

Supplementary Information

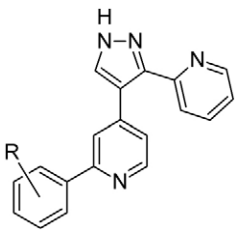
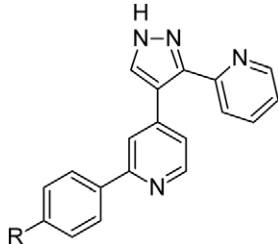
ALK-5 Inhibition: A Molecular Interpretation of the Main Physicochemical Properties Related to Bioactive Ligands

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Table S1. Structure and pIC₅₀ values of the studied compounds

Compound	General structure	X	R	R ²	pIC ₅₀
1		-	-H	-	6.97
2		-	2-F	-	7.23
3		-	2-CF ₃	-	5.03
4		-	3-CH ₃	-	6.72
5		-	3-CF ₃	-	6.62
6		-	3-OCH ₃	-	6.94
7		-	4-CH ₃	-	7.55
8		-	4-CF ₃	-	7.62
9		-	4-F	-	7.32
10		-	4-Pr	-	7.49
11		-	4-Cl	-	7.37
12		-	4-COOMe	-	7.57
13		-	4-CN	-	7.46
14		-	-H	-	6.97
15		-	-OCH ₃	-	7.62
16		-	-O(CH ₂) ₂ -cyclohexyl	-	7.09
17		-	-O(CH ₂) ₂ Cl	-	7.72
18		-	-OCH ₂ COCH ₃	-	7.60
19		-	-O(CH ₂) ₂ N(CH ₃) ₂	-	7.82
20		-	-(OCH ₂) ₂ -pyrrolidine	-	7.40
21		-	-O(CH ₂) ₂ -morpholine	-	7.92
22		-	-O(CH ₂) ₂ -(imidazol-1-yl)	-	7.52
23		-	-CH ₂ -pyrrolidine	-	7.72
24		-	-CH ₂ -morpholine	-	7.38
25		-	-CH ₂ NH-(tetrahydro-2H-pyran-4-yl)	-	7.33
26		-	-CONH(CH ₂) ₂ OCH ₃	-	7.04
27		-	-CO-morpholine	-	6.91
28		-	-CO-[N-(tetrahydro-2H-pyran-4-yl)amine]	-	7.74
29		-	-NHCO-(tetrahydro-2H-pyran-4-yl)	-	6.95

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Table S1. Structure and pIC_{50} values of the studied compounds (cont.)

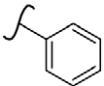
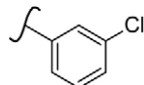
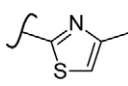
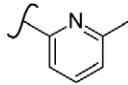
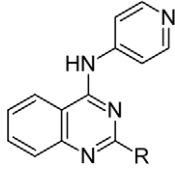
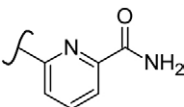
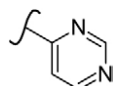
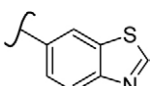
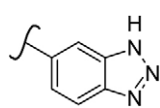
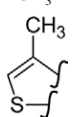


Compound	General structure	X	R	R ²	pIC_{50}
30		-		-	6.71
31		-		-	7.31
32		-		-	7.70
33		-		-	7.60
34		-		-	6.58
35		-		-	7.40
36		-		-	6.19
37		-		-	5.43
38		N	CH ₃	H	7.03
39		N		-	7.80
40		N		-	7.66
41		-		-	7.66

Table S1. Structure and pIC₅₀ values of the studied compounds (cont.)

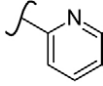
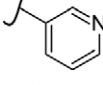
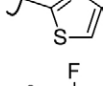
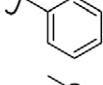
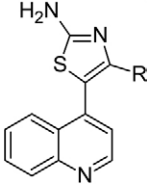
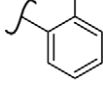
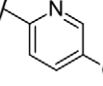
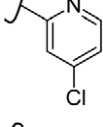
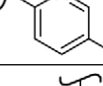
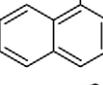
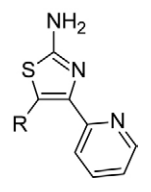
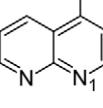
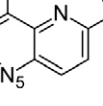
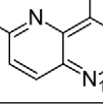
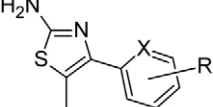
Compound	General structure	X	R	R ²	pIC ₅₀
42		-		-	6.14
43		-		-	5.40
44		-		-	5.93
45		-		-	5.90
46		-		-	5.00
47		-		-	5.75
48		-		-	5.99
49		-		-	5.00
50		-		-	4.96
51		-		-	5.10
52		-		-	7.52
53		-		-	6.42
54		N	H	-	7.40
55		N	6-CH ₃	-	7.60
56		CH	4-F	-	7.38
57		CH	3-Cl	-	7.64

Table S1. Structure and pIC₅₀ values of the studied compounds (cont.)

