Fluocinolone	Glucocorticoid Rc				45628.9
CPD000466308	Epirubicin	DNA Related				45628.9
CPD000469221	Balsalazide	GPCR	Prostaglandin Rc			45628.9
CPD000112594	Prostaglandin E1	GPCR	Prostaglandin Rc			45628.9
CPD001496939	Terbutaline	GPCR	Adrenergic Rc	beta-2	agonist	39806.7
CPD000466344	Topotecan	DNA Related				39806.7
CPD000466294	RU 24969	GPCR	Serotonergic Rc			39806.7
CPD000468732	CCPA	GPCR	Adenosine Rc			39806.7
CPD000058515	Artane	GPCR	mAChR			39806.7
CPD001491672	Phylloquinone	Vitamine K1				39806.7
CPD000058513	Salbutamol	GPCR	Adrenergic Rc	beta-2	agonist	33662.2
CPD000058420	Betaxolol	GPCR	Adrenergic Rc	beta-1	antagonist	33662.2
CPD000058383	Norepinephrine	GPCR	Adrenergic Rc	alpha, beta	agonist	33662.2
CPD000466920	Beclomethasone	Glucocorticoid Rc				33662.2
CPD000058570	Doxorubicin	DNA Related				33662.2
CPD000466296	SB 205607	GPCR	Opioid Rc			33662.2
CPD000035778	Hydrochlorothiazide	Transporter				33662.2
CPD000499581	Valproic acid	HDAC				33662.2
CPD000058745	Clobetasol	Glucocorticoid Rc				19273.3
CPD001491664	Amcinonide	Glucocorticoid Rc				19273.3
CPD000449294	Capsaicin	Vanilloid Rc				19273.3
CPD000466355	Idarubicin	DNA Related				19273.3
CPD000466319	Lamivudine	DNA Related				19273.3
CPD000468734	PD 81723	GPCR	Adenosine Rc			19273.3
CPD000469232	Lofexidine	GPCR	Adrenergic Rc	alpha-2	agonist	19273.3

Table S2. GPCR-associated drugs (in NCC library)

NCC_Structure_ID	Target GPCR	sRluc activity
CPD000058832	Acetylcholine	14504.4
CPD000058661	Acetylcholine	14504.4
CPD000058821	Acetylcholine	14084.4
CPD000449327	Acetylcholine	13964.4
CPD000469231	Acetylcholine	11964.4
CPD000449286	Acetylcholine	11773.3
CPD001906769	Acetylcholine	11711.1
CPD000058719	Acetylcholine	11673.3
CPD000449292	Acetylcholine	11620.0
CPD000058660	Acetylcholine	11517.8
CPD000471626	Acetylcholine	11308.9
CPD000058672	Acetylcholine	11186.7
CPD000469196	Acetylcholine	11055.6
CPD000058605	Acetylcholine	10964.4
CPD000469284	Acetylcholine	10846.7
CPD000058817	Acetylcholine	10846.7
CPD001906775	Acetylcholine	10647.8
CPD000059171	Acetylcholine	10613.3
CPD000449267	Acetylcholine	10588.9
CPD000059182	Acetylcholine	10124.4
CPD000466270	Acetylcholine	10033.3
CPD000469282	Acetylcholine	5960.0
CPD000057879	Acetylcholine	8077.8
CPD000058515	Acetylcholine	39806.7
CPD000058523	Acetylcholine	13266.7
CPD000471622	Acetylcholine	13113.3
CPD000059142	Acetylcholine	12557.8
CPD000059053	Acetylcholine	12497.8
CPD000058490	Acetylcholine	11915.6
CPD000058680	Acetylcholine	11593.3
CPD001906768	Acetylcholine	11055.6
CPD000058623	Acetylcholine	10682.2
CPD000466280	Acetylcholine	10601.1
CPD000058440	Acetylcholine	10257.8
CPD001496929	Acetylcholine	9533.3
CPD000058572	Acetylcholine	15577.8
CPD000449277	Acetylcholine	12695.6
CPD000471625	Acetylcholine	12031.1
CPD000875213	Acetylcholine	11786.7
CPD000058736	Acetylcholine	12324.4
CPD000468732	Adenosine	39806.7
CPD000468734	Adenosine	19273.3

CPD000048468	Adenosine	12986.7
CPD000466321	Adenosine	11606.7
CPD000466392	Adenosine	10846.7
CPD000449316	Adenosine	10733.3
CPD000058553	Adenosine	10555.6
CPD000449284	Adenosine	10148.9
CPD000469631	Adenosine	17306.7
CPD000466364	Adenosine	15860.0
CPD000469168	Adenosine	14800.0
CPD000471620	Adrenergic	81826.7
CPD000466295	Adrenergic	81826.7
CPD000058267	Adrenergic	81826.7
CPD000857209	Adrenergic	81826.7
CPD000058729	Adrenergic	45628.9
CPD001453712	Adrenergic	45628.9
CPD001496939	Adrenergic	39806.7
CPD000058513	Adrenergic	33662.2
CPD000058420	Adrenergic	16197.8
CPD000058383	Adrenergic	33662.2
CPD000469232	Adrenergic	19273.3
CPD000058800	Adrenergic	16197.8
CPD000058463	Adrenergic	15577.8
CPD000499584	Adrenergic	14606.7
CPD000469190	Adrenergic	14555.6
CPD000058525	Adrenergic	14412.2
CPD000466362	Adrenergic	14320.0
CPD000058423	Adrenergic	14320.0
CPD000059167	Adrenergic	14320.0
CPD000148117	Adrenergic	14146.7
CPD000449302	Adrenergic	14146.7
CPD000449280	Adrenergic	13964.4
CPD000466276	Adrenergic	13964.4
CPD000059120	Adrenergic	13964.4
CPD000466346	Adrenergic	13822.2
CPD000466347	Adrenergic	13660.0
CPD000472527	Adrenergic	13528.9
CPD000326828	Adrenergic	13222.2
CPD000550486	Adrenergic	13222.2
CPD000058388	Adrenergic	13148.9
CPD000449301	Adrenergic	12813.3
CPD000449266	Adrenergic	12733.3
CPD001370753	Adrenergic	12695.6
CPD001819784	Adrenergic	12466.7
CPD000466340	Adrenergic	12324.4
CPD000059081	Adrenergic	12310.0

