

SUPPLEMENTARY MATERIAL

Table 1S. Description of the Total Score of ligands with their substituents and pIC₅₀ values

Substituents					
Number	R, R ₁	X, Y	R ₂	Actual pIC ₅₀	Total Score
001	(CH ₃) ₂	CH	-Ph-4-OMe	5.85	3.96
002	(CH ₃) ₃	C	-Ph-4-OMe	5.68	3.50
003	(Me) ₂ N-	CH ₂	-Ph-4-OMe	7.36	5.31
004	Morpholine-4-yl	CH ₂	-Ph-4-OMe	7.68	5.42
005	Piperazine-1-yl	CH ₂	-Ph-4-OMe	7.48	5.37
006	Ethyl NH-	CH ₂	-Ph-4-OMe	6.89	4.92
007	N-methyl piperazine	CH ₂	-Ph-4-OMe	7.92	5.91
008	4-Aminomethylpiperidine	CH ₂	-Ph-4-OMe	7.92	5.86
009	4-Aminopiperidine	CH ₂	-Ph-4-OMe	8.10	6.44
010	4-Hydroxymethylpiperidine	CH ₂	-Ph-4-OMe	7.96	6.01
011	4-Amidepiperazine	CH ₂	-Ph-4-OMe	8.10	6.38
012	4-Amidinepiperazine	CH ₂	-Ph-4-OMe	8.16	6.62
013	H	CH ₂	-Ph-4-OMe	6.57	4.34
014	Benzyl	NH	-Ph-4-OMe	7.02	5.13
015	Phenyl	NH	-Ph-4-OMe	7.50	5.38
016	n-butyl	NH	-Ph-4-OMe	7.08	5.15
017	(Me) ₂ N	NH	-Ph-4-OMe	8.30	7.03

018	4-methylpiperazine	NH	-Ph-4-OMe	7.92	6.14
019	Morpholine-4-yl	NH	-Ph-4-OMe	7.75	5.55
020	Piperidine-1-yl	NH	-Ph-4-OMe	7.66	5.43
021	Pyrrolidine-1-yl	NH	-Ph-4-OMe	7.82	6.01
022	H	CH ₂	-Ph	6.62	4.61
023	H	CH ₂	-PH-4-Me	6.80	4.86
024	H	CH ₂	-PH-4-Et	6.55	4.48
025	H	CH ₂	-PH-4-n-Pr	6.31	4.25
026	H	CH ₂	-PH-4-OH	6.28	4.12
027	-Ph-4-NH ₂	CH ₂	-PH-4-OMe	7.42	5.27
028	H	CH ₂	-PH-4-NMe ₂	6.50	4.40
029	H	CH ₂	-PH-4-piperidine	6.05	4.07
030	H	CH ₂	-PH-4- morpholine	6.43	4.39
031	H	CH ₂	-PH-4-SMe	6.92	4.82
032	Morpholine	CH ₂	-PH-4-NMe ₂	7.44	5.31
033	4-(OH)piperidin-1-yl	CH ₂	-PH-4-NMe ₂	7.48	5.33
034	4-(Aminomethyl)piperidin-1-yl	CH ₂	-PH-4-NMe ₂	7.82	5.87
035	N-methylpiperazin-1-yl	CH ₂	-PH-4-NMe ₂	7.54	5.66
036	Morpholine	CH ₂	-PH-4- morpholine	7.43	5.30
037	4-(OH)piperidin-1-yl	CH ₂	-PH-4- morpholine	7.07	5.12

