

**Pharmacophore modeling, docking and virtual screening approaches in the discovery of
novel Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI's)**

Supporting Information Tables

Table S1. Scores and data related to training set.

Name	IC₅₀ (mM) Reported^a	IC₅₀ (mM) Estimated^b	Fit Value^c	Error	Activity Scale Est.^d	Observed Scale Rep.^d	HBA lipid^e	RA^e	HY^e
1	0.008	0.051	10.73	-6.4	++	+++	1	1	101
7	1.585	0.16	10.22	-9.7	++	++	1	1	101
8	3.98	2.3	9.07	-1.7	++	++	1	1	101
20	0.159	0.39	9.85	2.5	++	++	0	1	101
26	0.398	0.084	10.51	-4.7	+++	++	1	0	101
27	0.0004	0.0009	13.45	2.4	++	+++	1	1	111
40	1.995	0.18	10.18	-11	++	++	1	1	101
42	1	0.38	9.85	-2.6	++	++	1	0	101
43	1.995	0.13	10.31	-15	++	++	1	1	111
46	0.398	0.37	9.87	-1.1	++	++	1	1	111
54	0.05	0.2	10.14	4	++	++	1	1	101
57	0.003	0.03	10.96	10	+++	+++	1	0	111
60	0.004	0.0035	11.89	-1.1	+++	+++	1	1	111
61	0.001	0.0018	12.18	-5.5	+++	+++	1	1	111
63	0.005	0.003	11.97	-1.7	++	+++	1	1	101
66	0.05	0.012	11.43	-4.9	++	++	1	1	111
67	1.585	0.3	9.96	-5.3	++	++	1	1	111
68	1.258	1	9.43	-1.2	++	++	1	1	111
76	0.199	0.16	10.24	-1.3	+	++	1	1	111

83	100	36	6.97	-2.8	+	+	1	1	101
86	5.012	2.1	9.12	-2.4	+++	++	1	1	111
88	0.003	0.01	10.42	3.2	++	+++	1	1	111
92	0.01	0.2	10.15	2.1	+++	+++	1	0	111
94	0.02	0.13	10.34	6.3	++	+++	1	1	111
95	0.316	0.21	10.12	-1.5	++	++	1	0	111
96	0.079	0.17	10.22	2.1	++	++	1	1	111
97	0.1	0.16	10.22	1.6	++	++	1	1	111
99	0.02	0.041	10.82	2	+++	++	1	1	111
102	0.158	0.12	10.35	-1.3	+++	++	1	1	101
103	0.032	0.14	10.28	4.5		++	1	1	111

^a Reported activity, ^b Estimated Activity, ^c Ligand pharmacophore mapping based fit value, ^dActivity Scale HA (highly active, +++, 0.0004-0.01), MA (moderately active, ++, 0.01-5) and LA (least active, +, 5-100) according to their reported and estimated biological activity. ^e Feature Mapping based on Ligand pharmacophore mapping HBA, RA, HY.

Table S2. Test set prediction on training set pharmacophore.

Name	IC ₅₀ (nM) Reported ^a	IC ₅₀ (nM) Estimated ^b	Fit Value ^c	Activity Scale ^d	Observed Scale ^d	Mapped Features ^e		
				cat ⁱ	obs ⁱⁱ	HBA	RA	HY
2	0.004	0.031	6.866	++	+++	1	1	111
3	0.025	0.0099	7.146	+++	++	1	1	111
4	0.002	0.0005	8.415	+++	+++	1	1	111
5	0.316	0.04	8.851	+++	++	1	1	111
6	0.01	0.0004	8.561	+++	+++	1	1	111
9	0.006	0.0098	7.149	+++	+++	1	1	111
10	0.006	0.0051	7.429	+++	+++	1	1	111
11	0.002	0.0168	6.914	++	+++	1	1	111
12	0.005	0.0008	8.257	+++	+++	1	1	111
13	0.004	0.001	8.16	+++	+++	1	1	111
14	0.199	0.0002	8.76	+++	++	1	1	111
15	1.585	0.5	8.752	++	++	1	1	111
16	0.004	0.003	7.662	+++	+++	1	1	111
17	0.013	0.0066	7.323	+++	++	1	1	111
18	1.259	0.305	8.681	+++	++	1	1	111
19	0.1	0.0005	8.464	+++	++	1	1	111
21	0.04	0.0002	8.816	+++	++	1	1	111
24	0.013	0.0004	8.592	+++	++	1	1	111
25	0.008	0.0005	8.426	+++	+++	1	1	111
28	0.002	0.0005	8.468	+++	+++	1	1	111
29	0.002	0.001	8.162	+++	+++	1	1	111