CPD000058833	Adrenergic	12222.2
CPD000058355	Adrenergic	12160.0
CPD000449297	Adrenergic	12095.6
CPD000036768	Adrenergic	12047.8
CPD000058295	Adrenergic	12031.1
CPD000449270	Adrenergic	12020.0
CPD000059111	Adrenergic	11940.0
CPD000149600	Adrenergic	11915.6
CPD000058500	Adrenergic	11860.0
CPD001906782	Adrenergic	11860.0
CPD000058368	Adrenergic	11830.0
CPD000238156	Adrenergic	11711.1
CPD000469292	Adrenergic	11673.3
CPD000058230	Adrenergic	11555.6
CPD000469209	Adrenergic	11453.3
CPD000036827	Adrenergic	11453.3
CPD000449282	Adrenergic	11333.3
CPD001453705	Adrenergic	11308.9
CPD000097306	Adrenergic	11308.9
CPD001496977	Adrenergic	11240.0
CPD000059074	Adrenergic	11055.6
CPD000469177	Adrenergic	10942.2
CPD000059133	Adrenergic	10914.4
CPD000471619	Adrenergic	10846.7
CPD000058803	Adrenergic	10846.7
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CPD000058416	Adrenergic	10780.0
CPD000059045	Adrenergic	10588.9
CPD000449268	Adrenergic	10511.1
CPD000058180	Adrenergic	10424.4
CPD000449273	Adrenergic	10344.4
CPD000469141	Adrenergic	10257.8
CPD000058309	Adrenergic	10148.9
CPD000058486	Adrenergic	10103.3
CPD000469154	Adrenergic	10082.2
CPD000058365	Adrenergic	10082.2
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CPD000499582	Angiotensin	9868.9
CPD000466337	Angiotensin	9648.9
CPD000466306	Angiotensin	8517.8
CPD000466284	Cannabinoid	13028.9
CPD000449274	Cannabinoid	12324.4
CPD000466379	Dopamine	14555.6
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CPD000238142	Dopamine	10572.2
CPD000449298	Dopamine	10257.8
CPD000058411	Dopamine	9984.4
CPD001370746	Dopamine	9690.0
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CPD000058380	Dopamine	11333.3
CPD000449328	Dopamine	10148.9
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CPD001491654	GABA	12466.7
CPD000058418	GABA	12466.7
CPD000238177	GABA	12435.6
CPD000238180	GABA	12031.1
CPD000469176	GABA	12025.6
CPD000469160	GABA	11964.4
CPD000596519	GABA	11786.7
CPD000058501	GABA	11186.7
CPD000466325	GABA	10886.7
CPD000059151	GABA	10707.8
CPD000058302	GABA	10424.4
CPD000010931	GABA	10192.2
CPD000469145	GABA	9868.9
CPD000469226	GABA	6593.3
CPD000469289	GABA	6420.0
CPD000499581	GABA	33662.2
CPD000058410	GABA	18031.1
CPD000466378	GABA	15577.8
CPD000058433	GABA	14146.7
CPD000058855	GABA	10082.2
CPD000449307	GABA	11308.9
CPD000059075	GABA	10148.9
CPD000058464	GABA	10682.2
CPD000857229	GABA	18031.1
CPD000471616	Histamine	15860.0
CPD001370751	Histamine	14800.0
CPD000149358	Histamine	13964.4
CPD000058436	Histamine	13222.2
CPD000058462	Histamine	13131.1
CPD000059100	Histamine	12695.6
CPD000466384	Histamine	12617.8
CPD000469144	Histamine	12222.2
CPD001370748	Histamine	12222.2
CPD000469632	Histamine	12160.0
CPD001453715	Histamine	12095.6
CPD000466315	Histamine	11800.0
CPD000058353	Histamine	11773.3
CPD000653467	Histamine	11453.3
CPD000058255	Histamine	10846.7

CPD000058721	Histamine	10846.7
CPD000469183	Histamine	10445.6
CPD000058379	Histamine	9984.4
CPD000466271	Histamine	9788.9
CPD000469220	Histamine	9690.0
CPD000471617	Histamine	8755.6
CPD000718798	Histamine	8517.8
CPD000058961	Histamine	7140.0
CPD000469188	Leukotriene	14320.0
CPD000466377	Leukotriene	13477.8
CPD000466316	Leukotriene	13113.3
CPD000469147	Leukotriene	12064.4
CPD000058555	Leukotriene	10424.4
CPD000059165	Leukotriene	9868.9
CPD000466352	Leukotriene	9788.9
CPD000449311	NMDA	12047.8
CPD000449296	NMDA	11915.6
CPD000326694	NMDA	12095.6
CPD000058313	NMDA	10511.1
CPD000058445	NMDA	10445.6
CPD000058999	NMDA	10466.7
CPD000466296	Opioid	33662.2
CPD000449312	Opioid	13861.1
CPD000466389	Opioid	13822.2
CPD000058466	Opioid	13266.7
CPD000449308	Opioid	12222.2
CPD000449320	Opioid	11964.4
CPD000058908	Opioid	11593.3
CPD000469140	Opioid	10942.2
CPD000058766	Opioid	10124.4
CPD000449281	Opioid	8755.6
CPD000466297	Opioid	14800.0
CPD000058382	Platelets	10173.3
CPD000466348	Platelets	12733.3
CPD000112594	Prostanoid	45628.9
CPD000466354	Prostanoid	14800.0
CPD000042823	Prostanoid	8517.8
CPD000449318	Prostanoid	13861.1
CPD000718800	Prostanoid	13822.2
CPD000058785	Prostanoid	13528.9
CPD000469165	Prostanoid	13311.1
CPD000469178	Prostanoid	13148.9
CPD000058184	Prostanoid	13148.9
CPD000145728	Prostanoid	13113.3
CPD000466299	Prostanoid	12986.7

CPD000326718	Prostanoid	12813.3
CPD000466327	Prostanoid	12733.3
CPD000058991	Prostanoid	12047.8
CPD000040181	Prostanoid	12020.0
CPD000449291	Prostanoid	11860.0
CPD000058443	Prostanoid	11800.0
CPD000058746	Prostanoid	11692.2
CPD000059146	Prostanoid	11240.0
CPD000449290	Prostanoid	11186.7
CPD000058206	Prostanoid	11186.7
CPD000469285	Prostanoid	11108.9
CPD000469164	Prostanoid	10942.2
CPD000440694	Prostanoid	10733.3
CPD000058188	Prostanoid	10588.9
CPD000058461	Prostanoid	10344.4
CPD000469594	Prostanoid	10211.1
CPD000550473	Prostanoid	10082.2
CPD000058835	Prostanoid	9648.9
CPD000058286	Prostanoid	9271.1
CPD000466331	Prostanoid	8517.8
CPD000058723	Prostanoid	6593.3
CPD000058715	Prostanoid	6420.0
CPD000466294	Serotonin	39806.7
CPD000059115	Serotonin	5960.0
CPD000466283	Serotonin	18031.1
CPD000469200	Serotonin	15860.0
CPD000466268	Serotonin	13477.8
CPD000449310	Serotonin	13477.8
CPD000058254	Serotonin	13477.8
CPD001307702	Serotonin	13113.3
CPD000469228	Serotonin	12961.1
CPD000525252	Serotonin	12935.6
CPD000012114	Serotonin	12874.4
CPD000469138	Serotonin	12714.4
CPD000059131	Serotonin	12714.4
CPD000469203	Serotonin	12295.6
CPD000469191	Serotonin	12160.0
CPD000058507	Serotonin	12064.4
CPD000469211	Serotonin	11964.4
CPD000112269	Serotonin	11860.0
CPD000449305	Serotonin	11800.0
CPD000466269	Serotonin	11646.7
CPD000469179	Serotonin	11453.3
CPD000469156	Serotonin	11186.7
CPD000466298	Serotonin	11108.9