038	4-(Aminomethyl)piperidin-1-yl	CH ₂	-PH-4-morpholine	7.59	5.57
039	H	NH	3-thienyl	8.05	6.23
040	N-methylpiperazin-1-yl	CH ₂	-PH-4-morpholine	7.38	5.22
041	4-(Aminomethyl)piperidin-1-yl	CH ₂	Et	6.62	4.58
042	4-(Aminomethyl)piperidin-1-yl	CH ₂	Cyclopropyl	7.26	5.19
043	4-(Aminomethyl)piperidin-1-yl	CH ₂	Cyclohexane	7.02	5.05
044	H	NH	Cyclopropyl	6.85	4.84
045	H	CH ₂	4-Pyridyl	7.12	5.11
046	H	CH ₂	2-Thienyl	6.75	4.76
047	H	NH	2-Thienyl	7.96	5.99
048	H	NH	2-Thienyl-1.3-OMe	7.77	5.75
049	H	NH	2-Thienyl-1.5-Me	7.89	5.82
050	H	NH	2-Furanyl	7.07	5.05
051	H	NH	2-Thienyl-1.5-CO ₂ Et	6.89	4.90
052	H	NH	2-Thienyl-1.5-Cl	7.89	5.88
053	H	NH	3-Pyrrole.1-Me	7.59	5.56
054	Dimethylamine	NH	2-Thienyl	7.44	5.32

055	Dimethylamine	NH	5-(OMe) thien-2-yl	7.50	5.46
056	Dimethylamine	NH	5-(Me)thien-2-yl	7.60	5.51
057	Dimethylamine	NH	5(CO ₂ EtMe)thien-2-yl	7.55	5.48
058	Dimethylamine	NH	3-Thienyl	7.62	5.57
059	Dimethylamine	NH	5-(Cl) thien-3-yl	8.16	6.36
060	Dimethylamine	NH	2.5-(di-Me)thien-3-yl	7.59	5.43
061	Dimethylamine	NH	Furan-2-yl	7.59	5.47
062	Dimethylamine	NH	2.4-(di-Me)thiazole-5-yl	8.40	7.38
063	Morpholine-4-yl	NH	5-(Me) thien-2-yl	8.00	6.05
064	Morpholine-4-yl	NH	5-(CO ₂ EtMe) thien-2-yl	7.51	5.43
065	Morpholine-4-yl	NH	5-(Cl) thien-3-yl	8.00	6.18
066	4-(Methyl)piperazin-1-yl	NH	5-(CO ₂ EtMe) thien-2-yl	7.44	5.32
067	4-(Aminomethyl)piperidin-1-yl	CH ₂	Isopropyl	7.32	5.29
068	4-(Methyl)piperazin-1-yl	NH	2.5-(di-Me)thien-3-yl	7.92	6.00
069	4-(Methyl)piperazin-1-yl	NH	2.4-(di-Me)thiazole 5-yl	8.10	6.19
070	(Me) ₂ CHCONH-	NH	-Ph-4-OMe	7.72	5.67

071	4-(OH)Ph(CH ₂) ₂ CONH-	NH	-Ph-4-OMe	7.89	5.86
072	4-(Ome)PhCONH-	NH	-Ph-4-OMe	7.82	5.75
073	3-(NO ₂)PhCONH-	NH	-Ph-4-OMe	7.62	5.57
074	3,4,5-(tri-OMe)PhCONH-	NH	-Ph-4-OMe	7.70	5.63
075	3-(Me)PhCONH-	NH	-Ph-4-OMe	7.89	5.84
076	3,4-(di-OMe)PhCONH-	NH	-Ph-4-OMe	7.39	5.35
077	(4-OH,3-NH ₂)PhCONH-	NH	-Ph-4-OMe	7.62	5.52
078	2,5-(di-Cl)PhCONH-	NH	-Ph-4-OMe	7.44	5.45
079	3,4-(di-OH)PhCONH-	NH	-Ph-4-OMe	8.00	6.04
080	3,5-(di-NH ₂)PhCONH-	NH	-Ph-4-OMe	7.41	5.46
081	MeOCONH-	NH	-Ph-4-OMe	7.80	5.76
082	2-(OH)PhCONH-	NH	-Ph-4-OMe	8.05	6.13
083	Naphthalen-2-yl CONH-	NH	-Ph-4-OMe	7.46	5.45
084	BnCONH-	NH	-Ph-4-OMe	7.48	5.44
085	PhCONH-	NH	-Ph-4-OMe	7.92	5.94
086	4-pyridylCONH-	NH	-Ph-4-OMe	7.92	5.88
087	3-pyridylCONH-	NH	-Ph-4-OMe	7.80	5.79
088	MeCONH-	NH	-Ph-4-OMe	7.43	5.36
089	4-(OH)PhCONH-	NH	-Ph-4-OMe	8.05	6.07
090	H ₂ NCONH-	NH	-Ph-4-OMe	7.01	4.98
091	3-(NH ₂)PhCONH-	NH	-Ph-4-OMe	7.89	5.90
092	2,4-(di-OH)PhCONH-	NH	-Ph-4-OMe	7.80	5.75

