

Supplementary Table 1. Drug activation and affinity parameters in κ Light, δ Light, and μ Light cells.

Compound	κ Light		δ Light		μ Light	
	$\Delta F/F$ max (%)	EC50 (M)	$\Delta F/F$ max (%)	EC50 (M)	$\Delta F/F$ max (%)	EC50 (M)
β -endorphin	126.9 $\pm$ 8.55	1.77E-06	147.9 $\pm$ 4.07	4.18E-07	54.9 $\pm$ 2.78	1.61E-06
BAM18	99.5 $\pm$ 1.70	3.56E-08	155.0 $\pm$ 1.73	1.82E-07	13.2 $\pm$ 2.17	1.86E-07
β -neoendorphin	92.0 $\pm$ 1.40	2.59E-08	157.5 $\pm$ 3.66	3.31E-08	14.2 $\pm$ 4.45	6.31E-06
Buprenorphin	58.6 $\pm$ 3.31	1.58E-08	253.8 $\pm$ 29.88	8.10E-10	-8.3 $\pm$ 1.63	7.34E-11
DAMGO	52.9 $\pm$ 2.09	1.34E-06	101.5 $\pm$ 22.50	1.51E-05	50.5 $\pm$ 1.95	5.05E-07
Deltorphin I	37.8 $\pm$ 7.27	2.17E-09	253.8 $\pm$ 29.88	7.36E-09	43.1 $\pm$ 9.43	7.38E-06
DPDPE	20.5 $\pm$ 1.67	1.66E-10	17.1 $\pm$ 4.08	1.93E-10	n/a	n/a
DynA17	94.0 $\pm$ 6.42	9.20E-10	167.4 $\pm$ 3.65	1.96E-07	n/a	n/a
DynA13	93.6 $\pm$ 3.93	8.98E-11	232.6 $\pm$ 6.82	2.13E-07	45.6 $\pm$ 0.83	3.74E-06
DynA8	112.6 $\pm$ 2.21	1.05E-08	231.6 $\pm$ 15.57	1.97E-08	24.8 $\pm$ 0.63	6.51E-06
DynB9	177.2 $\pm$ 3.94	1.00E-08	217.1 $\pm$ 20.88	1.99E-08	42.3 $\pm$ 3.28	3.76E-06
Endomorphin I	41.7 $\pm$ 6.31	4.96E-08	11.6 $\pm$ 1.074	1.75E-10	26.6 $\pm$ 4.37	1.01E-07
Fentanyl	103.9 $\pm$ 11.88	2.09E-07	134.1 $\pm$ 5.97	6.00E-07	13.9 $\pm$ 2.20	3.58E-08
LE	95.9 $\pm$ 3.55	5.01E-06	214.9 $\pm$ 5.53	7.22E-09	27.0 $\pm$ 3.68	2.84E-06
ME	80.3 $\pm$ 1.79	6.64E-06	246.1 $\pm$ 4.56	6.58E-09	40.0 $\pm$ 1.55	4.27E-07
Methadone	149.9 $\pm$ 2.96	6.79E-06	146.7 $\pm$ 3.20	1.80E-05	26.7 $\pm$ 5.31	3.77E-06
Metorphinmide	105.3 $\pm$ 8.15	1.52E-08	161.3 $\pm$ 2.69	9.55E-08	40.9 $\pm$ 1.55	6.39E-08
Morphine	40.1 $\pm$ 2.78	3.77E-08	26.7 $\pm$ 1.25	1.18E-10	n/a	n/a
Nalfurafine	199.4 $\pm$ 25.33	9.61E-12	39.7 $\pm$ 3.24	3.22E-10	-12.8 $\pm$ 1.33	1.16E-09
Oxycodone	34.5 $\pm$ 4.44	1.08E-08	45.0 $\pm$ 6.45	6.97E-08	-12.8 $\pm$ 2.78	1.59E-11
SNC162	12.2 $\pm$ 2.39	8.28E-06	152.1 $\pm$ 5.20	1.03E-08	2.9 $\pm$ 1.69	8.73E-08
SNC80	42.4 $\pm$ 3.39	6.65E-09	209.4 $\pm$ 5.29	1.82E-07	38.8 $\pm$ 0	1.52E-06
U50,488	189.7 $\pm$ 2.79	5.29E-08	36.1 $\pm$ 0.87	4.1E-5	13.4 $\pm$ 1.61	1.08E-05
U69,593	163.4 $\pm$ 4.97	2.78E-07	23.9 $\pm$ 1.59	2.14E+10	30.8 $\pm$ 9.63	2.43E-12

Dose-response assays from (1pM - 100 μ M) of each compound screened on κ Light, δ Light, μ Light stable cell lines. $\Delta F/F$ max values are sensor responses at 100 μ M of each compound. EC50 values were calculated with the mean of $\Delta F/F$ values at each concentration of compounds. Data are represented by mean $\pm$ SEM, n/a = not applicable.