CPD000471618	Serotonin	11108.9
CPD001227191	Serotonin	11021.1
CPD000465669	Serotonin	10866.7
CPD000469233	Serotonin	10613.3
CPD000449271	Serotonin	10211.1
CPD000466277	Serotonin	10211.1
CPD000469158	Serotonin	10173.3
CPD000058431	Serotonin	9788.9
CPD000466272	Serotonin	9648.9
CPD000058452	Serotonin	7608.9
CPD000059105	Serotonin	6593.3
CPD000449269	Serotonin	4731.1
CPD000449272	Serotonin	12222.2
CPD000449287	Serotonin	11055.6
CPD000058269	Serotonin	6420.0
CPD001453706	Serotonin	10707.8
CPD000469181	Serotonin	10613.3
CPD000058926	Serotonin	12733.3
CPD000449299	Serotonin	13028.9

Table S3. AR-associated drugs (in NCC library)

NCC_STRUC_ID	Target AR	Agonist/ Antagonist	sRluc activity
CPD000469232	alpha	agonist	19273.3
CPD000058833	alpha	agonist	12222.2
CPD000059111	alpha	agonist	11940.0
CPD000058219	alpha	agonist	9533.3
CPD000058292	alpha	agonist	8517.8
CPD000499584	alpha	agonist	14606.7
CPD000466276	alpha	agonist	13964.4
CPD001370753	alpha	agonist	12695.6
CPD000058355	alpha	agonist	12160.0
CPD000469209	alpha	agonist	11453.3
CPD000058803	alpha	agonist	10846.7
CPD001906782	alpha	antagonist	11860.0
CPD000059133	alpha	antagonist	10914.4
CPD000059045	alpha	antagonist	10588.9
CPD000058180	alpha	antagonist	10424.4
CPD000058422	alpha	antagonist	9828.9
CPD000058520	alpha	antagonist	9760.0
CPD000058525	alpha	antagonist	14412.2
CPD000466362	alpha	antagonist	14320.0
CPD000466346	alpha	antagonist	13822.2
CPD000449301	alpha	antagonist	12813.3
CPD000466340	alpha	antagonist	12324.4
CPD000097306	alpha	antagonist	11308.9
CPD000466275	alpha	antagonist	10780.0
CPD000449268	alpha	antagonist	10511.1
CPD000058309	alpha	antagonist	10148.9
CPD001819784	alpha	antagonist	12466.7
CPD000471623	alpha	antagonist	9591.1
CPD000469190	alpha	antagonist	14555.6
CPD000449302	alpha	antagonist	14146.7
CPD000466347	alpha	antagonist	13660.0
CPD000550486	alpha	antagonist	13222.2
CPD000149600	alpha	antagonist	11915.6
CPD000058365	alpha	antagonist	10082.2
CPD000857209	alpha, beta	agonist	81826.7
CPD000058383	alpha, beta	agonist	33662.2
CPD000059081	alpha, beta	agonist	12310.0
CPD000058463	alpha, beta	antagonist	15577.8
CPD000466345	alpha, beta	antagonist	9731.1
CPD000449280	alpha, beta	antagonist	13964.4
CPD000058296	alpha, beta	antagonist	9591.1

CPD000058267	beta	agonist	81826.7
CPD000058729	beta	agonist	45628.9
CPD001453712	beta	agonist	45628.9
CPD000471620	beta	agonist	81826.7
CPD000466295	beta	agonist	81826.7
CPD001496939	beta	agonist	39806.7
CPD000058513	beta	agonist	33662.2
CPD000058420	beta	antagonist	33662.2
CPD000058800	beta	antagonist	16197.8
CPD000059167	beta	antagonist	14320.0
CPD000059120	beta	antagonist	13964.4
CPD000326828	beta	antagonist	13222.2
CPD000058388	beta	antagonist	13148.9
CPD000036768	beta	antagonist	12047.8
CPD000471619	beta	antagonist	10846.7
CPD000058975	beta	antagonist	10780.0
CPD000469141	beta	antagonist	10257.8
CPD001453705	beta	antagonist	11308.9