30	0.002	0.0103	7.126	+++	+++	1	1	111
32	0.002	0.09	6.467	++	+++	1	1	111
31	0.002	0.0043	7.51	+++	+++	1	1	111
33	0.004	0.0004	8.516	+++	+++	1	1	111
34	0.002	0.0006	8.352	+++	+++	1	1	111
35	0.05	0.0495	6.446	++	++	1	1	111
36	0.003	0.0006	8.367	+++	+++	1	1	111
37	0.079	0.0005	8.41	+++	++	1	1	111
38	0.398	0.088	8.519	+++	++	1	1	111
39	0.012	0.0084	7.215	+++	++	1	1	111
41	0.126	0.0044	7.496	+++	++	1	1	111
46	0.398	0.025	8.593	+++	++	1	1	111
47	0.398	0.176	7.579	+++	++	1	1	111
53	0.008	0.0035	7.599	+++	+++	1	1	111
56	0.001	0.0021	7.809	+++	+++	1	1	111
49	0.063	0.0377	6.4095	++	++	1	1	101
54	0.05	0.0007	8.3	+++	++	1	1	111
44	0.04	0.1	6.932	++	++	1	1	101
50	0.251	0.247	6.7159	++	++	1	1	111
55	0.01	0.0033	7.625	+++	+++	1	1	111
58	0.039	0.0019	7.861	+++	++	1	1	111
45	0.079	0.045	6.4	++	++	1	1	101
51	0.006	0.06	6.7159	+++	++	1	1	111
52	0.158	0.0055	8.3653	+++	++	1	1	111
62	0.003	0.0003	8.719	+++	+++	1	1	111
64	0.002	0.0028	7.687	+++	+++	1	1	111
65	0.005	0.0015	7.956	+++	+++	1	1	111

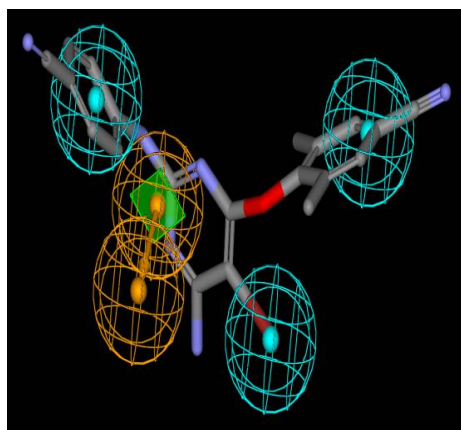
67	1.585	0.251	5.449	++	++	1	1	111
71	0.079	0.0044	7.498	+++	++	1	1	111
72	0.079	0.0014	7.991	+++	++	1	1	111
73	0.001	0.0009	8.175	+++	+++	1	1	111
74	0.012	0.0042	7.519	+++	++	1	1	111
75	0.158	0.0007	8.267	+++	++	1	1	111
76	1	0.239	7.956	+++	++	1	1	111
77	0.199	0.022	7.651	+++	++	1	1	111
78	0.063	0.0034	7.608	+++	++	1	1	111
79	0.001	0.0011	8.113	+++	+++	1	1	111
80	0.006	0.0012	8.069	+++	+++	1	1	111
81	0.003	0.0015	7.956	+++	+++	1	1	111
82	0.008	0.0012	8.069	+++	+++	1	1	111
84	0.063	0.049	6.829	++	++	1	1	111
85	0.039	0.0005	8.48	+++	++	1	1	111
86	0.015	0.015	7.435	++	++	1	1	111
88	0.016	0.0353	6.592	++	++	1	1	111
90	0.01	0.0003	8.626	+++	+++	1	1	111
91	0.003	0.0006	8.329	+++	+++	1	1	111
92	0.061	0.003	7.669	+++	++	1	1	111
94	0.199	0.0022	7.792	+++	++	1	1	111
99	0.063	0.003	7.662	+++	++	1	1	111
101	0.079	0.0005	8.486	+++	++	1	1	111

^a Reported activity, ^b Estimated Activity, ^c Ligand pharmacophore mapping based fit value, ^d Activity Scale HA (highly active, +++, 0.0004-0.01), MA (moderately active, ++, 0.01-5) and LA (least active, +, 5-100) according to their reported biological activity (ⁱ Estimated scale by catalyst software, ⁱⁱ Reported scale). ^e Feature Mapping based on Ligand pharmacophore mapping.