093	4-NH ₂ PhCONH-	NH	-Ph-4-OMe	8.00	6.00
094	2(Dimethylamine)ethylami n			7.68	5.69
095	2(Pyrrolidin-1- yl)ethylamine			7.60	5.47
096	2(Piperidin-1-yl)etilamine			7.51	5.52
097	2-(Morpholin-4- yl)etilamine			7.29	5.23
098	Piperidin-1-yl			7.60	5.55
099	3(Dimethylamine)Piperidi n-1-yl			7.62	5.57
100	4(Dimethylamine)Piperidin -1-yl			7.64	5.54
101	Piperazin-1-yl			7.42	5.38
102	4-(Ethyl)piperazin-1-yl			7.72	5.65
103	3-(Amine)pyrrolidin-1-yl			7.41	5.39
104	3-(Methylamine)pyrrolidin- 1-yl			7.96	6.10
105	3(Dimethylamine)pyrrolidi n-1-yl			7.36	5.23
106	Azepam-1-yl			7.64	5.59
107	4-(Methyl)piperazin-1-yl			7.50	5.41
108	[1,4]Diazepam-1-yl			8.22	7.14
109	4-(Methyl)-[1,4]diazepam- 1			7.82	5.86

110	4-(Ethyl)-[1,4]diazepam-1			7.85	5.78
111	H	H	C	4.59	3.51
112	Acetamide	H	C	6.29	4.27
113	H	NH ₂	C	3.68	2.56
114	NH ₂	H	C	5.08	4.09
115	H	H	N	5.33	4.27
116	OH	H	C	5.28	5.18
117	Formamide	H	C	7.10	5.07

Table 2S. Variance Analysis for the current pIC₅₀

Source	Sum of Squares	Gl	Mean Square	F-Ratio	P-Value
Model	8.79	10	0.88	3.69 x 10 ¹⁰	0.0
Residue	4.76 x 10 ⁻¹¹	2	2.38 x 10 ⁻¹¹		
Total	8.79	12			

Table 3S. Model for the current pIC₅₀

	% Variation		Mean Square	Prediction
Component	in Y	R-Squared	PRESS	R-Squared
1	88.33	88.33	0.91	84.78
2	9.48	97.81	0.85	85.82
3	1.98	99.78	0.99	83.44

4	0.18	99.96	0.89	85.11
5	0.03	99.99	0.91	84.82
6	4.9×10^{-3}	100.0	0.91	84.77
7	1.7×10^{-4}	100.0	0.64	89.37
8	3.8×10^{-6}	100.0	0.91	84.78
9	5.9×10^{-7}	100.0	0.91	84.78
10	1.3×10^{-8}	100.0	0.91	84.78

Table 4S. Independent and dependent variables of PLS statistical analysis

	% Variation in X	% Accumulated of X	% Variation in Y	% Accumulated of Y	Average Prediction R-Squared
1	13.04	13.04	88.33	88.33	84.78
2	13.10	26.14	9.47	97.81	85.82
3	8.53	34.67	1.98	99.79	83.44
4	9.21	43.88	0.18	99.96	85.11
5	7.85	51.73	0.03	99.99	84.82
6	6.50	58.22	4.9×10^{-3}	100.0	84.77
7	7.93	66.15	1.7×10^{-4}	100.0	89.37
8	6.87	73.02	3.8×10^{-6}	100.0	84.78
9	5.94	78.97	5.9×10^{-7}	100.0	84.78
10	8.58	87.55	1.3×10^{-8}	100.0	84.78