Table S4. mRNA seq data for GPCRs and related genes

TPM (transcripts per million)			TPM (transcripts per million)		
Gene name	HEK293T	HeLa	Gene name	C2C12	Neuro2A
ACKR1	NA	NA	Ackr1	NA	0.411135
ACKR2	0.0671921	0.00611861	Ackr2	0.0290849	0.0274002
ACKR3	NA	10.7309	Ackr3	10.5631	0.0218309
ACKR4	2.40158	1.43155	Ackr4	4.28392	0.273759
ADCYAP1R1	0.412282	0.0204383	Adcyap1r1	NA	10.1754
ADGRA1	0.014162	0.00209562	Adgra1	0.0280815	0.349205
ADGRA2	1.06185	1.11038	Adgra2	17.5953	3.67736
ADGRA3	1.52622	1.54665	Adgra3	4.41482	1.44618
ADGRB1	0.0186445	0.276368	Adgrb1	NA	0.139848
ADGRB2	0.99388	2.11289	Adgrb2	0.205729	0.369166
ADGRB3	0.55272	0.000928321	Adgrb3	NA	0.0175584
ADGRD1	0.00229335	0.0678718	Adgrd1	0.205819	4.37884
ADGRD2	0.00678628	0.569381	Adgre1	0.0296354	0.0217767
ADGRE1	0.00116175	0.00722024	Adgre5	20.6852	0.871518
ADGRE2	0.0053239	6.33217	Adgrf1	NA	0.00896804
ADGRE3	1.52864	9.58569	Adgrf2	0.0428473	0.292145
ADGRE4P	0.00135432	NA	Adgrf3	0.170553	0.0226834
ADGRE5	0.333102	16.6925	Adgrf4	NA	0.189065
ADGRF1	NA	0.00570313	Adgrf5	0.0398179	0.0858076
ADGRF2	0.00742829	NA	Adgrg1	4.8713	0.190748
ADGRF3	0.386397	0.331062	Adgrg2	0.119437	0.0467386
ADGRF4	0.00509844	0.0475298	Adgrg3	1.90625	0.134055
ADGRF5	0.00119993	0.0031073	Adgrg4	0.00656975	0.00530503
ADGRG1	0.00111871	4.58533	Adgrg5	0.214064	0.0142352
ADGRG2	0.161309	0.208143	Adgrg6	4.31215	3.71776
ADGRG3	NA	0.241309	Adgrg7	NA	0.0166323
ADGRG4	0.00318041	0.00164717	Adgrl1	11.9194	17.6022
ADGRG5	0.00125308	0.0986458	Adgrl2	5.19926	1.72021
ADGRG6	0.37275	0.133109	Adgrl3	0.298114	0.722868
ADGRG7	0.00572431	0.00370586	Adgrl4	0.0264586	0.0123546
ADGRL1	NA	NA	Adgrv1	0.00687546	0.0687879
ADGRL1	1.9325	1.72728	Adora1	14.243	0.173259
ADGRL2	0.00877483	0.00565755	Adora2a	0.406292	8.11576
ADGRL3	0.61066	0.000653147	Adora2b	5.09656	NA
ADGRL4	0.00125292	0.0629437	Adora3	NA	0.0292967
ADGRV1	0.776475	0.0175391	Adra1a	0.00181462	0.00923136
ADORA1	0.0640502	0.0514172	Adra1b	0.0915609	0.010461
ADORA2A	0.602473	0.759269	Adra1d	2.88152	0.0508989
ADORA2B	1.27165	1.93039	Adra2a	NA	0.31737
ADORA3	NA	NA	Adra2b	NA	1.47609
ADRA1A	0.0128956	NA	Adra2c	NA	0.0809359
ADRA1B	0.0142333	0.159227	Adrb1	0.0677892	0.0447038
ADRA1D	0.00643274	0.0666319	Adrb2	33.8209	NA
ADRA2A	0.0633666	NA	Adrb3	0.173753	0.0140304
ADRA2B	0.0498781	0.137773	Agtr2	NA	0.0301692
ADRA2C	5.97859	5.17038	Aplnr	0.666774	0.0565337
ADRB1	0.465069	1.36141	Avpr1a	NA	0.0281413
ADRB2	53.3648	2.82853	Avpr1b	NA	0.114702

ADRB3	NA	NA	Avpr2	0.217559	0.471402
AGTR1	0.134517	0.00985204	Bdkrb1	4.73498	0.118952
AGTR2	NA	0.030088	Bdkrb2	1.98779	2.53243
APLNR	NA	0.191354	Brs3	NA	NA
AVPR1A	0.0800601	NA	C3ar1	0.478302	0.015449
AVPR1B	0.0228353	NA	C5ar1	0.0481794	0.0980394
AVPR2	0.0397647	2.64984	C5ar2	0.0128861	NA
BDKRB1	NA	0.0798259	Calcr	0.00468096	0.0582096
BDKRB2	0.197633	0.538379	Calcr1	1.56514	0.0956025
BRS3	0.147463	NA	Casr	NA	0.00611045
C3AR1	0.0193726	0.0401332	Cckar	NA	0.0140395
C5AR1	0.0441064	0.572074	Cckbr	0.0409537	0.0077163
C5AR2	0.0121643	5.84222	Ccr1	0.037546	NA
CALCR	0.00245398	NA	Ccr10	1.76387	3.61776
CALCRL	0.0761653	0.00119536	Ccr2	NA	0.042035
CASR	NA	0.00235828	Ccr3	NA	NA
CCKAR	NA	NA	Ccr4	0.00844599	0.17664
CCKBR	0.074805	NA	Ccr5	0.047146	0.0239842
CCR1	NA	NA	Ccr6	0.0116896	0.0991128
CCR10	0.53764	5.2779	Ccr7	0.0679948	0.134518
CCR2	NA	NA	Ccr8	0.0883064	NA
CCR3	0.00178801	0.0265463	Ccr9	1.58616	12.525
CCR4	NA	0.108204	Ccr12	1.5039	0.252724
CCR5	NA	NA	Celsr1	0.0118511	0.024734
CCR6	0.0881316	0.02054	Celsr2	NA	1.93016
CCR7	NA	1.23996	Celsr3	0.101803	12.6988
CCR8	0.061883	0.0320499	Chrm1	0.0373716	0.225324
CCR9	0.0663445	0.0152714	Chrm2	0.000878779	0.00596071
CCRL2	NA	0.087313	Chrm3	0.00177855	0.196755
CELSR1	0.499838	2.56748	Chrm4	1.88405	15.5386
CELSR2	1.65504	14.6301	Chrm5	0.154246	0.0435935
CELSR3	2.55111	17.0353	Cmklr1	0.715827	0.0549255
CHRM1	NA	0.0145444	Cnr1	4.17697	17.3266
CHRM2	0.100533	NA	Cnr2	NA	0.039328
CHRM3	0.0216107	0.0973624	Crhr1	NA	0.486826
CHRM4	0.447351	1.64288	Crhr2	0.0114802	0.00162228
CHRM5	0.195597	0.0611029	Cx3cr1	6.74777	1.03732
CMKLR1	NA	NA	Cxcr1	NA	NA
CNR1	0.201771	NA	Cxcr2	NA	0.019208
CNR2	0.0100389	0.0118841	Cxcr3	NA	NA
CRHR1	NA	NA	Cxcr4	9.96798	NA
CRHR1	NA	NA	Cxcr5	0.288044	0.20178
CRHR1	0.0882128	NA	Cxcr6	0.839863	0.0923084
CRHR2	0.0395315	0.184925	Cysltr1	NA	NA
CX3CR1	0.0505316	NA	Cysltr2	0.0576947	0.275717
CXCR1	NA	NA	Drd1	NA	0.123292
CXCR2	NA	0.0425654	Drd2	0.00182558	0.00515951
CXCR3	0.0710128	NA	Drd3	0.00715863	0.0890204
CXCR4	4.20335	19.1741	Drd4	0.110626	0.140694
CXCR5	0.106131	23.1592	Drd5	NA	0.0442297
CXCR6	1.78908	0.154431	Ednra	0.843089	0.00794254
CYSLTR1	0.00218589	NA	Ednrb	NA	0.0468171