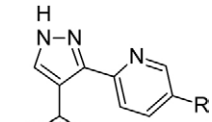
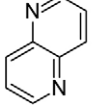
Compound	General structure	X	R	R ²	pIC ₅₀
58		-	H	-	7.52
59		-	CH ₃	-	7.64

Table S2. Values of the 8 selected descriptors for the training and test sets

Compound	MATS4v	EEig04x	ESpm12r	BELp5	SPH	Mor26e	R8m+	R5e+	Set
1	-0.092	3.500	17.435	1.355	0.908	0.188	0.021	0.028	test
2	-0.001	3.574	17.570	1.355	0.876	0.345	0.023	0.026	training
3	-0.249	3.772	18.094	1.355	0.878	-0.044	0.018	0.062	outlier
4	-0.074	3.636	17.501	1.365	0.872	0.224	0.018	0.026	test
5	-0.163	3.815	17.992	1.368	0.899	0.439	0.022	0.041	training
6	-0.127	3.559	17.510	1.403	0.903	0.535	0.018	0.040	training
7	-0.082	3.666	17.491	1.371	0.895	0.210	0.016	0.024	test
8	-0.175	3.823	17.983	1.375	0.916	0.209	0.032	0.031	training
9	-0.090	3.700	17.500	1.395	0.888	0.267	0.018	0.029	training
10	-0.051	3.767	17.609	1.540	0.896	0.651	0.016	0.025	training
11	-0.097	3.666	17.480	1.355	0.915	0.413	0.021	0.026	training
12	-0.150	3.800	17.631	1.481	0.947	0.381	0.018	0.029	training
13	-0.132	3.777	17.512	1.364	0.879	0.276	0.016	0.031	training
14	-0.092	3.500	17.435	1.355	0.869	0.354	0.018	0.025	test
15	-0.090	3.700	17.500	1.395	0.919	0.312	0.020	0.031	training
16	-0.123	3.709	17.592	1.591	0.885	0.554	0.013	0.020	training
17	-0.072	3.707	17.505	1.510	0.924	0.138	0.020	0.025	training
18	-0.115	3.708	17.508	1.586	0.920	0.497	0.014	0.024	training
19	0.074	3.707	17.529	1.589	0.949	0.534	0.013	0.023	training
20	0.089	3.707	17.576	1.615	0.944	0.155	0.014	0.026	training
21	0.042	3.707	17.572	1.600	0.937	0.564	0.011	0.023	test
22	-0.163	3.896	17.574	1.587	0.936	0.322	0.015	0.023	training
23	-0.079	3.744	17.594	1.588	0.888	0.588	0.014	0.018	test
24	-0.090	3.744	17.590	1.588	0.862	0.667	0.014	0.019	training
25	0.069	3.717	17.594	1.589	0.910	0.547	0.015	0.029	training
26	-0.182	3.801	17.647	1.587	0.912	0.547	0.015	0.026	training
27	-0.146	3.831	17.703	1.592	0.943	0.401	0.014	0.032	training
28	-0.260	3.801	17.719	1.597	0.939	0.636	0.014	0.021	training
29	-0.197	3.851	17.719	1.589	0.926	0.333	0.013	0.026	training
30	-0.190	3.456	17.279	1.193	0.830	0.042	0.014	0.035	training
31	-0.164	3.602	17.333	1.190	0.852	0.089	0.038	0.031	test
32	-0.048	3.564	17.301	1.243	0.876	0.283	0.057	0.032	training

Table S2. Values of the 8 selected descriptors for the training and test sets (cont.)

Compound	MATS4v	EEig04x	ESpm12r	BELp5	SPH	Mor26e	R8m+	R5e+	Set
33	-0.058	3.602	17.333	1.274	0.818	0.265	0.013	0.033	training
34	-0.299	3.677	17.487	1.405	0.880	-0.089	0.013	0.040	training
35	0.010	3.602	17.323	1.274	0.876	0.403	0.017	0.032	training
36	-0.224	3.706	17.588	1.355	0.834	0.140	0.029	0.027	training
37	-0.223	3.706	17.566	1.472	0.830	0.214	0.013	0.034	training
38	-0.021	3.456	16.856	1.268	0.813	0.472	0.015	0.029	test
39	-0.174	3.650	17.514	1.269	0.853	0.441	0.042	0.028	training
40	-0.011	3.603	17.287	1.280	0.833	0.499	0.027	0.030	training
41	0.191	3.456	17.299	1.183	0.882	0.368	0.017	0.042	training
42	-0.175	3.491	17.584	1.269	0.724	0.316	0.019	0.029	training
43	0.098	3.491	17.594	1.264	0.740	0.235	0.025	0.030	test
44	-0.131	3.491	17.553	1.321	0.760	0.108	0.039	0.029	test
45	0.079	3.493	17.715	1.269	0.723	-0.071	0.023	0.029	training
46	0.083	3.493	17.742	1.379	0.783	-0.022	0.020	0.033	test
47	-0.173	3.503	17.615	1.259	0.736	0.108	0.062	0.029	test
48	-0.193	3.497	17.623	1.265	0.750	0.179	0.052	0.029	training
49	-0.173	3.503	17.631	1.329	0.802	0.150	0.016	0.029	training
50	-0.166	3.491	17.598	1.291	0.732	-0.053	0.019	0.026	training
51	-0.191	3.491	17.570	1.266	0.743	0.226	0.022	0.028	training
52	-0.108	3.557	17.421	1.216	0.881	0.374	0.017	0.029	training
53	-0.254	3.607	17.621	1.293	0.838	0.647	0.021	0.025	training
54	-0.108	3.557	17.421	1.216	0.903	0.304	0.018	0.030	training
55	-0.091	3.577	17.481	1.296	0.864	0.396	0.016	0.029	training
56	0.004	3.586	17.482	1.217	0.882	0.255	0.031	0.028	training
57	0.054	3.577	17.483	1.211	0.874	0.081	0.045	0.028	training
58	0.159	3.356	17.414	1.281	0.920	0.421	0.017	0.033	training
59	0.177	3.496	17.475	1.328	0.868	0.482	0.014	0.029	training