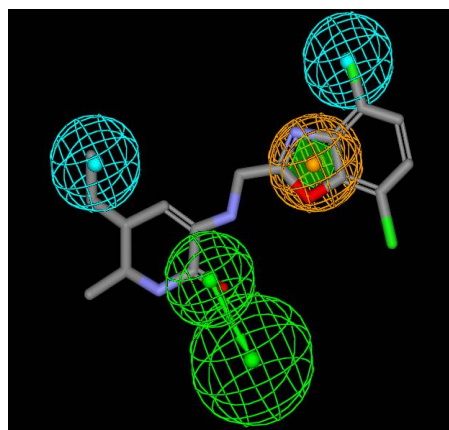
Table S3. Mapping of standard compounds and estimated activities using hypothesis 1.

Comp.	Fit Value	Estimated IC ₅₀ in (μM)	Reported IC ₅₀ in (μM)
Delavirdine	7.34	0.058	0.0161
DPC083	7.13	0.062	0.0004
HETP-1	6.06	1.117	5.06
Nevirapine	6.22	0.759	0.18
Efavirenz	7.35	0.057	0.004
TMC125	6.34	0.515	0.0014
L697.661	7.90	0.016	0.23
GW8248	7.47	0.043	0.0046

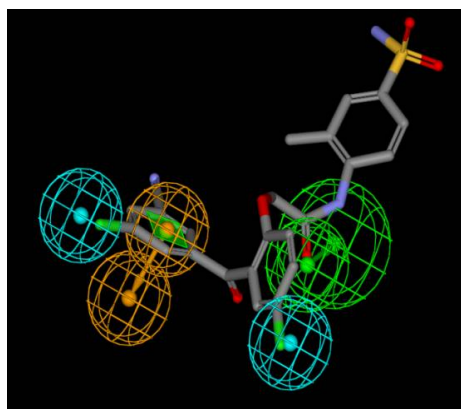
Figure S1. The ligand pharmacophore mapping of the external test set of compounds on the pharmacophore model.



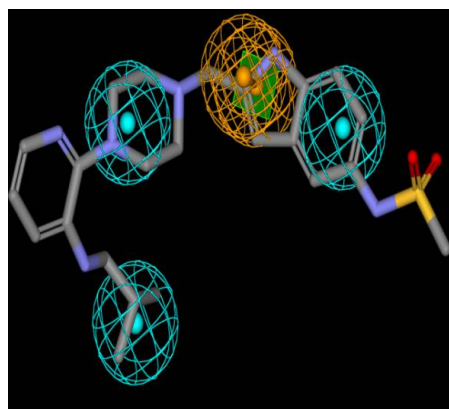
a. Mapping of TMC-125 on Hypo-1.



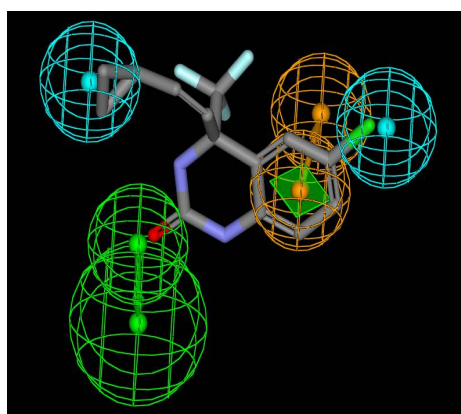
b. Mapping of L697,661 on Hypo-1.



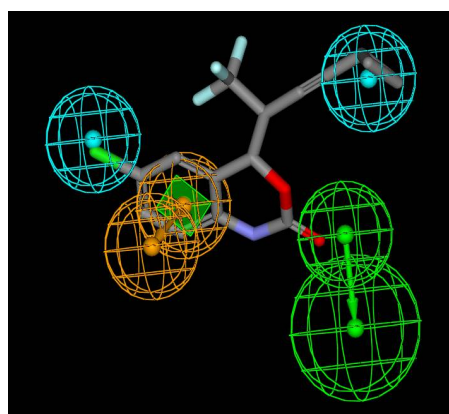
c. Mapping of GW8248 on Hypo- 1.



d. Mapping of Delavirdine on Hypo- 1.



e. Mapping of DPC083 on Hypo- 1.



f. Mapping of Efavirenz on Hypo- 1.