CYSLTR2	0.00213679	0.00885335	F2r	70.0968	41.9615
DRD1	NA	NA	F2rl1	NA	0.00516494
DRD2	0.0102281	NA	F2rl2	0.418957	17.5242
DRD3	0.00171103	NA	F2rl3	1.35992	0.663867
DRD4	NA	NA	Ffar1	NA	NA
DRD4	0.107242	1.38855	Ffar2	NA	NA
DRD5	NA	NA	Ffar3	NA	0.0376993
EDNRA	0.531609	1.98593	Ffar4	NA	0.158119
EDNRB	0.122824	0.00397576	Fpr1	0.0990521	NA
F2R	3.71295	5.43684	Fpr2	0.120724	0.0113731
F2RL1	3.50702	2.1796	Fpr3	0.0176537	0.353411
F2RL2	0.240159	NA	Fshr	0.00114331	0.0739958
F2RL3	NA	0.0705667	Fzd1	105.367	0.398605
FFAR1	NA	NA	Fzd10	0.0758892	0.021448
FFAR2	NA	NA	Fzd2	57.4348	0.837309
FFAR3	NA	NA	Fzd3	0.533685	2.26795
FFAR4	NA	0.351785	Fzd4	11.0258	4.82702
FPR1	0.0041704	0.0043198	Fzd5	39.3239	6.21095
FPR2	0.0132821	0.013758	Fzd6	4.64439	1.4546
FPR3	0.0396016	NA	Fzd7	53.3606	32.5613
FSHR	0.00223604	0.000992632	Fzd8	4.64462	0.0700094
FZD1	3.98434	2.89911	Fzd9	2.15124	0.425593
FZD10	1.42297	32.7759	Gabbr1	20.3612	3.95453
FZD2	4.03269	23.5639	Gabbr2	NA	0.0188241
FZD3	3.16524	0.552535	Galr1	NA	NA
FZD4	7.82272	12.8324	Galr2	0.698813	0.929413
FZD5	8.55875	5.40804	Galr3	0.221003	0.208202
FZD6	6.57078	5.44383	Gcgr	0.208311	0.0336419
FZD7	13.9492	7.43889	Ghrhr	NA	NA
FZD8	5.23009	6.82315	Ghsr	0.0185165	NA
FZD9	1.96702	6.68297	Gipr	0.489997	2.07726
GABBR1	NA	NA	Glp1r	0.563206	2.35901
GABBR1	NA	NA	Glp2r	0.328397	0.0902697
GABBR1	NA	NA	Gna12	5.04073	2.53181
GABBR1	NA	NA	Gna13	15.065	18.3693
GABBR1	NA	NA	Gna14	0.00845337	0.0314567
GABBR1	NA	NA	Gna15	0.180029	0.213061
GABBR1	0.47765	0.780732	Gnai1	0.0362626	0.0541713
GABBR2	0.0559262	0.0116465	Gnai2	147.998	12.1378
GALR1	NA	NA	Gnal	1.14441	0.293256
GALR2	0.0891546	0.138523	Gnao1	7.7029	3.62646
GALR3	0.0876185	0.0907574	Gnaq	1.65148	5.21112
GCGR	NA	NA	Gnas	88.98	48.5078
GCGR	0.0062215	4.46596	Gnat1	0.0470776	0.0532208
GHRHR	0.00450297	NA	Gnat2	1.75478	2.12892
GHSR	0.0356851	NA	Gnat3	0.00645812	0.0304202
GIPR	0.253695	5.20641	Gnaz	0.225656	1.45212
GLP1R	0.00289019	NA	Gnrhr	NA	NA
GLP2R	NA	7.13428	Gpbar1	NA	1.88044
GNA12	0.87518	3.39553	Gper1	11.4568	0.749527
GNA13	7.74662	7.70489	Gpr1	0.0348438	0.048144
GNA14	0.0103669	0.00989057	Gpr101	NA	0.0294948

GNA15	0.00443409	0.296244	Gpr107	7.54281	2.90739
GNAI1	0.37166	0.530017	Gpr119	0.0379446	NA
GNAI2	4.25137	30.8026	Gpr12	NA	3.55643
GNAL	1.0252	1.548	Gpr132	0.0284213	NA
GNAO1	0.0529181	1.52942	Gpr135	0.782983	1.6818
GNAQ	1.19176	1.04051	Gpr137	22.4674	15.4727
GNAS	20.9845	45.9669	Gpr139	0.0112475	0.00317879
GNAT1	NA	0.282336	Gpr141	0.0992168	0.0177593
GNAT2	2.02671	1.6222	Gpr142	0.268018	0.0534692
GNAT3	0.0046004	NA	Gpr143	0.00922846	0.0234735
GNAZ	2.29504	0.754277	Gpr146	5.65246	1.54911
GNRHR	1.05672	0.784998	Gpr149	0.194552	0.00549848
GPBAR1	0.253343	0.0728942	Gpr15	0.301147	NA
GPBR1	0.3388	7.21614	Gpr150	NA	0.0324818
GPR1	NA	NA	Gpr151	0.347968	0.118012
GPR1	0.0388267	0.210026	Gpr152	0.0414242	0.0117074
GPR101	NA	NA	Gpr153	5.56305	2.2093
GPR107	3.32241	8.076	Gpr156	0.0731507	0.0589593
GPR119	NA	NA	Gpr157	1.6874	0.0150204
GPR12	0.0329961	NA	Gpr158	0.00319615	0.051639
GPR132	0.00765682	0.21414	Gpr160	0.233226	0.0219717
GPR135	0.908525	2.66024	Gpr161	2.98769	0.434579
GPR137	3.14219	11.5587	Gpr162	3.27221	5.07067
GPR139	NA	NA	Gpr17	0.705746	0.440911
GPR141	0.00245811	0.0169744	Gpr171	NA	NA
GPR142	NA	NA	Gpr173	4.22904	2.40988
GPR143	0.006049	0.110694	Gpr174	0.012063	0.018751
GPR146	0.492734	3.53377	Gpr176	2.09097	0.0709292
GPR148	NA	NA	Gpr179	0.0494045	0.230387
GPR149	0.0135483	0.00534614	Gpr18	0.190603	0.0769552
GPR15	NA	NA	Gpr182	1.74314	0.563028
GPR150	NA	NA	Gpr183	0.0195049	0.0551254
GPR151	0.338292	NA	Gpr19	1.89041	2.93141
GPR152	NA	NA	Gpr20	0.0382328	0.0756382
GPR153	1.80603	9.25179	Gpr21	0.461872	0.163169
GPR156	0.0862185	0.951201	Gpr22	NA	5.34534
GPR157	1.21628	3.13415	Gpr25	NA	NA
GPR158	0.00460052	0.0735649	Gpr26	NA	0.142176
GPR160	1.99396	1.1079	Gpr27	NA	0.233521
GPR161	2.0774	0.900151	Gpr3	0.115721	5.29827
GPR162	0.802255	0.404062	Gpr33	NA	NA
GPR17	0.0816187	4.48076	Gpr34	0.140616	0.0953788
GPR171	0.981371	NA	Gpr35	0.32976	0.0706341
GPR173	0.00386149	0.553976	Gpr37	0.029773	0.0476824
GPR174	NA	NA	Gpr37l1	0.0331149	0.393079
GPR176	0.74089	1.01152	Gpr39	0.329491	0.0123926
GPR179	NA	NA	Gpr4	0.264931	0.155741
GPR179	0.0760753	0.0656672	Gpr45	0.0029865	0.098754
GPR18	1.2061	0.162953	Gpr50	NA	0.0124675
GPR182	0.233	0.273526	Gpr52	0.602663	0.0425816
GPR183	1.00816	0.445425	Gpr55	NA	0.00921631
GPR19	0.186169	0.151387	Gpr6	NA	0.120755

GPR20	NA	NA	Gpr61	0.18793	0.0743587
GPR20	0.0454468	0.841464	Gpr62	6.8615	2.18603
GPR21	0.778702	0.0467594	Gpr63	0.820654	0.00651047
GPR22	NA	NA	Gpr65	0.0307915	0.0261071
GPR22	1.16025	0.314493	Gpr68	1.43209	1.90206
GPR25	NA	NA	Gpr75	0.206221	0.566174
GPR26	NA	NA	Gpr82	0.243755	0.0688908
GPR27	15.4206	NA	Gpr83	NA	0.0131769
GPR3	0.327168	7.63495	Gpr84	0.103717	0.0586257
GPR31	NA	NA	Gpr85	0.764426	7.23112
GPR32	0.0484238	NA	Gpr87	NA	NA
GPR33	NA	NA	Gpr88	0.320311	0.0362109
GPR34	0.355244	0.298976	Gprc5a	6.95571	0.168239
GPR35	0.123708	0.211924	Gprc5b	27.9859	0.213647
GPR37	0.224392	13.1323	Gprc5c	2.46456	0.0389673
GPR37L1	0.207212	0.667753	Gprc5d	0.381205	0.0510334
GPR39	0.308081	0.137952	Gprc6a	NA	0.00837863
GPR4	0.00987224	0.132937	Grm1	0.0230273	0.141946
GPR42	NA	NA	Grm2	NA	0.0751374
GPR45	0.142492	0.368992	Grm3	0.00205851	0.0113447
GPR50	0.151044	0.0260759	Grm4	0.00249088	0.00915174
GPR52	1.20414	0.0804693	Grm5	0.00470225	0.0322748
GPR55	NA	0.117239	Grm6	NA	NA
GPR6	NA	NA	Grm7	0.023148	0.010059
GPR61	0.84237	0.372883	Grm8	0.00157724	0.0286909
GPR62	0.0579989	0.36046	Gpr	0.0999686	0.00584553
GPR63	2.46491	0.0205549	Hcar1	NA	0.0848779
GPR65	NA	NA	Hcar2	0.127793	0.0722342
GPR68	0.0143615	0.119008	Hcrtr1	0.0269758	0.0609918
GPR75	1.41955	3.72562	Hcrtr2	0.00251732	0.00853743
GPR78	0.387604	0.5235	Hrh1	0.0606768	0.200884
GPR82	0.330486	0.117674	Hrh2	NA	0.00949414
GPR83	0.132567	0.0580952	Hrh3	NA	1.94244
GPR84	NA	0.591959	Hrh4	NA	0.0350877
GPR85	0.598368	0.026948	Htr1a	NA	0.139909
GPR87	0.194607	0.0167982	Htr1b	1.91504	0.0251737
GPR88	0.0791267	NA	Htr1d	0.0590754	0.016696
GPRC5A	0.519478	179.4	Htr1f	0.0142979	0.0392545
GPRC5B	1.24038	0.557113	Htr2a	0.0808302	0.0111684
GPRC5C	0.414969	2.81886	Htr2b	1.00028	0.425398
GPRC5D	0.0324188	10.9975	Htr2c	0.135525	0.00682912
GPRC6A	0.0149476	NA	Htr4	0.0100159	0.0105141
GRM1	0.00824415	0.0080737	Htr5a	NA	0.0161606
GRM2	0.0691882	0.00551283	Htr6	0.0255797	0.583173
GRM3	0.108177	0.0483928	Htr7	0.0112366	0.0162314
GRM4	0.000897208	0.136614	Kiss1r	3.09288	1.57736
GRM5	0.00186089	0.000680313	Lgr4	3.70045	0.466818
GRM6	NA	NA	Lgr5	0.00897068	0.785441
GRM7	0.00120176	0.00746885	Lgr6	0.181983	0.00514326
GRM8	0.00588472	0.00265703	Lhcgr	NA	0.00830822
GRPR	0.00820589	0.495117	Lpar1	3.06418	0.0117504
HCAR1	0.051541	NA	Lpar2	1.3222	4.17079

HCAR2	NA	7.42854	Lpar3	0.308186	0.00106872
HCAR3	0.119552	6.25367	Lpar4	15.0574	0.0367537
HCRR1	13.6587	7.28215	Lpar5	NA	0.349656
HCRR2	0.00104648	NA	Lpar6	5.77777	3.1755
HRH1	0.00680265	1.98657	Ltb4r2	NA	0.0751345
HRH2	0.026805	0.00120718	Mas1	0.337176	0.0669631
HRH3	NA	0.203435	Mc1r	0.0677954	0.36405
HRH4	0.0540567	NA	Mc2r	0.187065	1.68558
HTR1A	NA	NA	Mc3r	NA	NA
HTR1B	NA	NA	Mc4r	2.0678	0.0248684
HTR1D	0.476859	8.06024	Mc5r	0.203372	0.0287388
HTR1E	NA	0.000804164	Mchr1	1.31646	0.160891
HTR1F	0.09785	NA	Mrgprd	NA	NA
HTR2A	0.0103156	NA	Mrgpre	11.7735	1.28328
HTR2B	1.07454	0.162791	Mrgprf	14.5498	0.391248
HTR2C	0.00113103	0.00488147	Mrgprg	NA	NA
HTR4	0.00271656	0.00759749	Mrgprx1	NA	0.0105185
HTR5A	NA	NA	Mrgprx2	0.0774361	12.2995
HTR6	0.087829	0.0632873	Mtnr1a	NA	0.00719732
HTR7	0.0644815	0.0179197	Mtnr1b	NA	0.0236863
KISS1R	0.0991392	NA	Nmbr	1.50229	49.4062
LGR4	3.37246	15.8887	Nmur1	0.0185323	0.0209506
LGR5	0.209288	0.00130332	Nmur2	NA	NA
LGR6	0.00878684	0.273049	Npbwr1	NA	0.0188803
LHCGR	0.0115847	0.00276917	Npffr1	0.0111858	0.0358288
LPAR1	0.30614	0.00154123	Npffr2	NA	0.0123785
LPAR2	0.163059	2.24396	Npsr1	0.00677573	0.00414911
LPAR3	1.02485	NA	Npy1r	0.924803	0.0435617
LPAR4	NA	NA	Npy2r	NA	0.136509
LPAR5	0.0071762	2.32662	Npy4r	0.203163	NA
LPAR6	0.454705	0.349783	Npy5r	0.0302107	0.0341529
LTB4R	NA	NA	Npy6r	NA	NA
LTB4R	4.66447	13.2965	Ntsr1	0.00274014	0.00154885
LTB4R2	NA	NA	Ntsr2	0.108081	0.336006
LTB4R2	19.3295	23.0131	Opn1mw	0.0211735	8.35383
MAS1	NA	0.00721669	Opn1sw	0.742135	0.0886244
MAS1L	NA	NA	Opn3	3.99339	1.40762
MAS1L	NA	NA	Opn4	0.103576	NA
MAS1L	NA	NA	Opn5	NA	0.00765818
MAS1L	NA	NA	Oprd1	0.0255691	0.251892
MAS1L	NA	NA	Oprk1	NA	0.0315662
MAS1L	NA	NA	Oprl1	0.0413132	2.05498
MAS1L	NA	NA	Oprm1	0.00264547	0.016698
MAS1L	NA	NA	Oxgr1	NA	NA
MC1R	1.04787	10.2072	Oxtr	0.0455027	0.0600138
MC2R	NA	NA	P2ry1	NA	0.0225294
MC3R	NA	NA	P2ry10	0.0149633	0.0422896
MC4R	0.143407	NA	P2ry12	0.00264635	0.0254292
MC5R	NA	NA	P2ry13	NA	0.163137
MCHR1	0.0302336	NA	P2ry14	0.0248104	0.00175299
MCHR2	0.0056801	0.000840513	P2ry2	3.9949	0.359243
MLNR	0.150612	0.124806	P2ry4	0.0522985	NA

MRGPRD	NA	0.263566	P2ry6	0.103266	0.176995
MRGPRE	NA	0.0344619	PrIhr	NA	0.0443141
MRGPRF	NA	0.899388	Prokr1	0.629131	0.69402
MRGPRG	NA	NA	Prokr2	NA	0.0701224
MRGPRX1	NA	NA	Ptafr	0.119233	0.0299537
MRGPRX2	NA	NA	Ptgd	NA	NA
MRGPRX3	0.0105186	0.00726363	Ptgd2	1.08297	0.481899
MRGPRX4	NA	NA	Ptger1	39.192	10.0268
MTNR1A	0.0813236	NA	Ptger2	0.181515	NA
MTNR1B	0.0119583	0.0206445	Ptger3	0.24821	0.0070591
NMBR	0.598969	0.515978	Ptger4	8.76749	2.31443
NMUR1	0.118515	NA	Ptgrfr	1.55615	0.0152533
NMUR2	0.0293856	0.00608767	Ptgir	16.0573	39.3517
NPBWR1	0.0944758	0.12582	Pth1r	0.167307	0.111258
NPBWR2	NA	NA	Pth2r	0.0207088	0.0565769
NPBWR2	NA	NA	Qrfpr	0.0172516	0.0162523
NPFFR1	NA	0.024297	Rho	0.743877	0.176599
NPFFR2	0.0269554	0.0136868	Rxfp1	0.00256196	0.0101369
NPSR1	0.00139586	0.000289172	Rxfp2	NA	0.00878048
NPY1R	0.176656	NA	Rxfp3	0.144234	0.0163055
NPY2R	0.116451	NA	Rxfp4	0.891469	0.111978
NPY4R	0.037932	14.8781	S1pr1	46.7234	0.600914
NPY5R	0.0382008	NA	S1pr2	12.391	2.64884
NPY6R	0.179997	0.173128	S1pr3	11.6448	0.0443078
NTSR1	0.00683586	2.96093	S1pr4	NA	0.116858
NTSR2	0.00511315	0.0211853	S1pr5	0.156045	0.113405
OPN1LW	0.0207741	NA	Sctr	0.0892628	0.980804
OPN1MW	0.0215371	NA	Smo	14.9102	0.0889417
OPN1SW	10.4651	18.0731	Sstr1	NA	0.0260778
OPN3	12.3259	13.9307	Sstr2	NA	1.02156
OPN4	NA	0.0103481	Sstr3	0.0803073	0.508405
OPN5	NA	NA	Sstr4	NA	0.195803
OPRD1	0.226568	0.0150715	Sstr5	NA	NA
OPRK1	NA	NA	Sucnr1	NA	NA
OPRL1	NA	NA	Taar1	NA	NA
OPRL1	0.116552	0.238359	Taar2	NA	NA
OPRM1	0.00935894	0.00403926	Taar5	NA	NA
OR1A1	NA	NA	Taar6	NA	NA
OR1G1	NA	NA	Taar9	NA	NA
OR2T11	NA	NA	Tacr1	NA	0.00441818
OR51E1	NA	NA	Tacr2	0.0272973	0.072005
OXER1	0.207018	NA	Tacr3	0.0046724	0.02509
OXGR1	0.0477306	NA	Tas1r1	0.694434	0.588788
OXTR	0.479552	1.0332	Tas1r2	0.0515582	NA
P2RY1	19.3826	NA	Tas1r3	1.95746	0.476622
P2RY10	NA	NA	Tbxa2r	0.268003	0.205591
P2RY11	27.7526	32.5348	Tpra1	15.236	4.63404
P2RY12	0.98374	NA	Trhr	0.0248016	0.0122666
P2RY13	0.189777	NA	Tshr	0.0246273	0.0236226
P2RY14	0.442191	0.00287468	Uts2r	0.0724133	0.0409313
P2RY2	0.0865239	2.76515	Vipr1	0.024469	0.0345775
P2RY4	0.11558	0.0399067	Vipr2	0.16374	0.0122049

P2RY6	NA	2.84855	Xcr1	0.0126938	NA
P2RY8	0.00164734	0.0307143	Cdc42	43.8568	21.657
PRLHR	NA	NA	Rac1	55.5175	23.4372
PROKR1	0.0376915	NA	Rhoa	46.2479	12.3628
PROKR2	0.0249188	NA	Rhog	9.19874	1.53146
PTAFR	0.110363	0.187806			
PTGDR	NA	NA			
PTGDR2	3.83296	5.86027			
PTGER1	0.0212703	0.308452			
PTGER2	0.133269	0.035624			
PTGER3	0.0154052	0.00293089			
PTGER4	0.182291	4.79882			
PTGFR	1.00315	0.0142452			
PTGIR	NA	0.0275427			
PTH1R	0.0683325	0.0439327			
PTH2R	0.00248387	0.00192964			
QRFPR	0.219221	NA			
RHO	0.0091634	NA			
RXFP1	0.00272656	0.0826561			
RXFP2	0.0019244	NA			
RXFP3	NA	NA			
RXFP3	NA	NA			
RXFP4	0.296654	0.965742			
S1PR1	1.12151	2.05386			
S1PR2	1.48363	1.69754			
S1PR3	1.08342	2.00844			
S1PR4	0.0153875	1.41057			
S1PR5	0.296001	NA			
SCTR	0.0287622	0.00372408			
SMO	6.11217	NA			
SSTR1	0.0356989	9.25679			
SSTR2	1.50664	0.109517			
SSTR3	NA	0.0154474			
SSTR4	NA	NA			
SSTR5	NA	3.13115			
SUCNR1	NA	NA			
TAAR1	NA	NA			
TAAR2	NA	NA			
TAAR3P	NA	NA			
TAAR5	NA	NA			
TAAR6	NA	NA			
TAAR8	NA	NA			
TAAR9	NA	NA			
TACR1	0.169425	0.218328			
TACR2	0.0236055	0.948704			
TACR3	0.00275241	0.00997854			
TAS1R1	0.0502677	0.0442583			
TAS1R2	0.00611928	0.025354			
TAS1R3	0.609168	2.96566			
TAS2R1	0.00147393	0.0183208			
TAS2R10	NA	NA			
TAS2R10	NA	NA			

TAS2R10	1.2974	1.83257
TAS2R13	NA	NA
TAS2R13	NA	NA
TAS2R13	1.31383	0.466594
TAS2R14	NA	NA
TAS2R14	NA	NA
TAS2R14	1.43412	0.57028
TAS2R16	NA	NA
TAS2R19	NA	NA
TAS2R19	NA	NA
TAS2R19	3.6183	3.9385
TAS2R20	NA	NA
TAS2R20	NA	NA
TAS2R20	3.60422	3.64116
TAS2R3	1.56276	0.404685
TAS2R30	NA	NA
TAS2R30	NA	NA
TAS2R30	2.76834	0.113191
TAS2R31	NA	NA
TAS2R31	NA	NA
TAS2R31	2.40744	1.1845
TAS2R38	0.0537618	NA
TAS2R39	0.120845	NA
TAS2R4	2.69409	0.202953
TAS2R40	0.294582	NA
TAS2R41	NA	NA
TAS2R41	NA	NA
TAS2R42	NA	NA
TAS2R42	0.260105	NA
TAS2R43	NA	NA
TAS2R43	NA	NA
TAS2R43	NA	NA
TAS2R45	NA	NA
TAS2R46	NA	NA
TAS2R46	NA	NA
TAS2R46	2.24655	0.342211
TAS2R5	2.93635	0.497707
TAS2R50	NA	NA
TAS2R50	NA	NA
TAS2R50	1.84349	0.827465
TAS2R60	NA	NA
TAS2R60	NA	NA
TAS2R7	NA	NA
TAS2R7	NA	NA
TAS2R7	NA	NA
TAS2R8	NA	NA
TAS2R8	NA	NA
TAS2R8	0.197747	NA
TAS2R9	NA	NA
TAS2R9	NA	NA
TAS2R9	0.0571626	NA
TBXA2R	0.0397444	3.14422

TPRA1	3.62526	7.53851
TRHR	0.11594	0.0564074
TSHR	0.0234475	0.00532329
UTS2R	NA	NA
VIPR1	0.392057	0.520812
VIPR2	0.0189574	0.147819
XCR1	0.028664	NA
CDC42	18.1935	12.5121
RAC1	14.4102	40.8616
RHOA	31.575	29.2585
RHOG	1.69644	10.5251

Table S5. Primer Sequences

Primer Name	Corresponding cDNA Name	Sequence
CDH-ADRB2F	β 2-AR	GTCGTGATCTAGAGCTAGCG CACC ATGGGGCAACCCGGGAACGGCAGC
CDH-ADRB2R	β 2-AR	CCAGAGGTTGATTGTCGACGC TTACAGCAGTGAGTCATTTGTACTACAATTCTCCCTTG
CIG-GNAQF	Gaq	TCGAGCTCAAGCTTCGCACC ATGACTCTGGAGTCCATCATGGCG
CIG-GNAQR	Gaq	TAGAAGCTTCTGCAGAT TTAGACCAGATTGTACTCCTTCAGGTTCAAC
Q_Q209LR	Gaq CA	CAGGCCCCCTACATCGACCAATTCTG
Q_Q209LF	Gaq CA	TGGTCGATGTAGGGGGCCTGAGGTGAGAGAGAAGAAAATGGATACACTGC
CIG-GNASF	Gas	TCGAGCTCAAGCTTCGCACC ATGGGCTGCCTCGGGAACAGTAAG
CIG-GNASR	Gas	TAGAAGCTTCTGCAGAT TTAGAGCAGCTCGTACTGACGAAGGTG
S_Q227LR	Gas CA	TCATCGCGCAGGCCACCCACGTCAAACATGT
S_Q227LF	Gas CA	GACGTGGGTGGCCTGCGGATGAACGCCGCAAG
CIG-GNAi2F	Gai	TCGAGCTCAAGCTTCGCACC ATGGGCTGCACCGTGAGCG
CIG-GNAi2R	Gai	TAGAAGCTTCTGCAGAT TCAGAAGAGGCCGAGTCCTTCAGGTTG
i2_Q205LF	Gai CA	GTGGGTGGTCTGCGGTCTGAGCGG
i2_Q205LR	Gai CA	CCGCTCAGACCGCAGACCAACCAC
CIG-EPAC2F	EPAC	TCGAGCTCAAGCTTCGCACC ATGGTCGCTGCGCACGCTG
CIG-EPAC2R	EPAC	TAGAAGCTTCTGCAGAT CTATGGTCGACGAGGCTCTAATCTGTG
R432KF	EPAC DN	CTAGTGAATGATGCCCCAAAGGCTGCCTCTATCGTCTTA
R432KR	EPAC DN	TAAGACGATAGAGGCAGCCTTTGGGGCATCATTCCTAG
CIG-RAP1AS17NF	RAP1A DN	TCGAGCTCAAGCTTCGCACC ATGCGTGAGTACAAGCTAGTGGTCCTTGTTTCAGGAGGCGTTGGGAAGAATGCTCTGACAGTTCAGTTTG
CIG-RAP1AS17NR	RAP1A DN	TAGAAGCTTCTGCAGAT CTAGAGCAGCAGACATGATTTCTTTTAGGCTTCTCTTTTCC